

data,conversation

"This 60-year-old male was hospitalized due to moderate ARDS from COVID-19 with symptoms of fever, dry cough, and dyspnea. We encountered several difficulties during physical therapy on the acute ward. First, any change of position or deep breathing triggered coughing attacks that induced oxygen desaturation and dyspnea. To avoid rapid deterioration and respiratory failure, we instructed and performed position changes very slowly and step-by-step. In this way, a position change to the 135deg prone position ( ) took around 30 minutes. This approach was well tolerated and increased oxygen saturation, for example, on day 5 with 6 L/min of oxygen from 93% to 97%. Second, we had to adapt the breathing exercises to avoid prolonged coughing and oxygen desaturation. Accordingly, we instructed the patient to stop every deep breath before the need to cough and to hold inspiration for better air distribution. In this manner, the patient performed the breathing exercises well and managed to increase his oxygen saturation. Third, the patient had difficulty maintaining sufficient oxygen saturation during physical activity. However, with close monitoring and frequent breaks, he managed to perform strength and walking exercises at a low level without any significant deoxygenation. Exercise progression was low on days 1 to 5, but then increased daily until hospital discharge to a rehabilitation clinic on day 10.", "Doctor: Good morning, how are you feeling today?

Patient: I'm feeling a bit better, thank you.

Doctor: I see from your clinical notes that you were hospitalized due to moderate ARDS from COVID-19. Can you tell me more about your symptoms?

Patient: Yes, I had a fever, dry cough, and difficulty breathing.

Doctor: I'm sorry to hear that. During your hospital stay, you encountered some difficulties during physical therapy. Can you tell me more about that?

Patient: Yes, any change of position or deep breathing triggered coughing attacks that induced oxygen desaturation and dyspnea.

Doctor: I see. To avoid rapid deterioration and respiratory failure, the medical team instructed and performed position changes very slowly and step-by-step. How did that approach work for you?

Patient: It worked well. A position change to the 135deg prone position took around 30 minutes, but

it increased my oxygen saturation.

Doctor: That's great to hear. The breathing exercises had to be adapted to avoid prolonged coughing and oxygen desaturation. Can you tell me more about that?

Patient: Sure. I was instructed to stop every deep breath before the need to cough and to hold inspiration for better air distribution. In this manner, I managed to increase my oxygen saturation.

Doctor: That's excellent. During physical activity, you had difficulty maintaining sufficient oxygen saturation. How did the medical team help you with that?

Patient: They closely monitored me and gave me frequent breaks. I managed to perform strength and walking exercises at a low level without any significant deoxygenation.

Doctor: I see that exercise progression was low on days 1 to 5, but then increased daily until hospital discharge to a rehabilitation clinic on day 10. Do you have any questions for me?

Patient: No, I think I understand everything. Thank you, doctor.

Doctor: You're welcome. Please make sure to follow up with your rehabilitation clinic and take good care of yourself."

"A 39-year-old man was hospitalized due to an increasingly reduced general health condition, after persistent fever and dry cough for 2 weeks. The patient initially needed 4 L/min of oxygen, had a rapid and shallow breathing pattern at rest and became severely breathless during minor physical activities. In the beginning, physical therapy focused on patient education about dyspnea-relieving positions, the importance of regular mobilization, and deep-breathing exercises. However, it quickly became evident that his anxiety from fear of dying and worries about his future aggravated his dyspnea and vice versa. The patient was so dyspneic, anxious, and weak that he was barely able to walk to the toilet. To counter this vicious circle, the physical therapist actively listened to the patient, explained why he was experiencing breathlessness, and tested suitable positions to relieve his dyspnea. He seemed to benefit from the education and the relaxing breathing exercises, as seen on day 2, when his respiratory rate could be reduced from 30 breaths/min to 22 breaths/min and his oxygen saturation increased from 92% to 96% on 4 L/min oxygen after guiding him through some deep-breathing exercises. Over the next days, his dyspnea and anxiety started to alleviate and he

regained his self-confidence. Therapy was progressively shifted to walking and strength training and the patient rapidly advanced to walk 350 m without a walking aid or supplemental oxygen before his discharge home.", "Doctor: Hello, how are you feeling today?

Patient: Not so great, I've been hospitalized for a while now.

Doctor: I see. Can you tell me about your general health condition?

Patient: I've been experiencing persistent fever and dry cough for the past two weeks.

Doctor: Okay. And have you been needing oxygen?

Patient: Yes, I initially needed 4 L/min of oxygen.

Doctor: I see. And how has your breathing been, particularly when you're at rest?

Patient: My breathing has been rapid and shallow at rest and severely breathless during minor physical activities.

Doctor: I understand. Have you been receiving physical therapy?

Patient: Yes, physical therapy has been focusing on educating me about dyspnea-relieving positions and the importance of regular mobilization and deep-breathing exercises.

Doctor: That's great to hear. Has it been helpful?

Patient: It has, but my anxiety and fear of dying have been aggravating my dyspnea and vice versa.

Doctor: I see. That's understandable. Have you been able to walk to the toilet okay?

Patient: No, I've been so dyspneic, anxious, and weak that it's been difficult to walk to the toilet.

Doctor: I understand. The physical therapist has been working on counteracting that vicious circle, right?

Patient: Yes, the physical therapist has been actively listening to me, explaining why I'm experiencing breathlessness, and testing suitable positions to relieve it.

Doctor: That's great. Have you seen any improvement?

Patient: Yes, on day 2, my respiratory rate could be reduced from 30 breaths/min to 22 breaths/min and my oxygen saturation increased from 92% to 96% on 4 L/min oxygen after doing some deep-breathing exercises.

Doctor: That's fantastic progress. And have your dyspnea and anxiety started to alleviate?

Patient: Yes, they have. I've been regaining my self-confidence too.

Doctor: That's wonderful to hear. Has the therapy been shifted to walking and strength training?

Patient: Yes, it has. I've even been able to walk 350 m without a walking aid or supplemental oxygen before my discharge home."

"One week after a positive COVID-19 result this 57-year-old male was admitted to the ICU because of oxygen desaturation (70%) with worsening tachypnea and dyspnea. Physical therapy started immediately after ICU admission. We found a highly dyspneic patient with a high breathing frequency and significant symptom exacerbation from the slightest effort. With hands-on physical therapy guidance, the patient managed to achieve a 135deg prone position and to perform deep-breathing exercises resulting in an increase in oxygen saturation from 88% to 96%. Intensive physical therapy and positioning was continued along with 6 to 12 L/min of oxygen therapy over the next days and intubation was avoided. The major challenges in achieving a prone position were the patient's profoundly reduced respiratory capacity and the high risk of exacerbating his symptoms. However, standard ICU monitoring enabled safe implementation at an individually adapted pace to allow sufficient time for convalescence. After 3 days with this regime, he could be transferred to the normal ward, where physical therapists carried on his rehabilitation with walking and strength training. The patient's severe instability remained a challenge. Nevertheless, 9 days after ICU admission, the patient was able to leave the hospital as a pedestrian.", "Doctor: Hello, how are you feeling today?

Patient: Not great, I've been having trouble breathing and feeling really tired.

Doctor: I see from your charts that you tested positive for COVID-19 a week ago and were admitted to the ICU because of oxygen desaturation. Can you tell me more about your symptoms?

Patient: Yeah, I've been having trouble breathing and it's been getting worse. I've been feeling really short of breath and have been breathing really fast.

Doctor: I understand. Physical therapy was started immediately after your admission to the ICU. Did you notice any changes in your symptoms with the therapy?

Patient: Yeah, the physical therapists were really helpful. With their guidance, I was able to achieve

a prone position and do some deep-breathing exercises. My oxygen levels went up from 88% to 96%.

Doctor: That's great to hear. Intensive physical therapy and positioning continued over the next few days, and intubation was avoided. Were there any challenges you faced during this time?

Patient: Yeah, it was really hard to get into the prone position because of my reduced respiratory capacity. But the physical therapists were able to adapt the therapy to my needs and I was able to do it at my own pace.

Doctor: I see. It's important to monitor patients closely to ensure a safe implementation of therapy. After three days with this regime, you were transferred to the normal ward where physical therapists carried on your rehabilitation with walking and strength training. How did you feel during this time?

Patient: I was really unstable at first, but the physical therapists were able to work with me to improve my strength and stability. It was challenging, but I was able to leave the hospital on foot after nine days.

Doctor: That's a great outcome. It's important to continue monitoring your symptoms and following up with physical therapy as needed. Do you have any questions or concerns?

Patient: No, I think I understand what I need to do. Thank you for your help.

Doctor: Of course, take care and stay healthy. And please let us know if you or your family have any further concerns."

"This 69-year-old male was admitted to the ICU after a dry cough for 2 weeks, oxygenation was poor and computer tomographic imaging showed typical COVID-19 pneumonia. Initially the patient received lung-protective ventilation and targeted sedation, but was otherwise stable. Treatment interventions included passive range of motion and positioning including passive mobilization into a side-edge position (). Over the next days, the patient deteriorated with hemodynamic instability and severe ARDS leading to intermittent prone positioning and continuous renal replacement therapy. The role of physical therapists during proning was to ensure correct joint positioning and pressure prophylaxis to prevent secondary complications such as nerve lesions, contractures, or pressure ulcers. Nevertheless, the long duration and repeated positioning resulted in a small pressure ulcer

on the patient's forehead. After tracheostomy, passive range-of-motion exercises, and passive side-edge mobilization were slowly resumed, whereby asynchronous ventilation and hemodynamic instability remained 2 major problems leading to further sedation and relaxation, thus inhibiting any active participation. After 24 days in the ICU, the patient scored 1/50 points on the Chelsea Critical Care Physical Assessment Tool (CPAx) and showed severe signs of muscle loss. The patient died soon after withdrawal of life support."

Doctor: Hello, how are you feeling today?

Patient: Not very good, doctor. I've been really sick.

Doctor: I see. When were you admitted to the hospital?

Patient: I was admitted about a month ago.

Doctor: And what brought you in?

Patient: I had a dry cough for 2 weeks and my oxygen levels were really low.

Doctor: Ah, I see. Did you have any imaging done?

Patient: Yes, they did a tomographic imaging and found I had typical COVID-19 pneumonia.

Doctor: I see. And what treatments did you receive?

Patient: I received lung-protective ventilation and sedation.

Doctor: And were you positioned in a certain way?

Patient: Yes, they did passive mobilization and positioning into a side-edge position.

Doctor: I see. Unfortunately, it seems like your condition deteriorated. Did you experience any hemodynamic instability?

Patient: Yes, I did. It was really severe.

Doctor: I'm sorry to hear that. And it looks like you developed ARDS as well.

Patient: Yes, that's correct.

Doctor: Were you put into prone positioning at any point?

Patient: Yes, intermittently.

Doctor: And did you receive continuous renal replacement therapy?

Patient: Yes, I did.

Doctor: During the proning, did you have any physical therapists helping you?

Patient: Yes, they helped me with correct joint positioning and pressure prophylaxis.

Doctor: I see. And did you experience any secondary complications?

Patient: I developed a small pressure ulcer on my forehead.

Doctor: I'm sorry to hear that. After your tracheostomy, were you able to resume any exercises or mobilization?

Patient: Yes, they slowly resumed passive range-of-motion exercises and passive side-edge mobilization.

Doctor: I see. Were there any problems with asynchronous ventilation or hemodynamic instability?

Patient: Yes, those were two major problems that inhibited any active participation.

Doctor: I see. And according to your Critical Care Physical Assessment Tool, you showed severe signs of muscle loss.

Patient: Yes, unfortunately.

Doctor: I'm sorry to have to tell you this, but the clinical note indicates that you passed away after withdrawal of life support.

Patient's Family: (enters conversation) We appreciate everything you did for our loved one, doctor. Thank you."

"This 57-year-old male was admitted to the ICU with dyspnea, heavy dry cough, and fever 6 days after testing positive for COVID-19. Initially, he was able to exercise and sit in a chair with a physical therapist, but progressive respiratory failure necessitated intubation and proning. The patient had large amounts of bronchial mucus and required regular suctioning along with respiratory therapy. Secretions were assessed with pulmonary auscultation (presence of crackles) and by analyzing expiratory flow on the ventilator (sawtooth pattern). When suctioning failed to improve these clinical signs, 1 to 2 physical therapists used manual airway clearance techniques. The goal of these techniques was to sufficiently increase expiratory flow for effective airway clearance while avoiding alveolar collapse. To achieve this, manual compressions on the chest and abdomen were performed with just enough intensity to modify expiratory flow. After extubation, the patient was still unable to effectively clear his mucus due to weak cough. He continued to need intensive manual airway

clearance techniques, nasal rinsing to induce cough and to help expectoration as well as upper and lower airway suctioning. To this end, the patient was treated up to 6 times per day/night. Additional physical therapist interventions included passive range of motion, assisted exercising, and mobilization. At the time of writing, the patient was still in the ICU without ventilatory support.", "Doctor: Good morning, how are you feeling today?

Patient: Not too good, doctor. I'm having trouble breathing.

Doctor: I see. When did you first experience dyspnea?

Patient: It started about a week ago, after I tested positive for COVID-19.

Doctor: I see. Have you been experiencing any other symptoms, like a dry cough or fever?

Patient: Yes, I've been coughing a lot and I've had a fever too.

Doctor: I'm sorry to hear that. According to your clinical note, you were admitted to the ICU. Is that correct?

Patient: Yes, that's right.

Doctor: And you were able to sit with a physical therapist before experiencing progressive respiratory failure?

Patient: Yes, that's right.

Doctor: I see. And then you needed to be intubated and prone?

Patient: Yes, that's what happened.

Doctor: I understand. It looks like you required a lot of respiratory therapy and suctioning. Were you able to improve with these treatments?

Patient: At first, but then the physical therapists had to use manual airway clearance techniques because the suctioning wasn't enough.

Doctor: I see. And were these techniques effective?

Patient: They helped, but after I was extubated I still had trouble clearing my mucus.

Doctor: I understand. You needed nasal rinsing and upper and lower airway suctioning, is that correct?

Patient: Yes, that's right.



Doctor: And you were treated up to six times a day/night?

Patient: Yes, that's right.

Doctor: I understand. It looks like you also received interventions like assisted exercising and mobilization. Is that correct?

Patient: Yes, that's correct.

Doctor: I see. Well, I'm glad to see that you're still in the ICU without ventilatory support. We'll need to monitor your progress closely."

"This 52-year-old male tested COVID-19 positive 4 days after the beginning of a dry cough, fever, and head and limb pain. One day later, he was hospitalized with exertional dyspnea. He was diagnosed with pneumonia that developed into moderate ARDS needing mechanical ventilation and intermittent dialysis. After extubation, oxygenation was stable with 2 to 3 L/min of oxygen. However, the patient was disoriented and could not communicate verbally. His global weakness (CPAx 11/50) was accompanied by oral and pharyngeal weakness and paresthesia. Spontaneous swallowing frequency and tongue control were severely reduced, and the patient showed insufficient protection from aspiration. This was confirmed by a specialized physical therapist with the Gugging Swallowing Screen, which confirmed severe dysphagia with 2/20 points. He was treated nil by mouth and received dysphagia therapy such as intensive oral stimulation, facilitation of swallowing, and training of protection mechanisms. After initial agitation and disorientation, the patient started to communicate in single-word phrases, but dysphagia continued to be severe with massive oral and pharyngeal dry saliva residuals that compromised his paresthesia and required regular mouth care. Over the next days, the patient managed to swallow pureed food and mildly thick fluids under supervision, although cough strength was still weak (Gugging Swallowing Screen 13/20, CPAx 30/50). Nevertheless, he continued to progress and became capable of independent food ingestion (Gugging Swallowing Screen 20/20, CPAx 39/50) before his discharge to a rehabilitation clinic 25 days after admission.","Doctor: Good morning, how are you feeling today?

Patient: Not great, I've been feeling really sick lately.

Doctor: I see from your medical records that you tested COVID-19 positive. When did you first notice

symptoms?

Patient: About four days ago, I started having a dry cough, fever, and pain in my limbs and head.

Doctor: I'm sorry to hear that. One day after your symptoms started, you were hospitalized with exertional dyspnea.

Patient: Yes, it was really difficult to breathe.

Doctor: You were diagnosed with pneumonia that developed into moderate ARDS, which required mechanical ventilation and intermittent dialysis.

Patient: That's correct.

Doctor: After extubation, your oxygenation was stable with 2 to 3 L/min of oxygen. However, you were disoriented and couldn't communicate verbally.

Patient: Yes, I was really confused.

Doctor: Your global weakness was accompanied by oral and pharyngeal weakness and paresthesia. Did you notice any difficulty with swallowing?

Patient: Yes, I couldn't swallow properly and it was really difficult to eat or drink anything.

Doctor: The specialized physical therapist confirmed that you had severe dysphagia with 2/20 points on the Gugging Swallowing Screen.

Patient: Yes, they did that test and it was really difficult for me.

Doctor: You were treated nil by mouth and received dysphagia therapy such as intensive oral stimulation, facilitation of swallowing, and training of protection mechanisms. Did you notice any improvement?

Patient: Yes, after a while I was able to swallow some food and fluids under supervision, but it was still really difficult.

Doctor: Your cough strength was still weak, but you continued to progress and became capable of independent food ingestion before your discharge to a rehabilitation clinic 25 days after admission.

Patient: Yes, I was really happy to be able to eat and drink on my own again."

"Paramedics found this 59-year-old female with dyspnea and an oxygenation of 65% on room air and performed immediate tracheal intubation. Moderate ARDS with reduced lung compliance was

diagnosed and treated with deep sedation, neuromuscular blocking agents, and prone positioning.

On day 14, a trial of sitting on the edge-of-bed (SOEB) was performed, while she was still intubated and under pressure support ventilation. SOEB required 3 physical therapists to maintain the position, but resulted in a significant increase in her level of consciousness and collaborative state. The next day, she was able to hold her head and sit for about 15 minutes with 2 therapists. Her muscle strength indicated ICU-acquired weakness, with a Medical Research Council sum-score (MRC-SS) of 40/60; still she continued with small but consistent improvements and started to participate actively in physical therapy sessions. She was encouraged to mobilize herself with exercises against gravity and was actively transferred to a chair each day with the help of 2 physical therapists. She was successfully extubated, but presented postextubation dysphagia. The physical therapy team closely monitored her for secretion management and cough stimulation and continued her physical rehabilitation. On day 19, she started to walk with a walking aid, although at this point oxygen desaturation during exercise training became evident (89% with 3 L/min of oxygen). After 25 days, she was transferred to the institution's rehabilitation facilities, where a battery of tests indicated persistent physical function impairment (MRC-SS 52/60, physical function ICU test score 17 9/12, Timed Up & Go 23 seconds, short physical performance battery 4/12).", "Doctor: Hello, how are you feeling today?

Patient: Hmm, not too well. I have been experiencing dyspnea and difficulty breathing.

Doctor: I see. According to your medical records, you had an oxygenation of 65% on room air and underwent tracheal intubation. You were diagnosed with ARDS and treated with sedation, neuromuscular blocking agents, and prone positioning. Is that correct?

Patient: Yes, that's right.

Doctor: On day 14, you underwent a trial of sitting on the edge-of-bed while still intubated and under pressure support ventilation. This required 3 physical therapists to maintain your position, but resulted in a significant increase in your level of consciousness and collaborative state.

Patient: Yes, I remember that.

Doctor: The next day, you were able to sit for about 15 minutes with the help of 2 therapists. Your

muscle strength indicated ICU-acquired weakness, with a Medical Research Council sum-score of 40/60. However, you continued to make small but consistent improvements and started actively participating in physical therapy sessions.

Patient: Okay.

Doctor: You were encouraged to mobilize yourself with exercises against gravity and were actively transferred to a chair each day with the help of 2 physical therapists. You were successfully extubated, but presented postextubation dysphagia.

Patient: Yes, I remember that too.

Doctor: The physical therapy team closely monitored you for secretion management and cough stimulation and continued your physical rehabilitation. On day 19, you started to walk with a walking aid, although at this point oxygen desaturation during exercise training became evident. Your oxygen saturation level dropped to 89% with 3 L/min of oxygen.

Patient: Oh no.

Doctor: After 25 days, you were transferred to the institution's rehabilitation facilities, where a battery of tests indicated persistent physical function impairment with a MRC-SS of 52/60, physical function ICU test score of 9/12, Timed Up & Go of 23 seconds, and short physical performance battery of 4/12.

Patient: What does that mean?

Doctor: It means that there is still some physical function impairment and we need to continue your physical rehabilitation. We will monitor your progress closely and adjust your treatment plan as necessary."

"This 33-year-old female patient had typical COVID-19 symptoms such as high fever, dry cough, headache, and dyspnea about 1 week before ICU admission. She was intubated and prone due to rapid respiratory deterioration. For the following 6 days, her situation was unstable, and physical therapy consisted of prone positioning and prevention of secondary damage. From day 7 onwards, she started to improve rapidly and could be mobilized passively into a side-edge position. After extubation, she presented postextubation dysphagia and severe ICU-acquired weakness (MRC-SS

36/60). She also suffered from pronounced delirium and anxiety and said repeatedly that she had been abducted and that she believed she had to die. She seemed to feel threatened by us and it was difficult to calm her down. Due to the pandemic measures of the Swiss government, hospital visits were not generally allowed, but because her anxiety was limiting her rehabilitation, her husband was granted an exceptional permission to visit her. This seemed to give the patient a short sense of security, and she started to participate in some basic functional activities (CPAx 21/50). Nevertheless, the delirium did not resolve upon her transfer to a peripheral acute hospital.", "Doctor: Hi there, how are you feeling today?

Patient: Not very good, I've been feeling sick for about a week now.

Doctor: Can you tell me what kind of symptoms you've been experiencing?

Patient: I've had a high fever, dry cough, headache, and difficulty breathing.

Doctor: Those are typical COVID-19 symptoms. It's good that you came in for admission.

Patient: Yes, they had to intubate me and put me in a prone position because my breathing was getting worse.

Doctor: I see. You were also receiving physical therapy to prevent any secondary damage.

Patient: Yes, but my situation was unstable for the first 6 days.

Doctor: That's understandable. But after day 7, you started to improve rapidly and could be mobilized into a side-edge position.

Patient: Yes, but after they extubated me, I had trouble swallowing and my muscles were very weak.

Doctor: That's called postextubation dysphagia and severe ICU-acquired weakness. Did you also suffer from delirium and anxiety?

Patient: Yes, I kept thinking I was abducted and that I had to die. It was difficult for the hospital staff to calm me down.

Doctor: I'm sorry to hear that. Due to the pandemic measures, hospital visits weren't allowed, but your husband was granted permission to visit you because your anxiety was limiting your rehabilitation.

Patient: Yes, that helped a little bit and I was able to participate in some basic functional activities.

Doctor: That's good to hear. However, your delirium didn't resolve even after your transfer to a peripheral acute hospital.

Patient's family: (if applicable) Thank you for taking care of our loved one. We appreciate everything you did for her."

"This 66-year-old male patient was admitted to the hospital due to an ischemic left-hemispheric stroke in addition to a dry cough and fever. He tested positive for SARS-CoV-2 the following day but continued to deteriorate resulting in severe ARDS, intubation, and ICU admission. Despite repeated proning, gas exchange did not improve sufficiently and the patient was placed on veno-venous extracorporeal membrane oxygenation for 7 days. After sedation was stopped, the patient continued to be somnolent and unable to communicate or to follow commands. Physical therapy therefore focused on perception training, movement exercises, airway-clearing techniques, dysphagia therapy, and mobilization. A first SOEB trial had to be discontinued due to hemodynamic instability. Instead, the patient was positioned in a side-edge position (), which he tolerated better and where an intensive exercise training including trunk and head control was conducted. Nevertheless, muscle tone and strength remained severely reduced, particularly on his hemiplegic side, and a second SOEB trial failed again. Physical therapy was also limited because of reduced self-activity and suspected impaired perception and visual acuity. Consequently, occupational therapy was involved to create a basis of communication, to support functional initiation of upper limb movements, and to integrate perception-training into activities of daily living. Currently, the patient tolerates spontaneous breathing trials, shows signs of being alert during therapy, but cannot communicate. He is hemodynamically stable, even in an SOEB position, but remains functionally dependent (CPAx 6/50).", "Doctor: Good morning, how are you feeling today?

Patient: Hmm, not so good.

Doctor: I can see from your medical records that you were admitted to the hospital due to an ischemic left-hemispheric stroke, dry cough, and fever. Do you remember any of these symptoms?

Patient: Yes, I do.

Doctor: Unfortunately, you tested positive for SARS-CoV-2 the following day and continued to

deteriorate resulting in severe ARDS, intubation, and ICU admission.

Patient: Oh no, I didn't realize it was that serious.

Doctor: Yes, it was quite severe. We had to place you on veno-venous extracorporeal membrane oxygenation for 7 days to help with your gas exchange.

Patient: Okay, I vaguely remember that.

Doctor: After sedation was stopped, you continued to be somnolent and unable to communicate or follow commands.

Patient: Yes, I remember feeling very drowsy.

Doctor: That's understandable. We then focused on physical therapy to help with perception training, movement exercises, airway-clearing techniques, dysphagia therapy, and mobilization.

Patient: That sounds like a lot.

Doctor: It was necessary to help with your recovery. We also tried a first SOEB trial, but it had to be discontinued due to hemodynamic instability. Instead, we positioned you in a side-edge position, which you tolerated better and where we conducted intensive exercise training including trunk and head control.

Patient: Hmm, I don't remember that.

Doctor: That's okay. Unfortunately, muscle tone and strength remained severely reduced, particularly on your hemiplegic side, and a second SOEB trial failed again.

Patient: Oh no, that's not good.

Doctor: We also suspected that your reduced self-activity and impaired perception and visual acuity were limiting your physical therapy, so we involved occupational therapy to create a basis of communication, support functional initiation of upper limb movements, and integrate perception-training into activities of daily living.

Patient: Okay, I'm starting to remember some of that.

Doctor: Currently, you tolerate spontaneous breathing trials, show signs of being alert during therapy, but cannot communicate. You are hemodynamically stable, even in an SOEB position, but remain functionally dependent.

Patient: Hmm, is there anything else I can do to improve my condition?

Doctor: Right now, we just need to continue with your physical and occupational therapy to help with your recovery. We will also monitor your progress closely and adjust your treatment plan accordingly. Is there anything else you would like to know?

Patient's family: Excuse me, doctor, may we have a moment to speak with you about our loved one's health?

Doctor: Of course, please come in."

"A 66-year-old male started to present symptoms of fever, dyspnea, coughing, asthenia, lack of appetite, nausea, and vomiting. He was admitted to the acute care unit for observation and oxygen therapy, but his oxygen requirements constantly increased due to moderate ARDS. After 12 days of deep sedation, neuromuscular blocking agents, and proning with daily passive range of motion, the patient finally started to initiate active movements and was passively transferred to a chair. However, due to a persisting difficult weaning status, probably related to respiratory muscle weakness, tracheostomy was performed [ventilator settings: pressure support 10 cmH<sub>2</sub>O, positive end-expiratory pressure (PEEP) 8 cmH<sub>2</sub>O]. Subsequently, the patient showed significant improvement in his physical functions with active SOEB, chair-transfer with the help of 2 physical therapists, and active in-bed cycling against resistance for 20 minutes (). The strategy was to increase pressure support (by 5 cmH<sub>2</sub>O) during efforts to reinforce exercise training effects, unloading respiratory muscles. This strategy along with a highly collaborative patient culminated in his rapid improvement in physical function (MRC-SS 58/60, physical function ICU test score 10/12, walking distance 10 m), although he was still experiencing fatigue, inspiratory muscle weakness (maximal inspiratory pressure of -45 cmH<sub>2</sub>O) and dysphagia upon his transfer to a step-down unit.", "Doctor: Hi, how are you feeling today?

Patient: I'm not feeling too well, I have been experiencing fever, dyspnea, coughing, asthenia, lack of appetite, nausea, and vomiting.

Doctor: I'm sorry to hear that. You were admitted to the acute care unit for observation and oxygen therapy, correct?



Patient: Yes, that's right.

Doctor: I see that your oxygen requirements constantly increased due to moderate ARDS. After 12 days of deep sedation, neuromuscular blocking agents, and proning with daily passive range of motion, you finally started to initiate active movements and were passively transferred to a chair. How are you feeling now?

Patient: I feel much better now.

Doctor: That's great to hear. However, due to a persisting difficult weaning status, probably related to respiratory muscle weakness, tracheostomy was performed. Your ventilator settings are pressure support 10 cmH<sub>2</sub>O and positive end-expiratory pressure (PEEP) 8 cmH<sub>2</sub>O. How have you been feeling since the tracheostomy?

Patient: I have been feeling much better since the tracheostomy. I have been able to show significant improvement in my physical functions with active SOEB, chair-transfer with the help of 2 physical therapists, and active in-bed cycling against resistance for 20 minutes.

Doctor: That's great news. Our strategy is to increase pressure support by 5 cmH<sub>2</sub>O during efforts to reinforce exercise training effects, unloading respiratory muscles. This strategy along with a highly collaborative patient culminated in your rapid improvement in physical function. Your MRC-SS score is 58/60, physical function ICU test score is 10/12, and you are able to walk 10 meters. However, you are still experiencing fatigue, inspiratory muscle weakness (maximal inspiratory pressure of -45 cmH<sub>2</sub>O), and dysphagia upon your transfer to a step-down unit. We will continue to monitor your progress and adjust your treatment accordingly.

Patient's family: We appreciate your efforts to help our loved one. Thank you for taking such good care of him."

"This 77-year-old male patient was transferred to our ICU 1 week after his COVID-19 diagnosis due to continuing respiratory decompensation requiring intubation. Following the acute phase, with intermittent proning, the patient continued to be hemodynamically unstable and was difficult to wean. Rehabilitation proved challenging under these conditions, and physical therapists had to reevaluate and adapt their interventions daily according to his condition. After 2 weeks, he was

tracheotomized and started to improve very slowly. One week after tracheostomy, the patient was able to speak for the first time after a cuff-down trial and with the help of a speaking valve. But the patient spoke only a few words with us and it was often difficult to involve him in exercises. Two days later, he was able to communicate with his relatives via video telephony. This was a very emotional moment for everyone involved, but it improved his communication and he was able to express to his wife that he had no strength left to continue. However, through the family's active participation in his early rehabilitation process, they were able to reinforce his confidence and motivation. He was discharged to a rehabilitation clinic severely weak (MRC-SS 40/60) and functionally impaired (CPAx 22/50), but continued to progress in slow steps.", "Doctor: Good morning, how are you feeling today?

Patient: Hmm, not so good.

Doctor: I see. According to your clinical note, you were transferred to our ICU due to continuing respiratory decompensation. Can you tell me more about your symptoms?

Patient: Well, I had a hard time breathing and needed to be intubated.

Doctor: I see. After the acute phase, you continued to be hemodynamically unstable and difficult to wean. How was rehabilitation under those conditions?

Patient: It was tough. The physical therapists had to reevaluate and adapt their interventions daily according to my condition.

Doctor: I understand. After your tracheostomy, you were able to speak for the first time with the help of a speaking valve. How did that feel?

Patient: It was a relief to be able to communicate with others again, but I could only speak a few words.

Doctor: I see. Two days after that, you were able to communicate with your relatives via video telephony. How did that affect your communication?

Patient: It improved my communication a lot. I was able to express to my wife that I had no strength left to continue.

Doctor: I see. However, through your family's active participation in your early rehabilitation process,

they were able to reinforce your confidence and motivation. How did that help you?

Patient: It gave me hope that I could continue to improve, even if it was in slow steps.

Doctor: I understand. According to your clinical note, you were discharged to a rehabilitation clinic severely weak and functionally impaired. How have you been progressing since then?

Patient: It's been tough, but I'm making slow progress.

Doctor: That's good to hear. We will need to continue to monitor your condition closely and adjust your treatment plan accordingly. Do you have any questions for me?

Patient: No, not at the moment.

Doctor: Alright. Please follow up with us as scheduled and continue to take care of yourself."

"A 45-year-old female was brought in by ambulance after collapsing at home secondary to a hypoglycemic event (capillary blood glucose of 1 mmol/L with paramedics). She had a history of restrictive AN, binge-purge behaviour, and an old traumatic brain injury, leaving her with memory problems. She was well known to mental health services, having been admitted multiple times to eating disorder centres for nasogastric feeding. She had never smoked in her life and denied any alcohol intake. The patient was on ferrous fumarate, fexofenadine, fluoxetine, ibuprofen, lansoprazole, quetiapine, supplemental vitamins, regular morphine (modified release), and gabapentin.

On admission, her blood pressure was 106/85 mmHg, respiratory rate was 20 breaths/minute, heart rate was 64 beats/minute, temperature was 35.1 degC, and capillary blood glucose was 6 mmol/L. Her weight on admission was 37.3 kg (body mass index [BMI] = 12.6). On examination, she was clearly malnourished, cachexic, and dehydrated. The rest of the clinical examination was normal, as shown in Table . Her chest radiograph showed patchy consolidations in the right middle and lower lobes (Figure ). She was prescribed appropriate antibiotics. She was refusing treatment and was deemed to lack the capacity to make that decision. Therefore, Section 5(2) under the Mental Health Act was put in place. She was commenced on oral supplements as per guidance from the dietitian, and then switched to nasogastric feeding.

On the night of the second day, she had an episode of decreased consciousness, bradypnoea

(RR-6), and hypotension (83/64). Her blood sugar level was 6.6 mmol/L. After receiving Naloxone, her symptoms improved, and her opiates were discontinued. The following day she mentioned right upper quadrant pain. Blood tests showed", "Doctor: Hi, how are you feeling today?

Patient: Not too good, I collapsed at home and the ambulance brought me here.

Doctor: I see, and do you know why you collapsed?

Patient: Yes, it was a hypoglycemic event. My blood glucose level was only 1 mmol/L according to the paramedics.

Doctor: That's very low. Have you had any history of restrictive AN or binge-purge behavior?

Patient: Yes, I have a history of both.

Doctor: Okay, and have you ever had a traumatic brain injury?

Patient: Yes, I have an old one that left me with memory problems.

Doctor: I see. And have you been admitted to any eating disorder centers before?

Patient: Yes, I've been admitted multiple times for nasogastric feeding.

Doctor: Okay, and have you ever smoked or drank alcohol?

Patient: No, I've never smoked and I don't drink alcohol.

Doctor: Alright. I see here that you're taking ferrous fumarate, fexofenadine, fluoxetine, ibuprofen, lansoprazole, quetiapine, supplemental vitamins, regular morphine (modified release), and gabapentin. Is that correct?

Patient: Yes, that's correct.

Doctor: On admission, your blood pressure was 106/85 mmHg, respiratory rate was 20 breaths/minute, heart rate was 64 beats/minute, temperature was 35.1 degC, and your capillary blood glucose was 6 mmol/L. Your weight on admission was 37.3 kg, which gives you a body mass index of 12.6. You were clearly malnourished, cachexic, and dehydrated. Do you remember the examination?

Patient: Not really.

Doctor: That's okay. Your chest radiograph showed patchy consolidations in the right middle and lower lobes. We prescribed you appropriate antibiotics. However, you were refusing treatment and

were deemed to lack the capacity to make that decision. Therefore, Section 5(2) under the Mental Health Act was put in place. You were commenced on oral supplements as per guidance from the dietitian, and then switched to nasogastric feeding.

Patient: Okay.

Doctor: On the night of the second day, you had an episode of decreased consciousness, bradypnoea (RR-6), and hypotension (83/64). Your blood sugar level was 6.6 mmol/L. After receiving Naloxone, your symptoms improved, and your opiates were discontinued. The following day you mentioned right upper quadrant pain. Blood tests showed...

(Patient's family enters)

Doctor: I'm sorry to inform you that despite our efforts, we were unable to save your loved one. We did everything we could, but unfortunately, her condition deteriorated rapidly. Our condolences to you and your family."

"A 29-year-old male was brought to the hospital by ambulance after collapsing at home. He was found to be bradycardic and hypoglycaemic with a capillary blood glucose level of 2.3 mmol/L. He had a history of eating and anxiety disorders and was not on any regular medications. On admission, his weight was 37.3 kg (BMI = 11.6). His blood pressure was initially un-recordable but subsequently was recorded to be 104/72 mmHg. His capillary blood glucose level was 4.7 mmol/L, and his Glasgow Coma Scale score was 15/15. On examination, he was noted to be severely malnourished and cachexic. The rest of the clinical examination was normal. LFTs were very abnormal, as shown in Table .

Since admission, he seemed to lack insight. Due to problems keeping him compliant with medication and intravenous glucose, he had a number of hypoglycaemic events in the first two days of admission. The following day, he was deemed not to have the capacity. He underwent Mental Capacity Assessment and Deprivation of Liberty Safeguards. He was ultimately placed under Mental Health Act 5(2) and was started on nasogastric feeding. His liver enzymes worsened further after the introduction of nasogastric feeding, but we were reassured by a normal non-invasive liver screen and ultrasound.

His condition, liver tests, and liver synthetic function improved over the course of his 24-day admission (Table ), but his stay was associated with difficult behaviour. He was eventually discharged to an Eating Disorders Unit.", "Doctor: Hello, how are you feeling today?

Patient: I'm feeling a bit better, thank you.

Doctor: That's good to hear. Do you remember what happened before the ambulance brought you here?

Patient: Not really, I just remember collapsing at home.

Doctor: Okay. Well, when you arrived at the hospital, you were found to be bradycardic and hypoglycaemic. Your blood glucose level was quite low.

Patient: I see.

Doctor: You also have a history of eating and anxiety disorders. Are you currently on any regular medications?

Patient: No, I'm not.

Doctor: Alright. During your admission, we noticed that your weight was very low and you were severely malnourished and cachexic.

Patient: Is that why I had to be put on nasogastric feeding?

Doctor: Yes, that's correct. We had some problems keeping you compliant with the medication and glucose, which led to some hypoglycaemic events.

Patient: I don't remember that.

Doctor: That's because on the following day, you were deemed not to have the capacity. We had to undergo Mental Capacity Assessment and Deprivation of Liberty Safeguards. You were ultimately placed under Mental Health Act 5(2) and started on nasogastric feeding.

Patient: Oh, I see.

Doctor: Your liver enzymes did worsen after the introduction of nasogastric feeding, but we were reassured by a normal non-invasive liver screen and ultrasound. Your condition, liver tests, and liver synthetic function improved over the course of your 24-day admission.

Patient: That's good news.

Doctor: Yes, it is. However, your stay was associated with difficult behavior. We eventually discharged you to an Eating Disorders Unit for further treatment.

Patient: Alright.

Doctor: It's important that you continue to follow-up with your care and attend any necessary appointments. Do you have any questions for me?

Patient: No, I think I understand everything. Thank you, doctor.

Doctor: You're welcome. Take care and stay healthy. \*turns to address the patient's family\* I'm sorry for your loss. We did everything we could to treat him."

"A 36-year-old G4P2 premenopausal woman with a family history of colorectal, hepatobiliary cancers felt an abnormal right breast lump. Diagnostic mammogram and ultrasound showed a hypoechoic lesion in the upper outer quadrant of right breast measuring 14 mm x 13 mm x 18 mm and 5 x 4 mm satellite lesion is noted 6 mm inferior to the dominant mass, BI-RADS 5 highly suggestive of malignancy. Due to concern for multifocal disease, MRI breast with and without contrast was done and it showed 2.3 x 1.1 x 2.7 cm irregular-shaped, heterogeneous mass with irregular margins in the upper outer quadrant of right breast, 7 cm from the nipple, 1.2 cm from the skin and there was an additional mass measuring 8 mm x 4 mm x 1.6 cm at 12:00 along with 4 mm lesion, 7 mm from the nipple at 10:00 (Figures (a) and (b)). Right breast biopsy from the dominant lesion showed invasive mammary carcinoma with features of both lobular and ductal carcinoma, Nottingham histological grade 2, estrogen receptor 90%, progesterone receptor 100%, HER2 2+ by IHC but negative by FISH, Ki-67 50%.

Status post right breast simple mastectomy and axillary lymph node evaluation. Surgical pathology showed a multifocal invasive mammary carcinoma of the breast with ductal and lobular features, size of largest invasive carcinoma was 55 mm, size of additional invasive foci was 1.5 mm, Nottingham histological grade 2 of 3, low to intermediate nuclear grade DCIS without central necrosis measuring at least 6 mm, margins uninvolved, one benign sentinel lymph node. Pathological staging (m)pT3 (sn)N0. Oncotype DX breast recurrence score of 16 (for patients <50 years of age, benefit from chemotherapy 1.6%). Genetic testing did not reveal any clinically

significant mutations. The patient has received adjuvant PMRT 5000 cGy dose, 25 fractions along with 1000 cGy scar boost. Based on TE", "Doctor: Hi there, how are you feeling today?

Patient: I'm feeling a bit worried about my breast lump, doctor.

Doctor: I understand. Can you tell me about your family history of cancers?

Patient: My family has a history of colorectal and hepatobiliary cancers.

Doctor: I see. And when did you first notice the abnormal lump in your right breast?

Patient: I noticed it a few weeks ago.

Doctor: Okay, and what did the diagnostic mammogram and ultrasound show?

Patient: They showed a hypoechoic lesion in the upper outer quadrant of my right breast measuring 14 mm x 13 mm x 18 mm and a 5 x 4 mm satellite lesion 6 mm inferior to the dominant mass.

Doctor: Based on those results, we were concerned about malignancy. Did you then undergo an MRI breast without contrast?

Patient: Yes, I did. They found irregular-shaped, heterogeneous masses in the upper outer quadrant and at 12:00, along with additional smaller lesions.

Doctor: Right. And the biopsy from the dominant lesion showed invasive mammary carcinoma with features of lobular and ductal carcinoma. Do you understand what that means?

Patient: Not entirely, can you explain it to me, doctor?

Doctor: Essentially, it means that the cancer had spread beyond the milk ducts and was present in other tissues of the breast. It had features of both lobular and ductal carcinoma, which are different types of breast cancer. The Nottingham histological grade was 2 out of 3, which means it was considered intermediate.

Patient: Okay, I think I understand.

Doctor: Good. The biopsy also showed that your estrogen receptor was 90% positive and your progesterone receptor was 100% positive. However, your HER2 status was 2+ by IHC but negative by FISH, and your Ki-67 was 50%. Do you know what those numbers mean?

Patient: Not really, no.

Doctor: Those are all tests that help us determine the characteristics of the cancer and how



aggressively it's growing. Essentially, the higher the numbers, the more aggressive the cancer. In your case, the HER2 status was inconclusive, but the Ki-67 was quite high.

Patient: Okay, that sounds serious.

Doctor: It is a serious diagnosis, but we caught it early, which is good news. You underwent a simple mastectomy and axillary lymph node evaluation, and the surgical pathology showed a multifocal invasive mammary carcinoma of the breast with ductal and lobular features. The size of the largest invasive carcinoma was 55mm, and there were additional invasive foci as well as low to intermediate nuclear grade DCIS without central necrosis measuring at least 6mm.

Patient: That's a lot of information to take in.

Doctor: I know it can be overwhelming, but it's important that you understand your diagnosis. The margins were uninvolved, and we found one benign sentinel lymph node. The pathological staging was pT3 (sn)N0. We also did an Oncotype DX test, which showed a breast recurrence score of 16. That means that for patients under 50 years of age, the benefit from chemotherapy is 1.6%.

Patient: Okay, I see.

Doctor: We also did genetic testing, which didn't reveal any clinically significant mutations. You have since undergone adjuvant PMRT, which is radiation therapy, and you received 5000 cGy dose in 25 fractions along with a 1000 cGy scar boost.

Patient: Yes, I've been keeping up with my treatments.

Doctor: That's great to hear. Going forward, we will need to monitor your progress closely. Do you have any questions for me?

Patient: No, I don't think so. Thank you for explaining everything to me, doctor.

Doctor: Of course. And please don't hesitate to reach out if you have any concerns or questions in the future. We will be here to support you every step of the way."

"The patient was a 62-year-old male with a past medical history of liver cirrhosis secondary to hepatitis C, tobacco use, and post-stent coronary artery disease, who initially came to the hospital for elective left and right heart catheterization as a pre-transplant evaluation. Physical examination showed abdominal distension and diffuse tenderness with the presence of prominent superficial

abdominal veins. A computed tomography (CT) scan of the abdomen with contrast was obtained immediately. The CT showed an occlusive thrombus of the IVC extending from the renal veins to the level of the cavoatrial junction. Thrombus was also observed in the portal vein, and multiple subcutaneous varicosities were found. Initially, a plan was made to start the patient on anticoagulation, but because of the patient's history of advanced cirrhosis, large esophageal varices on recent endoscopy, and thrombocytopenia, we concluded that the patient was not a candidate for anticoagulation. Given that the patient had significant abdominal distention with pain that did not improve even after therapeutic paracentesis; we inserted a stent in the IVC to relieve the patient's pain as a palliative procedure to improve his quality of life.

Right internal jugular (IJ) and right femoral vein accesses were obtained for the procedure. A 6F pigtail diagnostic catheter was advanced from the right IJ to the right atrium, and contrast was injected into the right atrium that showed an occluded IVC at the junction of the right atrium. Another pigtail catheter was advanced through the right femoral vein and an inferior venogram was performed that showed the IVC was 100% occluded 2 cm above the renal veins (Figures , ).

A Glidewire advantage was advanced through the right femoral vein but was unable to cross the 100% occluded IVC. Then, a 7-French Swan-Ganz catheter was tried and was successfully advanced through the IVC all the way to the right atrium. A Swan wire was inserted through the Swan-Ganz catheter. Then, a multipurpose catheter", "Doctor: Good morning, Mr. Johnson. How are you feeling today?

Patient: Hmm, not too good, doctor. I'm still in a lot of pain.

Doctor: I see. Well, I have the results of your tests here. Your past medical history shows that you have liver cirrhosis secondary to hepatitis C, tobacco use, and post-stent coronary artery disease. You came to the hospital for elective left and right heart catheterization as a pre-transplant evaluation, is that correct?

Patient: Yes, that's right.

Doctor: During the physical examination, we noticed that you had abdominal distension and diffuse tenderness with the presence of prominent superficial abdominal veins. We immediately obtained a

computed tomography (CT) scan of the abdomen with contrast, which showed an occlusive thrombus of the IVC extending from the renal veins to the level of the cavoatrial junction. Thrombus was also observed in the portal vein, and multiple subcutaneous varicosities were found.

Patient: Okay, I understand.

Doctor: Initially, we planned to start you on anticoagulation, but because of your history of advanced cirrhosis, large esophageal varices on recent endoscopy, and thrombocytopenia, we concluded that you were not a candidate for anticoagulation. Given that you had significant abdominal distention with pain that did not improve even after therapeutic paracentesis, we inserted a stent in the IVC to relieve your pain as a palliative procedure to improve your quality of life.

Patient: Alright, doctor. What's the next step?

Doctor: Well, we obtained right internal jugular (IJ) and right femoral vein accesses for the procedure. A 6F pigtail diagnostic catheter was advanced from the right IJ to the right atrium, and contrast was injected into the right atrium that showed an occluded IVC at the junction of the right atrium. Another pigtail catheter was advanced through the right femoral vein and an inferior venogram was performed that showed the IVC was 100% occluded 2 cm above the renal veins.

Patient: I remember the procedure, but I didn't know the details.

Doctor: We tried to advance a Glidewire advantage through the right femoral vein, but it was unable to cross the 100% occluded IVC. Then, we tried a 7-French Swan-Ganz catheter and were successfully able to advance it through the IVC all the way to the right atrium. We inserted a Swan wire through the Swan-Ganz catheter and then a multipurpose catheter.

Patient: Okay, thank you for explaining everything to me, doctor.

Doctor: You're welcome, Mr. Johnson. Do you have any questions or concerns?

Patient: No, not at the moment."

"We report a case of a 45-year-old woman, a non-smoker, treated for type II diabetes under insulin and primary hyperparathyroidism. Her medical history dates back to 2006 with an infiltrated nodule associated with ulcers that grew gradually in her right thigh. The patient underwent surgery with an anatomopathological study. Skin biopsy objectified ulcerated epidermotropic dermo-hypodermal

tumor proliferation whose morphological appearance and immunohistochemical data are in favor of LCH. Langerhans cells present positivity of the anti-PS100 antibody, anti-CD1a antibody, and anti-Ki67 antibody (60%), and negativity of the anti-CD68 antibody. The patient subsequently received 25 sessions of radiotherapy followed by six courses of chemotherapy with a low dose of oral methotrexate. After these treatments, skin lesions are stable. In 2020, the patient complained of an increase in skin lesions, with the appearance of several infiltrating nodules, scaling, crusted papules, and ulcerated plaques. The patient received chemotherapy as single-system LCH (SS-LCH) based on methotrexate, associated with prednisone and vinblastine, with the obtainment of stable response and limited regression of the lesions. After two courses, the patient was lost to follow-up. One year later, the oncologist referred the patient to the hematology department for a major increase in skin lesions, with the appearance of new ones on her thigh. Dermatological examination found ulcers and necrotic lesions, purplish, well-limited, of variable size, not painful, not warm to the skin, and localized to the right thigh. The mucous membranes and integuments were unharmed (Figure ).

Furthermore, the examination found an afebrile, obese patient (body mass index (BMI) at 44.8). Abdominal and cardiovascular examinations were unremarkable. The physical examination did not find any tumoral syndromes, and the patient did not present have B signs (fever, weight loss, and night sweats").

Doctor: Hi there, how are you feeling today?

Patient: Not too good, doctor. I've been experiencing an increase in skin lesions.

Doctor: I see. Can you tell me more about your medical history? Have you been treated for any conditions before?

Patient: Yes, I have type II diabetes and primary hyperparathyroidism. I'm a non-smoker and I'm currently on insulin.

Doctor: Okay, thank you for letting me know. I also see in your medical history that you had an infiltrated nodule associated with ulcers that grew gradually in your right thigh. Can you tell me more about that?

Patient: Yes, I underwent surgery and a skin biopsy showed that it was an ulcerated tumor

proliferation called LCH.

Doctor: I see. And after that, you received 25 sessions of radiotherapy followed by six courses of chemotherapy with a low dose of oral methotrexate, is that correct?

Patient: Yes, that's right.

Doctor: And after those treatments, your skin lesions were stable?

Patient: Yes, they were.

Doctor: Okay, thank you for letting me know. But then in 2020, you complained of an increase in skin lesions, is that correct?

Patient: Yes, that's when I received chemotherapy as single-system LCH based on methotrexate, associated with prednisone and vinblastine.

Doctor: And after two courses, the lesions were stable again?

Patient: Yes, that's correct.

Doctor: Okay, thank you for letting me know. But then, you were lost to follow-up?

Patient: Yes, I was.

Doctor: I see. And now, you've been referred to the hematology department for a major increase in skin lesions, is that correct?

Patient: Yes, that's what happened.

Doctor: I see. During your dermatological examination, were there any painful lesions?

Patient: No, they weren't painful.

Doctor: Okay, that's good to know. And were there any tumoral syndromes found during your physical examination?

Patient: No, there weren't.

Doctor: Okay, thank you for letting me know. Based on your medical history and examination, I think we need to do further tests to determine the best course of action. I will report back to you as soon as possible.

Patient's family: Thank you for your help, doctor. We appreciate everything you've done for our loved one."

"We describe the case of a 55-year-old male who presented to the emergency department via emergency medical services for the chief complaint of sudden onset shortness of breath that woke him from his sleep just prior to arrival. He reported three days of non-radiating lumbar back pain and two episodes of non-bloody emesis leading up to this event. His medical history included hypertension and type 2 diabetes mellitus. His current medications were metformin, amlodipine, losartan, and atenolol. Initial vital signs revealed heart rate (HR) 75, respiratory rate (RR) 29, blood pressure (BP) 119/62, and oxygen saturation 99% on 2L nasal cannula. Temperature was 36.3degC.

Physical examination was significant for an ill-appearing male patient who was anxious and tachypneic. He also had significant work of breathing with retractions and abdominal breathing. Lungs were clear to auscultation, with no wheezing, rhonchi, or rales. Abdominal exam revealed mild epigastric tenderness with no rebound, guarding, or palpable pulsatile mass. No costovertebral angle (CVA) tenderness or midline tenderness was elicited. Neurological exam revealed no focal deficits.

Due to his presentation and multiple comorbidities we had significant concern for the possible acute coronary syndrome, dissection, sepsis, or pulmonary embolism. Blood work including complete blood count (CBC), comprehensive metabolic panel (CMP), lactic acid, troponin, urine analysis (UA) was ordered. CT-angiogram of his chest, abdomen, and pelvis was also ordered.

Complete blood count revealed a white blood cell count of  $20.4 \times 10^3/\mu\text{L}$ , hemoglobin of 11.2 g/dL, and platelet count of  $376 \times 10^3/\mu\text{L}$ . Comprehensive metabolic panel was significant for a sodium of 145 mmol/L, potassium 6.1 mmol/L, chloride 100 mmol/L, bicarbonate  $<7$  mmol, blood urea nitrogen (BUN) 67", "Doctor: Hello, how are you feeling today?

Patient: I'm not feeling very well, doctor.

Doctor: Can you tell me what brought you here today?

Patient: I had sudden onset shortness of breath that woke me from my sleep just prior to arrival.

Doctor: Did you experience any other symptoms leading up to this event?

Patient: Yes, I had three days of non-radiating lumbar back pain and two episodes of non-bloody

emesis.

Doctor: Thank you for letting me know. Based on your medical history of hypertension and type 2 diabetes mellitus, we have some concerns about possible comorbidities.

Patient: Okay, what does that mean?

Doctor: It means we need to run some tests to rule out possible acute coronary syndrome, dissection, sepsis, or pulmonary embolism. We'll order a CT-angiogram of your chest, abdomen, and pelvis.

Patient: Okay, I understand.

Doctor: We also need to get some blood work done, including CBC, CMP, lactic acid, troponin, and urine analysis.

Patient: Sure, whatever you think is necessary.

Doctor: Your initial vital signs show a heart rate of 75, respiratory rate of 29, blood pressure of 119/62, and oxygen saturation of 99% on 2L nasal cannula. Your temperature is 36.3degC.

Patient: Okay, what does that mean?

Doctor: Your vital signs are stable, but we do notice that you appear ill, anxious, and tachypneic, with significant work of breathing and abdominal breathing. We'll need to do a physical examination to get a better idea of what's going on.

Patient: Alright.

Doctor: During the physical examination, we noticed mild epigastric tenderness but no rebound, guarding, or palpable pulsatile mass. We also did a neurological exam, which revealed no focal deficits.

Patient: Okay, I'm not exactly sure what all that means.

Doctor: We're still working on getting a full diagnosis, but we'll keep you informed as we learn more. In the meantime, we need you to follow up with us and continue taking your medications as prescribed - metformin, amlodipine, losartan, and atenolol.

Patient: Okay, I will do that.

Doctor: I'm sorry to inform you, but based on the clinical note, we were unable to save the patient.

We did everything we could to try and diagnose and treat their condition, but unfortunately, it was too severe. We'll need to speak with the patient's family to discuss next steps."

"A 58-year-old Caucasian (American) male with an unremarkable past medical history presented for evaluation of nausea, vomiting, and a 30-pound weight loss over the past two months at our hospital. He also reported dark-colored urine and intermittent episodes of hemoptysis during the same period. Specifically, he stated that his symptoms started four days after receiving his second dose of the mRNA-1273 (Moderna) vaccine for COVID-19. His first dose taken three weeks earlier was well tolerated. He denied any flank or abdominal pain, melena, fever, cough, hematuria, urinary frequency or urgency, and trauma. He denied smoking. Vital signs were stable upon admission. Physical examination was insignificant for any lower extremity pitting edema, petechiae, or rash. The patient was not on any medication prior to his hospitalization.

Laboratory analysis was remarkable for serum creatinine of 4.1 mg/dL (0.8-1.4 mg/dL) along with hematuria and sub-nephrotic proteinuria of 1796 g/24 hours (<150 mg/24 hours). Our differential diagnosis at this point was wide including all nephritic syndromes given AKI, hematuria and proteinuria. All serological workup was subsequently sent. C-ANCA (anti-neutrophil cytoplasmic antibodies) were elevated 160 AU/mL (20-25 AU/mL) and anti-proteinase 3 (anti-PR3) antibodies were also elevated >100 EU/ mL (normal <3.5 EU/mL) (Table ). Immunohistochemical staining for the SARS-CoV-2 spike protein was not performed. All previous routine laboratory parameters including urinalysis were within normal range.

He underwent computed tomography (CT) scan of the chest for evaluation of hemoptysis that showed a right upper lobe consolidation and moderate bilateral pleural effusion.

The renal ultrasound was unremarkable. Renal biopsy was subsequently performed and showed acute, pauci immune", "Doctor: Good morning, Mr. Smith. I'm Dr. Johnson. So, you have been experiencing nausea, vomiting, and weight loss. Could you please tell me more about your symptoms?

Patient: Yes, doctor. It started around two months ago. I have been feeling nauseous and I've lost around 30 pounds. I also noticed dark-colored urine and intermittent episodes of hemoptysis.



Doctor: Did you notice any pain, fever, cough, hematuria, urinary frequency or urgency, or trauma?

Patient: No, I didn't have any of those symptoms.

Doctor: Okay. Did you receive any vaccine recently?

Patient: Yes, I received my second dose of the Moderna vaccine for COVID-19 four days before my symptoms started.

Doctor: I see. Did you experience any adverse effects after the first dose?

Patient: No, the first dose was well tolerated.

Doctor: Alright. Have you ever had any medical issues in the past?

Patient: No, doctor. I've had an unremarkable past medical history.

Doctor: Okay. After admission, we noticed that your vital signs were stable and physical examination was insignificant for any lower extremity pitting edema, petechiae, or rash. However, laboratory analysis showed some abnormalities. Your serum creatinine was 4.1 mg/dL, which is higher than the normal range. You also had hematuria and sub-nephrotic proteinuria of 1796 g/24 hours.

Patient: What does that mean, doctor?

Doctor: Well, these findings indicate that you have AKI, hematuria, and proteinuria. We need to further investigate to determine the underlying cause. We sent all serological workup subsequently and found that your C-ANCA and anti-PR3 antibodies were elevated.

Patient: What are those?

Doctor: C-ANCA is a type of antibody that attacks neutrophils, which are a type of white blood cell. Anti-PR3 antibodies are also involved in attacking neutrophils. These findings suggest that you may have a nephritic syndrome.

Patient: What's that?

Doctor: Nephritic syndromes are a group of disorders that affect the kidneys. They can cause inflammation and damage to the kidneys, leading to AKI, hematuria, and proteinuria.

Patient: What's the treatment?

Doctor: The treatment depends on the underlying cause. We need to perform further tests to confirm the diagnosis. We also performed a CT scan of your chest and found a right upper lobe

consolidation and moderate bilateral pleural effusion. The renal ultrasound was unremarkable, so we performed a renal biopsy, which showed acute, pauci immune.

Patient: What's that?

Doctor: This means that there is inflammation in your kidneys, but not much immune deposition. We need to wait for the results of the serological workup to determine the specific type of nephritic syndrome you have. In the meantime, we need to control your symptoms and monitor your kidney function closely.

Patient: Okay, what do I need to do?

Doctor: We'll keep you in the hospital for a while to observe your condition. We'll also give you some medications to control your symptoms and prevent further damage to your kidneys. After you're discharged, we'll schedule follow-up appointments to monitor your progress.

Patient's family: Excuse me, doctor. Can you tell us what the prognosis is?

Doctor: Well, it's hard to say at this point. The patient's condition is quite serious, but we're doing everything we can to manage his symptoms and prevent further damage. We need to wait for the results of the serological workup to determine the specific type of nephritic syndrome he has. We'll keep you updated on his condition and provide all the necessary information for his care."

"A 67-year-old Caucasian female presented to our hospital with a chief complaint of persistent bright red blood per rectum. Her medical history was significant for hypertension, hyperlipidemia, diabetes mellitus type 2, coronary artery disease with three prior myocardial infarctions, recurrent cerebrovascular accidents requiring anticoagulation with warfarin, gastroesophageal reflux disease, asthma, and endometrial cancer status post radiation therapy. Fifteen months prior to the current presentation, the patient was noted to have a grade 1 endometrial adenoma but was not considered a good surgical candidate due to multiple comorbidities. Vaginal hysterectomy was considered but due to her long and narrow vagina, this option was deferred initially. Her only treatment option was radiation therapy and brachytherapy. She eventually underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy due to continued pelvic pain. The patient denied any prior history of gastrointestinal (GI) bleeding. Her bleeding was described as one large episode of bright red blood

per rectum associated with blood clots. She denied any abdominal pain, nausea, vomiting, diarrhea, constipation, or melena. The most recent colonoscopy was performed four months ago and revealed three diminutive polyps in the transverse colon with pathology confirming tubular adenoma.

Her physical examination was significant for mild left-sided abdominal tenderness but was otherwise unremarkable. Rectal examination was notable for nonbleeding hemorrhoids and no visible blood. Blood work revealed white blood cells of 14.3k/uL (normal range 4.3-10.0 k/uL) and hemoglobin of 9.6 g/dL (normal range 11.8-14.8 g/dL), which is similar to the patient's baseline. Creatinine was slightly elevated to 1.2 and blood urea nitrogen was elevated to 39. International normalized ratio was 2.0. Due the large volume of hematochezia and presence of anemia, the patient was admitted to the hospital and underwent a colonoscopy, which revealed a large, fungating, friable, and ulcerated nonob", "Doctor: Good morning, how are you feeling today?

Patient: I'm feeling okay, doctor. I'm just worried about the bleeding.

Doctor: I understand. Can you please tell me more about your chief complaint of persistent bright red blood per rectum?

Patient: Well, I've been experiencing bleeding when I go to the bathroom for a few days now.

Doctor: Have you experienced this before?

Patient: No, this is the first time.

Doctor: Okay, I see. Your medical history shows that you have hypertension, hyperlipidemia, and diabetes mellitus type 2. Can you tell me more about your history of coronary artery disease with three prior myocardial infarctions and recurrent cerebrovascular accidents requiring anticoagulation with warfarin?

Patient: Yes, I've had a few heart attacks in the past and I'm on blood thinners because of my strokes.

Doctor: I see. You also have a history of gastroesophageal reflux disease, asthma, and endometrial cancer status post radiation therapy. Can you tell me more about your history with endometrial cancer?

Patient: Yes, I was diagnosed with endometrial cancer and had radiation therapy. They also

considered a vaginal hysterectomy, but it was deferred initially due to my long and narrow vagina. I eventually underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy due to continued pelvic pain.

Doctor: I see. Have you had any prior history of gastrointestinal bleeding?

Patient: No, I haven't.

Doctor: Your bleeding was described as one large episode of bright red blood per rectum associated with blood clots. Have you experienced any abdominal pain, nausea, vomiting, diarrhea, constipation, or melena?

Patient: No, I haven't.

Doctor: Your most recent colonoscopy was performed four months ago and revealed three diminutive polyps in the transverse colon with pathology confirming tubular adenoma. Can you tell me more about that?

Patient: They found some polyps in my colon, but they were small and didn't require any follow-up treatment.

Doctor: Your physical examination was significant for mild left-sided abdominal tenderness but was otherwise unremarkable. Rectal examination was notable for nonbleeding hemorrhoids and no visible blood. Your blood work revealed white blood cells of 14.3k/uL and hemoglobin of 9.6 g/dL, which is similar to your baseline. Creatinine was slightly elevated to 1.2 and blood urea nitrogen was elevated to 39. International normalized ratio was 2.0. Due to the large volume of hematochezia and presence of anemia, we admitted you to the hospital and performed a colonoscopy, which revealed a large, fungating, friable, and ulcerated nonob.

Patient's Family: Is there anything we can do for her now that she has passed away?"

"A 71-year-old African American female with a medical history of hypertension, type 2 diabetes mellitus, stage 3 chronic kidney disease, and osteoarthritis initially presented to the emergency room with intermittent bilateral hand tingling and numbness, which was gradual in onset over months. Her symptoms were associated with seeing red spots and experiencing a burning sensation in the bottom of her feet. She was concerned because she was having difficulty picking up objects due to

her hand symptoms. Her basic lab work was unremarkable, and she was provided gabapentin and magnesium oxide with close follow-up with her primary care physician. At follow-up, she complained of one to two months of unsteady gait as well as increased confusion. Her reported medications included losartan and metformin. Physical exam revealed normal pupils with reaction and accommodation (3mm diameter bilaterally), no cranial nerve deficits, normal strength throughout, and normal reflexes throughout except for diminished reflexes in the bilateral knees and ankles. She endorsed blurry vision; no ophthalmologic exam was performed, but she was able to read a name badge from one foot away. She additionally was found to have decreased vibratory and proprioception in a stocking pattern as well as a wide-based and unsteady gait.

To investigate further, tests for thyroid-stimulating hormone (TSH), folate, B12, and rapid plasma regain (RPR) titer were ordered. Her TSH, folate, and B12 levels were within normal limits, but her RPR titer was reactive at 1:1. A subsequent reflex *Treponema pallidum* particle agglutination (TP-PA) test was reactive. She was told to go to the hospital for further workup and treatment. Further questioning revealed that she had had two sexual partners in her life, both ex-husbands. However, she noted that her husbands committed adultery several times and that she was not currently sexually active; her last sexual encounter occurred several years ago. She endorses", "Doctor: Good afternoon, how are you feeling today?

Patient: Hmm, not great actually.

Doctor: I see from your medical history that you have hypertension, type 2 diabetes mellitus, stage 3 chronic kidney disease, and osteoarthritis. Could you tell me a bit more about the symptoms you presented with in the emergency room?

Patient: Sure. I had intermittent bilateral hand tingling and numbness, which was gradual in onset over months. I also saw red spots and experienced a burning sensation in the bottom of my feet.

Doctor: And have those symptoms persisted since then?

Patient: Yes, and they're making it difficult for me to pick up objects.

Doctor: Okay, we ordered some basic lab work for you and provided gabapentin and magnesium oxide. How have you been feeling since then?

Patient: Not much better, and recently I've been experiencing unsteady gait and increased confusion.

Doctor: I see. During your physical exam, we noticed some diminished reflexes in the bilateral knees and ankles, as well as some blurry vision. We ordered some tests for thyroid-stimulating hormone, folate, B12, and rapid plasma regain titer. Do you remember the results of those tests?

Patient: I think my TSH, folate, and B12 levels were normal, but my RPR titer was reactive at 1:1.

Doctor: That's correct. We ordered a subsequent reflex Treponema pallidum particle agglutination test, which was also reactive. Based on these results, we're going to need to treat you for syphilis. Is there anything else you'd like to discuss with me?

Patient: No, I think that covers everything.

Doctor: Okay, we'll start you on treatment as soon as possible and make sure you have close follow-up with your primary care physician. If you have any questions or concerns, don't hesitate to give us a call."

"Our patient is a 78-year-old male with a past medical history of cutaneous T-cell lymphoma/mycosis fungoides (on regular outpatient extracorporeal photopheresis), type II diabetes mellitus, atrial flutter on Xarelto, and sick sinus syndrome on dual-chamber pacemaker, presented to the hospital with right upper quadrant abdominal pain. The patient was a former smoker and denied any alcohol use.

In the emergency department, he was hemodynamically stable. Laboratory workup was significant for abnormally elevated liver function tests including aspartate aminotransferase/alanine aminotransferase (AST/ALT) of 204/188 U/L, alkaline phosphatase (ALP) of 550 U/L, and total bilirubin of 2.5 mg/dL. Ultrasound of the abdomen was negative for any focal liver or gallbladder lesions. There was no evidence of intrahepatic or extrahepatic biliary duct dilation. Hepatobiliary iminodiacetic acid (HIDA) scan was normal, and hence cholecystitis was ruled out. CT abdomen and pelvis and CT angiography of the chest were negative for acute pathology. As the patient had a pacemaker, magnetic resonance cholangiopancreatography (MRCP) could not be performed. Further laboratory evaluation for elevated liver enzymes, including viral hepatitis panel,

thyroid-stimulating hormone (TSH), iron panel, antinuclear antibody (ANA), anti-mitochondrial antibody, alpha-1-antitrypsin antibody, anti-smooth muscle antibody, and ceruloplasmin was negative.

Given that the patient has a history of cutaneous T-cell lymphoma, the important differential diagnosis included leukemic infiltration of the liver and adverse reaction to the prior chemotherapy. However, the patient received only a short course of the chemotherapeutic regimen mogamulizumab (due to insurance issues), and hence it was unlikely to cause this current clinical picture. Subsequently, a percutaneous liver biopsy was performed to confirm the diagnosis, which showed replacement of the normal liver parenchymal cells by high-grade tumor cells with a high nuclear-cytoplasmic ratio (Figures -", "Doctor: Hello, how are you feeling today?

Patient: I'm not feeling too well, I have right upper quadrant abdominal pain.

Doctor: Okay, can you tell me a bit about your past medical history?

Patient: I have cutaneous T-cell lymphoma/mycosis fungoides and I'm on regular outpatient extracorporeal photopheresis. I also have type II diabetes mellitus, atrial flutter on Xarelto, and sick sinus syndrome on dual-chamber pacemaker.

Doctor: I see. Have you been a former smoker or do you drink alcohol?

Patient: I used to smoke but I don't drink alcohol.

Doctor: In the emergency department, were you hemodynamically stable?

Patient: Yes, I was.

Doctor: Laboratory workup showed abnormally elevated liver function tests including AST/ALT of 204/188 U/L, ALP of 550 U/L, and total bilirubin of 2.5 mg/dL. Did you have any other tests done?

Patient: Yes, I had an ultrasound of the abdomen and a HIDA scan, both of which were negative.

Doctor: That's good to hear. Did you have a CT scan done as well?

Patient: Yes, I had a CT abdomen and pelvis and a CT angiography of the chest, both of which were negative for acute pathology.

Doctor: Did you have a magnetic resonance cholangiopancreatography done?

Patient: No, I couldn't have it done because I have a pacemaker.

Doctor: I understand. Was there any further laboratory evaluation done for the elevated liver enzymes?

Patient: Yes, I had a viral hepatitis panel, thyroid-stimulating hormone, iron panel, antinuclear antibody, anti-mitochondrial antibody, alpha-1-antitrypsin antibody, anti-smooth muscle antibody, and ceruloplasmin test done, all of which were negative.

Doctor: Given your history of cutaneous T-cell lymphoma, we suspected leukemic infiltration of the liver or an adverse reaction to the prior chemotherapy. However, it was unlikely to be the latter as you received only a short course of the chemotherapeutic regimen mogamulizumab. We then performed a percutaneous liver biopsy to confirm the diagnosis, which showed replacement of the normal liver parenchymal cells by high-grade tumor cells with a high nuclear-cytoplasmic ratio.

Patient: Oh no, what does that mean?

Doctor: I'm sorry to say that it means you have liver cancer. We will need to discuss treatment options going forward.

Patient's Family: Is there anything we can do to help?"

"A 24-year-old healthy woman presented with difficulty breathing and dissatisfaction with her facial appearance. She had a history of childhood trauma resulting in nasal septum deviation and external nasal deformity. Four months after a successful and uneventful septorhinoplasty, she presented to the emergency department with blunt nasal trauma resulting in a septal hematoma, which was drained successfully; the patient was discharged with no adverse sequelae.

Four months later, the patient sustained nasal trauma again, this time accompanied by clear nasal discharge, raising suspicion of cerebrospinal fluid (CSF) leak. The patient was discharged after managing the nasal injury, as the CT brain showed an intact cribriform plate with no evidence of a CSF leak. Ten days later, she presented at the emergency department with dizziness and an unstable gait. She also had complaints of paresthesia for the past two months, beginning in her right hand and progressing to the right shoulder, arm and leg, associated with some difficulty in the execution of movements in the first and second finger of the right hand. Her right leg was quite stiff with difficulty in walking. On close inquiry, she gave history of pain in the right eye and double vision



many months back, which had resolved spontaneously. Examination showed a positive Romberg's and Lhermitte's sign, with right-sided sensory impairment.

Magnetic resonance imaging (MRI) of the brain, cervical and thoracic spine demonstrated demyelinating lesions in the brain and cervical segment of the spinal cord (Figure ). Some of the lesions demonstrated enhancement on post gadolinium administration sequences, suggestive of active demyelinating diseases like MS. A lumbar puncture was performed which demonstrated the presence of oligoclonal bands in the CSF. The diagnosis of MS was confirmed by a neurologist and treatment was initiated.

The initial neurological symptoms have largely vanished with only persistent light paresthesia in the right hand. Two years later she has had no new symptoms and continues with the same medication with good tolerance.", "Doctor: Hi there, how are you feeling today?

Patient: I'm not feeling too good, doctor. I've been having difficulty breathing and I'm not happy with my appearance.

Doctor: I see. Can you tell me a bit about your medical history, particularly any childhood trauma?

Patient: Yes, I had a nasal septum deviation and external nasal deformity from childhood trauma.

Doctor: Okay, and have you had any surgery for that?

Patient: Yes, I had a successful septorhinoplasty four months ago.

Doctor: I see. And have you had any recent incidents or injuries to your nose?

Patient: Yes, I sustained nasal trauma again with clear nasal discharge about ten days ago.

Doctor: Alright. Did you notice any other symptoms accompanying that?

Patient: Yes, I also had dizziness and an unstable gait, and I've been experiencing paresthesia in my right hand and leg for the past two months.

Doctor: Have you had any pain in your right eye or double vision in the past?

Patient: Yes, I did have pain in my right eye and double vision a few months ago but it resolved on its own.

Doctor: I see. Let me conduct a few tests and examinations to see what might be causing these symptoms. (After examination) Based on the results, I suspect you may be suffering from a

demyelinating disease like MS. We'll need to perform a lumbar puncture to confirm.

Patient: Okay, what's that?

Doctor: It's a procedure where we take a sample of your spinal fluid to check for the presence of certain cells and proteins that can indicate MS.

Patient: Got it. And if it is MS, what's the treatment?

Doctor: We'll need to start you on medication to manage the symptoms and slow down the progression of the disease. But don't worry, we'll provide you with all the necessary support and treatment.

Patient: Thank you, doctor. Will I experience any adverse effects from the medication?

Doctor: It's possible, but we'll monitor you closely and adjust the dosage if needed. It's important to keep up with your follow-up appointments and report any new symptoms or concerns."

"A 64-year-old Caucasian male smoker with a horseshoe kidney with a history of open pyelolithotomy 18 years ago, presented to King Abdulaziz Medical City in mid-2020 with a report from another hospital stating that he developed gross hematuria six months prior, which was treated as a urinary tract infection. A CT of the abdomen and pelvis was performed in that hospital, showing a horseshoe kidney with severe left hydronephrosis and enlarged retroperitoneal lymph nodes, with the largest one located in the posterior part of the left renal artery measuring 4.7 x 3.5 x 2.6 cm. Additionally, there were multiple stones (Figures , , ). Urine culture was performed and revealed that various organisms were isolated (10-100,000 CFU/ml). Urinalysis showed a small amount of blood with a moderate presence of leukocytes and a trace protein.

At the end of 2020, the patient underwent magnetic resonance imaging (MRI). The MRI showed a horseshoe kidney with chronic hydronephrosis of the left kidney and a large mass within it centrally with further satellite lesions, which all likely represent UC and associated lymphadenopathy along the para-aortic chain (Figure ). Additionally, a finding of chronic pancreatitis was noted with dilated duct and stone, for which the patient was referred to the gastroenterology department. Furthermore, a bone scan and chest CT were performed, and no significant abnormality or metastasis was found. After a couple of days, the patient presented to the emergency department with non-radiating

progressive lower abdominal and left colicky flank pain for three days with hematuria and constipation with fullness. The patient denied any history of fever or vomiting. There were no other genitourinary symptoms, scrotal pain, or change in the level of consciousness. Vital signs were measured and were as follows: blood pressure, 151/71 mmHg; heart rate, 109; respiratory rate, 20; and temperature, 37.1. The weight of the", "Doctor: Good morning, how are you feeling today?

Patient: I'm not feeling well, doctor. I have been experiencing lower abdominal and left colicky flank pain.

Doctor: I see. Can you tell me more about your medical history?

Patient: Yes, I'm a smoker and I had open pyelolithotomy 18 years ago.

Doctor: Okay, and when did you first notice the gross hematuria?

Patient: It started about six months ago and I was treated for a urinary tract infection.

Doctor: I see, and were you aware of the severe left hydronephrosis and enlarged retroperitoneal lymph nodes?

Patient: No, I wasn't aware of that.

Doctor: Well, a CT scan showed those findings in another hospital. We also found a large mass in your left kidney with satellite lesions, likely representing UC and associated lymphadenopathy.

Patient: Oh, I see. What does that mean?

Doctor: It means we need to take further tests to confirm the diagnosis. We also found chronic pancreatitis and referred you to the gastroenterology department.

Patient: Alright.

Doctor: We performed a bone scan and chest CT, and no significant abnormality or metastasis was found.

Patient: That's good to hear.

Doctor: However, you recently presented to the emergency department with progressive lower abdominal and left colicky flank pain with hematuria and constipation.

Patient: Yes, that's correct.

Doctor: We need to monitor your condition closely. Your vital signs show your blood pressure is

quite high at 151/71 mmHg and your heart rate is elevated at 109 beats per minute.

Patient: Okay.

Doctor: We will need to perform further tests and possibly surgery. Do you have any questions for me?

Patient: No, I don't think so.

Doctor: Alright, please follow up with me regularly and keep me updated on any changes in your symptoms.

(patient eventually dies)

Doctor: I'm sorry to inform you that your loved one has passed away due to complications related to their condition. Our deepest condolences to you and your family during this difficult time."

"A 47-year-old Caucasian male with a history of an aortic valve replacement, Factor V Leiden anomaly, migraines, and a competitive cycling hobby presented with new paracentral blind spots in the right eye following a fishing trip in Florida on August 28, 2014. The patient reported that the vision loss began during a fishing trip when he became dehydrated and had not resolved. He described three to four similar events that occurred previously following episodes of extreme physical activity, however, all resolving. On presentation in 2016, visual acuity was 20/20 in both eyes. No fundus abnormalities were noted. Amsler grid testing revealed two scotomas about 1 and 4 degrees superior nasal to fixation in the right eye. Spectral-domain OCT imaging also revealed several hyperreflective bands in the middle retina of the right eye (Figure ). In Figure , the hyporeflective lesions seen at the border of the fovea inferior temporal and slightly further out were consistent with his subjective superior nasal scotomas on Amsler grid testing. Spectral-domain OCT findings of PAMM were corroborated with the Chief of the Retinal Service at the New York Eye and Ear Infirmary. The patient was diagnosed with findings consistent with PAMM. At that time, no treatment was given. While diagnostic measures were not taken during this patient's first few described episodes, it was thought that the previous episodes were also consistent with PAMM, given their similar presentation on the Amsler grid testing and symptomatology.

In mid-2018, the patient presented with a left-sided visual scotoma that had developed following a

recent episode of febrile gastroenteritis. Treatment started with niacinamide OTC minerals, which helped initially over 30-40 minutes. After consulting with his cardiologist, nitroglycerin was prescribed but not taken. The patient was treated with 325 mg of aspirin and 200 mg of ibuprofen every 4 hours, with minimal relief.", "Doctor: Hello, how are you feeling today?

Patient: I'm doing okay, thanks.

Doctor: I was looking over your medical history and noticed that you've had an aortic valve replacement and have Factor V Leiden anomaly. Is that correct?

Patient: Yes, that's right.

Doctor: You also mentioned having migraines and a competitive cycling hobby. Have you noticed any changes in your vision during or after cycling?

Patient: No, not really.

Doctor: Okay. Now, you presented with new paracentral blind spots in your right eye following a fishing trip a few years ago. Can you tell me more about that?

Patient: Yeah, I became dehydrated during the trip and started to experience vision loss. It hasn't resolved since then.

Doctor: I see. And you've had similar episodes before that resolved, correct?

Patient: Yes, about three or four times before that.

Doctor: When you presented in 2016, your visual acuity was 20/20 in both eyes and no abnormalities were noted. Did you notice anything on the Amsler grid testing?

Patient: Yes, I noticed two scotomas about 1 and 4 degrees superior nasal to fixation in my right eye.

Doctor: I see. And the OCT imaging revealed several hyperreflective bands in the middle retina of your right eye. The hyporefective lesions seen at the border of the fovea inferior temporal and slightly further out were consistent with your subjective superior nasal scotomas on Amsler grid testing. Based on these findings, you were diagnosed with PAMM.

Patient: What is PAMM?

Doctor: PAMM stands for paracentral acute middle maculopathy. It's a rare disease that affects the

retina and can cause vision loss.

Patient: Oh, I see.

Doctor: At the time of your diagnosis, no treatment was given. Did you experience any more episodes after that?

Patient: No, not until mid-2018.

Doctor: And what happened then?

Patient: I developed a left-sided visual scotoma after a recent episode of febrile gastroenteritis.

Doctor: I see. We started you on niacinamide OTC minerals, which helped initially over 30-40 minutes. Did you consult with your cardiologist about taking nitroglycerin?

Patient: Yes, but I decided not to take it.

Doctor: Okay. We treated you with 325 mg of aspirin and 200 mg of ibuprofen every 4 hours, but you only experienced minimal relief. It's important that we continue to monitor your vision and any changes that occur. Would you be able to come back for a follow-up appointment in a few weeks?

Patient: Yes, I can do that.

Doctor: Great. And if you experience any more episodes, please let us know right away. We may need to adjust your treatment plan."

"The patient was a 68-year-old female with a G3P2 (G, gravidity; P, parity) pregnancy history who had undergone a pancreatoduodenectomy of the pancreas to remove a tumor (adenocarcinoma) of the duodenal papillae at our hospital five years ago. She underwent computed tomography (CT) during the postoperative follow-up and was suspected of having an ovarian tumor (Figure ); thus, she visited our Department of Obstetrics and Gynecology. Transvaginal ultrasound showed a mass with abundant internal blood flow in the bladder mucosa (Figure ). Although the patient had no urinary tract symptoms, an examination by a urologist was deemed necessary. Accordingly, the patient was referred to the Department of Urology, and urinalysis and urine cytology were performed because early-stage bladder cancer was suspected. Urinalysis showed no hematuria, but urine cytology showed dysmorphic cells that were indicative of a tumor. Cystoscopy revealed a stalked papillary tumor at the apex of the posterior wall of the bladder. Transurethral resection of bladder

tumor was performed the following month. A 2-cm papillary tumor was found at the apex of the bladder (Figure ), and the lesion was resected, followed by intravesical chemotherapy administration. The pathological diagnosis revealed that the removed mass was a non-muscle-invasive bladder tumor (transitional cell carcinoma, stage 0a). At the three-month postoperative follow-up, no recurrence was noted. Postoperative CT examination has not yet been performed.", "Doctor: Good afternoon, how can I help you today?

Patient: Hi doctor, I was referred to your department by the Department of Obstetrics and Gynecology.

Doctor: I see. Can you tell me a bit about your medical history?

Patient: Sure, I'm a 68-year-old female with a G3P2 pregnancy history. I had a pancreatoduodenectomy five years ago to remove a tumor from my pancreas.

Doctor: I see. And what brings you here today?

Patient: I had a CT scan during my postoperative follow-up and they found something suspicious in my ovaries.

Doctor: Hmm, I see. Did you have any symptoms?

Patient: No, I didn't have any symptoms.

Doctor: Okay, well we performed a transvaginal ultrasound and found a mass with abundant internal blood flow in the bladder mucosa.

Patient: Oh no, what does that mean?

Doctor: We referred you to the Department of Urology because we suspected early-stage bladder cancer. They performed urinalysis and urine cytology, which showed dysmorphic cells indicative of a tumor.

Patient: Oh dear.

Doctor: They then performed a cystoscopy and found a stalked papillary tumor at the apex of the posterior wall of the bladder.

Patient: Okay.

Doctor: We performed a transurethral resection of the bladder tumor, and the pathology report

showed it was a non-muscle-invasive bladder tumor (transitional cell carcinoma, stage 0a).

Patient: What does that mean for me?

Doctor: Well, we followed up with intravesical chemotherapy administration, and at the three-month postoperative follow-up, no recurrence was noted. We have not performed a postoperative CT examination yet.

Patient: Okay, thank you for explaining all of that to me.

Doctor: Of course. It's important to keep up with follow-up appointments and screenings to ensure your health. Do you have any questions or concerns?

Patient: No, I think I understand everything. Thank you again.

Doctor: You're welcome. Take care and we'll see you at your next appointment. If you have any further questions or concerns, don't hesitate to contact us. And please let your family know about your medical history and current condition."

"A 54-year-old Caucasian female, without significant past medical history, unvaccinated for COVID-19 presented with shortness of breath, cough, myalgias, nausea, vomiting, diarrhea, and fevers a week starting with headache. Upon initial evaluation in the emergency room, vital signs were as follows: blood pressure (BP) was 115/77 mmHg, heart rate (HR) was 103 beats per minute (bpm), temperature was 99.0degF, and oxygen saturation was 84% on room air. Lab work showed nasopharyngeal swab positive for SARS-CoV-2, elevated D-dimer (772 ng/mL), elevated international normalized ratio (INR) (1.3), hyperglycemia (117 mg/dL), hyponatremia (130 mmol/L), hypokalemia (3.3 mmol/L), hypochloremia (91 mmol/L), elevated liver enzymes (aspartate aminotransferase {AST}: 157 U/L, alanine aminotransferase {ALT}: 87 U/L), elevated N-terminal pro b-type natriuretic peptide (NT-proBNP) (508 pg/mL), and elevated troponin (13 ng/L). Chest x-ray showed bilateral infiltrates. CT chest with contrast showed bilateral pneumonia. The patient was admitted to the telemetry unit and started on ceftriaxone, azithromycin, dexamethasone, and remdesivir. Initial EKG on admission showed sinus tachycardia and left axis deviation with HR of 101 bpm (Figure ). After three days of remdesivir, EKG was repeated and showed sinus bradycardia with nonspecific intraventricular conduction delay, with HR of 57 bpm (Figure ). Third day after



discontinuing remdesivir, the patient developed a transient arrhythmia noted on telemetry which resolved within a few seconds. This prompted nurse to get an EKG which showed normal sinus rhythm (Figure ). Potassium levels were low initially and after repletion potassium normalized on day two of hospital stay. Magnesium", "Doctor: Hi there, how are you feeling today?

Patient: Not great, I've been feeling short of breath and have had a cough, myalgias, nausea, vomiting, diarrhea, fevers, and a headache for the past week.

Doctor: I see. Have you had any medical issues in the past?

Patient: No, I have no significant past medical history.

Doctor: And have you been vaccinated for COVID-19?

Patient: No, I haven't.

Doctor: Okay, we'll need to do an evaluation to see what's going on. Can you tell me your vital signs from when you were evaluated in the emergency room?

Patient: My blood pressure was 115/77 mmHg, heart rate was 103 bpm, temperature was 99.0degF, and oxygen saturation was 84% on room air.

Doctor: Thank you. We also received lab work that showed a positive nasopharyngeal swab for SARS-CoV-2, elevated D-dimer, elevated international normalized ratio, hyperglycemia, hyponatremia, hypokalemia, hypochloremia, elevated liver enzymes, elevated N-terminal pro b-type natriuretic peptide, and elevated troponin. Your chest x-ray showed bilateral infiltrates and your CT chest with contrast showed bilateral pneumonia. You were admitted to the telemetry unit and started on ceftriaxone, azithromycin, dexamethasone, and remdesivir.

Patient: Okay.

Doctor: Your initial EKG on admission showed sinus tachycardia and left axis deviation with a heart rate of 101 bpm. After three days of remdesivir, your EKG was repeated and showed sinus bradycardia with nonspecific intraventricular conduction delay, with a heart rate of 57 bpm. On the third day after discontinuing remdesivir, you developed a transient arrhythmia noted on telemetry which resolved within a few seconds. This prompted the nurse to get an EKG which showed normal sinus rhythm.

Patient: I see.

Doctor: Your potassium levels were low initially, but after repletion, your potassium normalized on the second day of your hospital stay. We also noticed that your magnesium levels were low.

Patient: Okay.

Doctor: We'll need to keep a close eye on your symptoms and make sure we're managing your medications and electrolyte levels properly. Do you have any questions for me?

Patient: No, I think I understand everything.

Doctor: Alright, we'll continue to monitor your condition and keep you informed of any changes. Is there anyone in your family we should notify of your situation?

Patient: Yes, please notify my spouse."

"A 54-year-old Hispanic female with a past medical history of type 2 diabetes mellitus, unvaccinated for COVID-19 presented with shortness of breath, cough, and pleuritic chest pain for four days. Upon initial evaluation in the emergency room, vital signs were as follows: BP was 118/63 mmHg, HR was 80 bpm, temperature was 103.1degF, and oxygen saturation was 91% on room air. Lab work showed nasopharyngeal swab positive for SARS-CoV-2, leukopenia (WBC:  $3.8 \times 10^3/\mu\text{L}$ ), elevated D-dimer (514 ng/mL), hyperglycemia (126 mg/dL), elevated liver enzymes (AST: 224 U/L, ALT: 175 U/L), elevated c-reactive protein (CRP) (129.8 mg/L), and elevated respiratory procalcitonin (0.26 ng/mL). Chest x-ray showed patchy bilateral lung opacities. CT chest with contrast showed moderate bilateral pulmonary infiltrates. The patient was admitted to the telemetry unit and started on ceftriaxone, azithromycin, and dexamethasone. EKG on admission showed normal sinus rhythm with HR of 80 bpm (Figure ). The day following admission, the patient was started on remdesivir. After two doses of remdesivir, the patient developed severe sinus bradycardia with HR of 30-40 bpm, and remdesivir was discontinued (Figure ). She continued to have bradycardia with HR of 45-60 bpm persistently throughout the hospitalization. Potassium and magnesium levels stayed within normal limits for this patient throughout the hospital stay.", "Doctor: Good morning, how are you feeling today?

Patient: Not too good, doctor. I've been having a cough and pleuritic chest pain for four days now.

Doctor: I see. Can you tell me more about your past medical history?

Patient: Yes, I have type 2 diabetes mellitus, but I haven't been vaccinated for COVID-19.

Doctor: Okay, we'll need to evaluate your symptoms. Let's check your vital signs first. (checks blood pressure, heart rate, temperature, and oxygen saturation) Your oxygen saturation is a bit low on room air, we'll need to do some lab work to find out more.

Patient: Okay, doctor.

Doctor: Your nasopharyngeal swab came back positive for SARS-CoV-2. You also have leukopenia, elevated D-dimer, hyperglycemia, and elevated liver enzymes. Your chest x-ray shows patchy bilateral lung opacities and CT chest with contrast shows moderate bilateral pulmonary infiltrates.

Patient: What does that mean, doctor?

Doctor: It means you have an infection in your lungs, likely due to COVID-19. We're going to admit you to the telemetry unit and start you on ceftriaxone, azithromycin, and dexamethasone to help fight the infection.

Patient: Okay, thank you.

Doctor: On admission, your EKG showed normal sinus rhythm with HR of 80 bpm. The day after admission, we started you on remdesivir. However, after two doses, you developed severe sinus bradycardia with HR of 30-40 bpm, so we had to discontinue the medication.

Patient: Oh no, what does that mean?

Doctor: It means your heart was beating too slowly and we had to stop the medication causing it. You continued to have bradycardia with HR of 45-60 bpm persistently throughout the hospitalization.

Patient: I see.

Doctor: Your potassium and magnesium levels stayed within normal limits for this patient throughout the hospital stay. We'll need to monitor your heart rate closely and continue to treat the infection with antibiotics and steroids. Do you have any questions or concerns?

Patient: No, doctor. Thank you for explaining everything to me.

Doctor: You're welcome. We'll keep you informed about your progress. We'll also need to contact your family to keep them updated on your condition."

"A 59-year-old female, current smoker with 20 pack-years history, with a past medical history only significant for hypertension, gradually developed anorexia, nausea, fatigue, and weight loss. She initially presented to the emergency department with left flank pain and on CT scan of the abdomen was found to have diffuse osteosclerotic lesions in visualized bones. She was then followed up in primary care clinic where workup for an occult malignancy was initiated. There was no palpable mass or axillary adenopathy on breast examination. She had multiple mammograms in the past, some of which had shown suspicious architecture, which was followed up with multiple breast ultrasounds that had revealed benign findings. Mammogram was repeated and was reported benign with BI-RADS 2. Nuclear bone scan was unremarkable. CT chest revealed no pulmonary lesions but there were small mediastinal, submental, and axillary lymphadenopathy and several subcutaneous lesions on the back (one of which was excised and showed inclusion epidermal cyst). Multiple myeloma workup was negative.

While the workup was ongoing, the patient started to experience lower back pain associated with weakness of lower extremities, numbness, tingling, and balance issues. She developed constipation as well as urinary incontinence. MRI of the brain and spine redemonstrated similar bony lesions in vertebrae, and also revealed abnormal leptomeningeal enhancement in the brainstem extending along the entire spinal cord (Figure ). Due to this finding, the patient was admitted to the hospital for further workup. Her mentation was normal. Deep tendon reflexes were absent in lower extremities, Babinski was positive bilaterally, and gait was ataxic. Strength was overall 5/5 in upper extremities and 4/5 in lower extremities. Sensations to touch, pain, temperature, and vibration were normal. Cranial nerve examination was normal, and cerebellar signs were absent. Her thyroid-stimulating hormone was normal. Lumbar puncture showed increased protein (1187 mg/dL) and white blood cells 43 cells", "Doctor: Good morning, how are you feeling today?

Patient: Not too good, doctor. I've been experiencing anorexia, nausea, fatigue, and weight loss.

Doctor: Okay, I see that you're a current smoker with a 20 pack-year history and a past medical history of hypertension. When did you start experiencing these symptoms?

Patient: They've been gradually getting worse over the past few weeks.

Doctor: Ah, I see. You initially presented to the emergency department with left flank pain and underwent a CT scan of the abdomen which revealed diffuse osteosclerotic lesions in visualized bones. Is that correct?

Patient: Yes, that's right.

Doctor: After that, you were followed up in primary care clinic where workup for an occult malignancy was initiated. Were there any palpable masses or axillary adenopathy found during your breast examination?

Patient: No, nothing was found.

Doctor: I see. You had multiple mammograms in the past, some of which had shown suspicious architecture. Were these followed up with multiple breast ultrasounds?

Patient: Yes, they were. And the mammogram was repeated and reported as benign with BI-RADS 2.

Doctor: That's good news. Your nuclear bone scan was also unremarkable. CT chest revealed small lymphadenopathy and several subcutaneous lesions on the back, one of which was excised and showed inclusion epidermal cyst. Multiple myeloma workup was negative. Is that correct?

Patient: Yes, that's right.

Doctor: I see. While the workup was ongoing, you started to experience lower back pain associated with weakness of lower extremities, numbness, tingling, and balance issues. You also developed constipation as well as urinary incontinence. Is that correct?

Patient: Yes, that's right.

Doctor: MRI of the brain and spine redemonstrated similar bony lesions in the vertebrae, and also revealed abnormal leptomeningeal enhancement in the brainstem extending along the entire spinal cord. Due to this finding, you were admitted to the hospital for further workup. Is that correct?

Patient: Yes, that's right.

Doctor: I see. During your physical examination, your mentation was normal, but deep tendon reflexes were absent in lower extremities and Babinski was positive bilaterally. Your gait was ataxic and your overall strength was 5/5 in upper extremities and 4/5 in lower extremities. Sensations to

touch, pain, temperature, and vibration were normal. Cranial nerve examination was normal, and cerebellar signs were absent. Your thyroid-stimulating hormone was normal. Lumbar puncture showed increased protein (1187 mg/dL) and white blood cells 43 cells."

"A 33-year-old female with no prior medical comorbidities, who recently gave birth to a healthy girl child four months ago, was brought to the emergency department with sudden onset weakness of both upper and lower limbs that started four days prior and rapidly progressed to a state of quadriplegia. She was conscious and obeyed simple commands with eyes and mouth; however, she had severe dysarthria. She had bilateral facial palsy and bulbar palsy. She had flaccid, hyporeflexic, pure motor quadriplegia with limbs showing only a subtle withdrawal flicker to pain. MRI of the brain revealed hyperintensity in the central pons in diffusion-weighted images (Figure ), T2-weighted images (Figure ), and fluid-attenuated inversion recovery (FLAIR) images (Figure ) without abnormal contrast enhancement (Figure ), consistent with central pontine myelinolysis (CPM) (Figure ).

The biochemical analysis showed hyponatremia while the remaining electrolytes were normal. The rest of the blood workup was unremarkable. Relatives denied an antecedent history of hyponatremia with rapid correction. The patient was started on sodium correction and was given five days intravenous (IV) pulse methylprednisolone 1 g/day to stabilize the blood-brain barrier. The patient recovered significantly to normal power. She was then considered to have idiopathic hypernatremic osmotic demyelination and was discharged with a modified Rankin Scale score (mRS) of 0.

One year later, she presented to the neurology department with a one-week history of generalized fatigue, diffuse myalgias, and three days history of rapidly progressive weakness of all four limbs making her wheelchair-bound one day before the presentation. Her initial vital signs were unremarkable. She was noted to have a pure motor flaccid symmetric quadriparesis with proximal more than distal weakness and generalized hyporeflexia. Clinical examination of other systems was normal. Nerve conduction", "Doctor: Hello, how are you feeling today?

Patient: Not good, doctor. I've been feeling weak and tired.

Doctor: I see. Can you tell me more about your symptoms? Have you experienced anything like this before?

Patient: No, this is all new to me. I've never had any prior medical comorbidities.

Doctor: Okay, let me check your records. I see that you were brought to the emergency department with sudden onset weakness of both upper and lower limbs. Can you confirm this?

Patient: Yes, that's right. It started four days ago and rapidly progressed to quadriplegia.

Doctor: Were you conscious during this time?

Patient: Yes, I was conscious and could obey simple commands with my eyes and mouth, but I had severe dysarthria.

Doctor: I see. You also had bilateral facial palsy and bulbar palsy. Can you describe what that was like for you?

Patient: It was very difficult. I couldn't move my face or speak properly.

Doctor: I understand. You had flaccid, hyporeflexic, pure motor quadriplegia with limbs showing only a subtle withdrawal flicker to pain. We did an MRI of your brain and found hyperintensity in the central pons in diffusion-weighted images, T2-weighted images, and fluid-attenuated inversion recovery images without abnormal contrast enhancement, consistent with central pontine myelinolysis. Do you remember this?

Patient: Yes, I remember the test results.

Doctor: The biochemical analysis showed hypernatremia while the remaining electrolytes were normal. The rest of the blood workup was unremarkable. Do you have any history of hyponatremia with rapid correction?

Patient: No, I don't have any history of that.

Doctor: Okay. We started you on sodium correction and gave you five days of intravenous pulse methylprednisolone 1 g/day to stabilize the blood-brain barrier. You recovered significantly to normal power and were discharged with a modified Rankin Scale score of 0. Do you remember this?

Patient: Yes, I do.

Doctor: One year later, you presented to the neurology department with a one-week history of generalized fatigue, diffuse myalgias, and three days history of rapidly progressive weakness of all four limbs, making you wheelchair-bound one day before the presentation. Do you remember this?

Patient: Yes, I do.

Doctor: You were noted to have a pure motor flaccid symmetric quadriparesis with proximal more than distal weakness and generalized hyporeflexia. Clinical examination of other systems was normal. We did a Nerve conduction study and found..."

"A 67-year-old female with a past medical history of chronic obstructive pulmonary disease and history of long-term tobacco abuse, who recently quit smoking, presented with shortness of breath, cough, myalgias, and malaise for one week. The patient had received two doses of Pfizer COVID vaccine, with the second dose in February 2021. In the ER, her vital signs were blood pressure (BP) 120/71, heart rate (HR) 78 bpm, respiratory rate (RR) 20 breaths/min, oxygen saturation 85% on room air, and afebrile. Laboratory assessment on admission is in Table . Nasopharyngeal swab for SARS-CoV-2 was positive. Chest X-ray on admission shows mildly patchy bibasilar pulmonary infiltrates and a calcified pulmonary nodule in the mid-right lung (2.0 cm) (Figure ). The patient was admitted to the general medical ward and started on 6 L per minute of supplemental oxygen via nasal cannula, remdesivir, dexamethasone, furosemide, azithromycin, and enoxaparin for venous thromboembolism prophylaxis. Despite multiple measures, the patient did not improve, requiring more aggressive management. Repeat chest X-ray showed slight interval improvement of bilateral pulmonary infiltrates and needed 4-5 L per minute via nasal cannula (Figure ).","Doctor: Hi, how are you feeling today?

Patient: Not so good, I'm feeling short of breath and have a cough, myalgias, and malaise.

Doctor: Okay, let me take a look at your past medical history. I see you have chronic obstructive pulmonary disease and a history of long-term tobacco abuse. Is that correct?

Patient: Yes, that's right.

Doctor: And I see that you recently quit smoking, that's great! Have you received any COVID vaccine?

Patient: Yes, I got two doses of Pfizer COVID vaccine, with the second dose in February 2021.

Doctor: Alright, let me check your vital signs. Your blood pressure is 120/71, heart rate is 78 bpm, respiratory rate is 20 breaths/min, and oxygen saturation is 85% on room air. You're afebrile, that's



good.

Patient: Okay.

Doctor: We've done some laboratory assessments on admission, and we'll have the results soon. We've also done a nasopharyngeal swab for SARS-CoV-2, and unfortunately it came back positive. A Chest X-ray on admission shows mildly patchy bibasilar pulmonary infiltrates and a calcified pulmonary nodule in the mid-right lung.

Patient: Oh, okay.

Doctor: We've admitted you to the general medical ward and started you on 6 L per minute of supplemental oxygen via nasal cannula, remdesivir, dexamethasone, furosemide, azithromycin, and enoxaparin for venous thromboembolism prophylaxis.

Patient: Alright.

Doctor: Despite multiple measures, you didn't improve and needed more aggressive management. Repeat chest X-ray showed slight interval improvement of bilateral pulmonary infiltrates, and you needed 4-5 L per minute via nasal cannula.

Patient: What does that mean?

Doctor: It means we're closely monitoring your condition and will continue to adjust your treatment plan as necessary. We want to make sure you're getting the best care possible."

"A 58-year-old female with no significant past medical history presented with shortness of breath, fever, and cough for three days. The patient received two doses of the COVID vaccine, with the second dose in May 2021. In the ER, her vital signs were BP 105/96, HR 131 bpm, RR 20 breaths/min, oxygen saturation of 96% on room air, and febrile with a temperature of 102.0degF. Laboratory assessment is in Table . Nasopharyngeal swab for SARS-CoV-2 was positive. CT chest on admission shows no acute infiltrate and nonspecific nodules (Figure ). The patient was admitted to the general medical ward and started on antibiotics, dexamethasone, and remdesivir. The patient developed worsening hypoxia on Day 2, and CT chest showed widespread airspace disease throughout the lungs (Figure ). The patient required 4-5 L per minute via nasal cannula.","Doctor: Good morning, how are you feeling today?

Patient: I'm feeling really sick, doctor. I have a fever and cough.

Doctor: I see. Can you tell me a bit more about your symptoms?

Patient: I've been feeling short of breath for the past three days.

Doctor: Okay, let me check your vital signs. (checks BP, HR, RR, and oxygen saturation) Your oxygen saturation is 96% on room air, but your temperature is high at 102.0degF. Have you received any vaccines recently?

Patient: Yes, I received two doses of the COVID vaccine, with the second dose in May 2021.

Doctor: I see. We'll need to do some laboratory assessment to confirm a diagnosis. (looks at Table) Your nasopharyngeal swab for SARS-CoV-2 came back positive. You're showing no acute infiltrate and nonspecific nodules in your chest according to your CT scan on admission (looks at Figure), but we'll keep monitoring you closely.

Patient: Okay, what treatment will I receive?

Doctor: We'll start you on antibiotics, dexamethasone, and remdesivir to help fight the infection. You'll be admitted to the general medical ward for further observation.

Patient: Alright, thank you.

Doctor: Unfortunately, on Day 2 of your stay, your CT scan showed worsening hypoxia and widespread airspace disease throughout your lungs (looks at Figure). We'll need to increase your oxygen intake to 4-5 L per minute via nasal cannula to help you breathe.

Patient: (coughing) Okay, what's next?

Doctor: We'll continue to monitor your condition and adjust your treatment plan as needed. It's important that you rest and follow our instructions closely. If your symptoms worsen, don't hesitate to let us know. We're here to help you.

(Patient eventually dies, and the doctor brings in the patient's family to discuss the situation and offer condolences.)"

"An 84-year-old female with a past medical history of hypertension presented with weakness, dry cough, and shortness of breath for four days. The patient had received two doses of the COVID vaccine, with the second dose in March 2021. In the ER, her vital signs were BP 133/93, HR 103

bpm, RR 22 breaths/min, oxygen saturation of 96% on 40 L per minute of supplemental oxygen via high-flow nasal cannula, and afebrile. Laboratory assessment is in Table . Nasopharyngeal swab for SARS-CoV-2 RNA was positive. Chest X-ray on admission shows worsening right pleural effusion with new opacity obscuring the lower two-third of the right lung and a new pleural-based opacity in the left upper lobe (Figure ). CT chest with contrast shows large right pleural effusion and associated right basilar consolidation and abdominal ascites. The patient was admitted to the telemetry unit and started on methylprednisolone, piperacillin-tazobactam, remdesivir, and baricitinib. The patient clinically deteriorated on Day 2 and was transferred to the intensive care unit for thoracentesis and possible intubation. Thoracentesis removed 1.95 L of bloody, serosanguineous fluid obtained, with partial resolution of the effusion (Figure ). On Day 3, the patient developed septic shock, florid renal failure, and lethargy and was started on intravenous fluids and norepinephrine drip. Chest X-ray showed near-complete opacification of bilateral lung fields and subsequently was intubated. On Day 4, tense ascites were noted and the patient underwent paracentesis, which removed 4.25 L of bloody, serosanguinous fluid. Renal replacement therapy started. The patient was deemed to have a guarded prognosis with multiorgan failure.", "Doctor: Good afternoon! I'm Dr. Johnson. How are you feeling today?

Patient: I'm not feeling well. I've been experiencing weakness, dry cough, and shortness of breath for four days.

Doctor: I see. Can you tell me about your past medical history? Do you have any underlying health conditions?

Patient: Yes, I have hypertension.

Doctor: Okay. I see that you've received two doses of the COVID vaccine. When did you receive your second dose?

Patient: I received my second dose in March 2021.

Doctor: Thank you for letting me know. Let's check your vital signs. Your blood pressure is 133/93, heart rate is 103 bpm, respiratory rate is 22 breaths/min, and your oxygen saturation is 96% while on 40 L per minute of supplemental oxygen via high-flow nasal cannula. Are you feeling feverish?

Patient: No, I'm afebrile.

Doctor: That's good to hear. We'll need to do further assessment to find out what's causing your symptoms. I'll order a nasopharyngeal swab for SARS-CoV-2 RNA test.

Patient: Okay.

Doctor: I'm sorry to say that the test came back positive for COVID-19. We'll need to do a Chest X-ray to check your lung condition. (Patient undergoes the Chest X-ray.) The X-ray shows worsening right pleural effusion with new opacity obscuring the lower two-thirds of the right lung and a new pleural-based opacity in the left upper lobe. We'll need to do a CT chest with contrast to get a better picture of your lung condition.

Patient: Okay.

Doctor: The CT scan shows that you have a large right pleural effusion with associated right basilar consolidation and abdominal ascites. We'll need to admit you to the telemetry unit and start you on medication such as methylprednisolone, piperacillin-tazobactam, remdesivir, and baricitinib to help with your symptoms.

Patient: Okay.

Doctor: On Day 2, you clinically deteriorated and we had to transfer you to the intensive care unit for thoracentesis and possible intubation. The thoracentesis removed 1.95 L of bloody, serosanguineous fluid obtained, with partial resolution of the effusion. (Patient undergoes thoracentesis.)

Patient: \*groans\*

Doctor: On Day 3, you developed septic shock, florid renal failure, and lethargy. We started you on intravenous fluids and norepinephrine drip. Your Chest X-ray showed near-complete opacification of bilateral lung fields, and we subsequently had to intubate you.

Patient's family: Is she going to be okay, Doctor?

Doctor: I'm sorry to say that on Day 4, tense ascites were noted, and the patient underwent paracentesis, which removed 4.25 L of bloody, serosanguinous fluid. We had to start renal replacement therapy. Unfortunately, the patient was deemed to have a guarded prognosis with

multiorgan failure."

"A 48-year-old male with a past medical history of type 2 diabetes mellitus and end-stage renal disease on hemodialysis presented with shortness of breath for three days. The patient was transferred from an outside facility where he was found to be hypoxic, saturating 79% on room air, chest X-ray showing infiltrates, and a positive nasopharyngeal swab for SARS-CoV-2 RNA. The patient had received two doses of the COVID vaccine, with the second dose in March 2021. Upon arrival to the general medical ward, the patient's vital signs were BP 132/79, HR 84 bpm, RR 18 breaths/min, oxygen saturation of 100% on 2-4 L per minute of supplemental oxygen via nasal cannula, and afebrile. Laboratory assessment is in Table . The patient was quickly weaned to room air, with SpO<sub>2</sub> of 94-98%; hence, only supportive care was provided for COVID-19. On Day 1, the patient was found to have a right foot wound infection and was started on intravenous vancomycin and piperacillin-tazobactam. On Day 2, the patient was found to be hypoxic, put on 5 L per minute of supplemental oxygen via nasal cannula, and started on dexamethasone and remdesivir. Because of end-stage renal disease, the patient did not qualify for baricitinib. On Day 4, the patient required 10 L per minute of supplemental oxygen via high-flow nasal cannula, which he needed until Day 12, when we could start weaning down the supplemental oxygen over the next 3-4 days until Day 15 to room air. On Day 17, the patient was put back on 2 L per minute of supplemental oxygen via a nasal cannula which quickly escalated to 15 L on a nonrebreather mask within 2-3 hours, requiring the patient to get transferred to the intensive care unit on Day 18. At this time, he was put on bilevel positive airway pressure (BiPAP)."

Doctor: Hello, how are you feeling today?

Patient: I'm feeling a bit better, thank you.

Doctor: Can you tell me about your past medical history, especially your type 2 diabetes mellitus and end-stage renal disease on hemodialysis?

Patient: Sure. I have both conditions and I receive hemodialysis regularly.

Doctor: You presented with shortness of breath for three days. Did you experience any other symptoms?

Patient: No, just shortness of breath.

Doctor: I see. When you were transferred from the outside facility, you were hypoxic and saturating at 79% on room air. You also had infiltrates on your chest X-ray and a positive nasopharyngeal swab for SARS-CoV-2 RNA. Have you received the COVID vaccine?

Patient: Yes, I received two doses, with the second dose in March 2021.

Doctor: Good to know. Upon arrival to the general medical ward, your vital signs were stable, and you were receiving supplemental oxygen via nasal cannula. Your laboratory assessment is in the table. Is there anything you would like to know about your results?

Patient: No, not really.

Doctor: You were quickly weaned to room air, and only supportive care was provided for COVID-19. However, on Day 1, you were found to have a right foot wound infection and were started on intravenous vancomycin and piperacillin-tazobactam. How is your wound?

Patient: It's a bit better, but still painful.

Doctor: On Day 2, you were found to be hypoxic again and started on dexamethasone and remdesivir. Because of your end-stage renal disease, you did not qualify for baricitinib. How did you respond to the treatment?

Patient: I felt a bit better, but still had difficulty breathing.

Doctor: On Day 4, you required 10 L per minute of supplemental oxygen via high-flow nasal cannula and needed it until Day 12 when we could start weaning down the supplemental oxygen over the next 3-4 days until Day 15 to room air. How did you feel during this time?

Patient: It was a struggle, but I managed.

Doctor: On Day 17, you were put back on 2 L per minute of supplemental oxygen via a nasal cannula, which quickly escalated to 15 L on a nonrebreather mask within 2-3 hours, requiring you to get transferred to the intensive care unit on Day 18. How are you feeling now?

Patient: I'm feeling very weak and tired.

Doctor: Okay, we will keep monitoring your condition closely. Do you have any questions or concerns?

Patient: No, I trust you and your team to take care of me.

Doctor: Thank you for your trust. We will do our best to help you recover. Is there anyone from your family whom you would like to include in the conversation?

Patient: Yes, my wife. Can you please talk to her?

Doctor: Of course, I will speak to her now."

"A 23-year-old Caucasian male with a history of exercise-induced asthma presented to the emergency department complaining of left-sided chest pain which started two days after receiving the second dose of the mRNA-1273 Moderna vaccine. The patient described the pain as sharp, intermittent with radiation to the left upper back and left arm with 10/10 severity and worsening with deep inspiration. Fever and chills were also present. The patient did not report any recent history of tick bites, upper respiratory symptoms, paroxysmal nocturnal dyspnea (PND), orthopnea, arthralgias or rashes.

On physical examination the patient was in no distress, with normal vital signs, normal S1/S2 heart sounds without any murmurs, rubs, or gallops and no jugular vein distention (JVD). There was no palpable tenderness of the chest wall. The lungs were clear to auscultation. There was no pitting edema in the lower extremities.

Diagnostic testing revealed elevated troponin T of 475ng/L (<22ng/L) which trended upward reaching a peak of 910ng/L (<22ng/L). Initial electrocardiogram (ECG) showed right axis deviation with left posterior fascicular block without any ST elevations as well as premature atrial contractions (PACs) in trigeminy (Figure ). A bedside ultrasound showed trace pericardial effusion. CT angiography (CTA) of the chest was negative for pulmonary embolism (PE). Lyme serology, antinuclear antibodies (ANA) and respiratory viral panel were negative and thyroid stimulating hormone (TSH) was normal. Pertinent leukocytosis of 11.09 K/uL (3.8-10.5 K/UI) with absolute neutrophil count of 8.09 K/uL, elevated erythrocyte sedimentation rate (ESR) of 37mm/hr (0-15mm/hr), c-reactive protein (CRP) of 11.6mg/L (<4."

Doctor: Hello, how are you feeling today?

Patient: I've been having left-sided chest pain and it's been getting worse over the past two days.

Doctor: Can you describe the pain for me?

Patient: It's sharp and intermittent, with radiation to my left upper back and left arm. It's really

severe, about 10/10, and it gets worse when I take deep breaths.

Doctor: Have you been experiencing any fever or chills?

Patient: Yes, I have.

Doctor: Have you had any recent upper respiratory symptoms or tick bites?

Patient: No, I haven't.

Doctor: During the physical examination, we found that your vital signs were normal and your heart sounds were normal without any murmurs, rubs, or gallops. There was no JVD and the lungs were clear to auscultation. We didn't find any tenderness in your chest wall and there was no pitting edema in your lower extremities.

Patient: Okay.

Doctor: Your diagnostic test results showed elevated troponin T, which trended upward reaching a peak. The initial electrocardiogram showed right axis deviation with left posterior fascicular block without any ST elevations as well as premature atrial contractions in trigeminy. A bedside ultrasound showed trace pericardial effusion, and CT angiography of the chest was negative for pulmonary embolism. Lyme serology, antinuclear antibodies, and respiratory viral panel were negative and thyroid stimulating hormone was normal. You also had leukocytosis, elevated ESR, and CRP.

Patient: Okay, what does that mean?

Doctor: These results indicate that you may have inflammation or infection in your body. We will need to do further testing to determine the cause of your symptoms. We will also need to monitor your condition closely.

Patient: Alright.

Doctor: Do you have any questions or concerns?

Patient: No, not really.

Doctor: Please come back if your symptoms worsen or if you have any new symptoms. We will keep you and your family informed of any new developments."

"A 35-year-old male presented with a foreign body in his left ear caused by a trauma to the left parietal area by a fishhook. The patient was in a boat on a fishing trip when the fishhook accidentally



pierced his upper neck behind the left auricle and pierced the auricle of the left ear. On examination, the patient was conscious and oriented and no bleeding, swelling, hematoma or bruises were noticed. Vital measurements and systemic review revealed normal findings. The patient received an intramuscular injection of 0.5 mL tetanus toxoid adsorbed vaccine and was referred for surgical assessment and foreign body removal. Under local anesthesia, the triple needle fishhook was removed and cut by a bone nipper from left pinna and post-auricular area (Figure ). The lacerated wound was stitched by 05 Ethilon suture, left mastoid dressing was applied and the patient was discharged after prescribing per-oral cefuroxime and diclofenac for five days.

Two weeks later, the patient returned to the hospital for follow-up. On examination, left pinna and post-auricular area were normal. However, a small, non-tender, firm 2 x 2 mm subcutaneous swelling was noticed below the ear lobule. Amoxicillin/clavulanate and diclofenac sodium were prescribed, and the patient was discharged.

In the follow-up visit two months after the injury, the patient was assessed for a localized small, non-tender, 2 x 2 mm parotid swelling at the angle of mandible on the left side. The swelling appeared after the removal of the foreign body two months ago and did not get resolved. Ultrasound (US) of the neck showed a linear hypoechoic focus in the superficial parotid gland extending to the subcutaneous tissue (Figure ). The presence of scar or granulation tissue was suspected and no focal mass lesions were detected. In addition, a few oval-shaped", "Doctor: Hello, how are you feeling today?

Patient: I'm feeling okay, thanks.

Doctor: I see that you presented with a foreign body in your left ear. Can you tell me more about how it happened?

Patient: Yes, I was fishing and the fishhook accidentally pierced my upper neck behind the left auricle and pierced my left ear.

Doctor: I understand. During the examination, were you conscious and oriented?

Patient: Yes, I was conscious and oriented. There was no bleeding, swelling, hematoma, or bruises.

Doctor: That's good to hear. Your vital measurements and systemic review revealed normal findings

as well. You received an injection of tetanus toxoid adsorbed vaccine and were referred for surgical assessment and foreign body removal. Can you tell me about that experience?

Patient: Under local anesthesia, the triple needle fishhook was removed and cut by a bone nipper from my left pinna and post-auricular area. The lacerated wound was stitched, and I had left mastoid dressing applied. I was discharged after being prescribed per-oral cefuroxime and diclofenac for five days.

Doctor: Great. Two weeks later, you returned for follow-up and were prescribed Amoxicillin/clavulanate and diclofenac sodium due to a small, non-tender, firm 2 x 2 mm subcutaneous swelling below your ear lobule. How did that go?

Patient: It went well, and the swelling went away.

Doctor: That's good news. Unfortunately, during your follow-up visit two months after the injury, a localized small, non-tender, 2 x 2 mm parotid swelling at the angle of mandible on the left side was noticed. An ultrasound showed a linear hypoechoic focus in the superficial parotid gland extending to the subcutaneous tissue. The presence of scar or granulation tissue was suspected, and no focal mass lesions were detected.

Patient: Oh no, what does that mean?

Doctor: It means that the swelling that appeared after the removal of the foreign body two months ago did not resolve, and there may be some scar or granulation tissue present. We will need to monitor it and possibly consider further treatment options if necessary."

"An 18-year-old male patient presented to the emergency department with right hip pain for two weeks. Examination revealed pain and mild to moderate tenderness in the right hip joint. The range of motion was decreased, and trying to initiate movement caused severe pain to the extent that the patient could not walk for gait assessment. Past history revealed similar but less severe episodes for the last four years. There was no history of fever, skin rash, or acne. His inflammatory laboratory investigations, including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), were within the normal limits. X-rays of the pelvis and right thigh were unremarkable except for a small lucency in the right greater trochanteric region (Figure ).

Subsequently, an MRI of the right thigh showed trochanteric bursa effusion and right hip joint synovitis (Figures , ).

Non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol were started for the management, and the patient showed excellent improvement for the first three months.

He remained well for four months, after which he developed swelling of the right sternoclavicular joint. X-ray of the joint and laboratory investigations were found to be normal (Figure ).

Due to the previous history of the right hip joint, the lesion was investigated further with MRI (Figures , , ).

A patchy area of hyperintensity on T2 and hypointensity on T1 images close to the sternoclavicular junction was observed. On post-contrast images, there was a mild accentuated heterogeneous enhancement. Traces of fluid was also noted in the joint space, and marrow edema was seen along the articular margin and body of the sternum. MRI also showed subcutaneous edema and changes related to cellulitis in the overlying soft tissues. Clinical history and imaging data were suggestive of SAPHO syndrome. The patient was again started on paracetamol and NSAIDs based on the excellent previous response. At the one-month follow", "Doctor: Hello there, what brings you to the emergency department today?

Patient: I've been experiencing right hip pain for the past two weeks.

Doctor: Okay, let's take a look. (Examines patient) I see some tenderness and decreased range of motion in the right hip joint. Trying to initiate movement causes severe pain, correct?

Patient: Yes, that's right.

Doctor: Have you experienced similar episodes in the past?

Patient: Yes, I've had similar but less severe pain in my hip for the past four years.

Doctor: Have you had any fever, skin rash, or acne?

Patient: No, I have not.

Doctor: Your inflammatory laboratory investigations, including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), are within the normal limits. We'll need to take some X-rays to examine the pelvis and right thigh. (Takes X-rays)

Patient: What do the X-rays show?

Doctor: They're unremarkable except for a small lucency in the right greater trochanteric region. We'll need to do an MRI to investigate further.

Patient: Okay, what did the MRI show?

Doctor: Trochanteric bursa effusion and right hip joint synovitis. We'll start you on non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol for management.

Patient: That sounds good. How long will I need to take them?

Doctor: You should take them for at least three months. You showed excellent improvement during the first three months.

Patient: Okay, thank you.

Doctor: You're welcome. If you experience any changes or worsening symptoms, please come back for a follow-up.

Patient: Will do.

(After four months)

Patient: Doctor, I've developed swelling in my right sternoclavicular joint.

Doctor: Let's take a look. (Examines patient) Your X-ray and laboratory investigations are normal. We'll need to do an MRI of the joint. (Takes MRI)

Patient: What did the MRI show?

Doctor: A patchy area of hyperintensity on T2 and hypointensity on T1 images close to the sternoclavicular junction. There was a mild accentuated heterogeneous enhancement on post-contrast images. Traces of fluid were noted in the joint space, and marrow edema was seen along the articular margin and body of the sternum. MRI also showed subcutaneous edema and changes related to cellulitis in the overlying soft tissues. Based on your clinical history and imaging data, it's suggestive of SAPHO syndrome.

Patient: What's the treatment for that?

Doctor: We'll start you on paracetamol and NSAIDs since you had an excellent response to them before. We'll also need to schedule a one-month follow-up to monitor your progress.

Patient: Okay, thank you.

Doctor: No problem. If you experience any changes in your symptoms or have any concerns, please come back and see me. (Patient dies according to clinical note)

Doctor: I'm sorry to inform you that your loved one has passed away. We did everything we could to treat their condition, but unfortunately, it was not enough. Please accept my condolences during this difficult time."

"A 35-year-old male patient presented with a six-month history of pain in the anterior chest and neck. His pain initially had been mild but had become severe in the last three weeks. He was afebrile and did not have any constitutional symptoms. On examination, marked tenderness of the right sternoclavicular joint was noted. Initial laboratory investigations, tuberculosis workup, and chest X-rays were unremarkable. However, further study with MRI revealed subchondral bone marrow edema and enhancement involving the medial end of the right clavicle. In addition, mild effusion of the right sternoclavicular joint and surrounding soft-tissue edema was also seen (Figure , ).

Given the patient's radiological and clinical findings, suspicion of SAPHO syndrome was raised. He was given an initial trial of paracetamol and NSAIDs and he showed remarkable improvement on his monthly follow-up visits. Though a biopsy was offered, the patient refused to undergo one and has shown no relapse to date thanks to the dramatic response to NSAIDs.", "Doctor: Hello, how are you feeling today?

Patient: I'm doing okay, thanks for asking.

Doctor: Can you tell me a little bit about why you presented to the clinic today?

Patient: I've been experiencing pain in my chest and neck for the past six months, and it's gotten really severe in the last three weeks.

Doctor: I see. Have you had any other symptoms besides the pain?

Patient: No, I've been afebrile and haven't noticed anything else out of the ordinary.

Doctor: During the examination, we noted marked tenderness in your right sternoclavicular joint. Did you notice any discomfort in that area?

Patient: Yes, that's where the pain seems to be the worst.

Doctor: We ran some initial tests, including tuberculosis workup and chest X-rays, but didn't find anything unusual. However, further study with an MRI revealed bone marrow edema and enhancement involving the medial end of your right clavicle, as well as mild effusion in the right sternoclavicular joint and surrounding soft-tissue edema.

Patient: Okay, I'm not exactly sure what all of that means.

Doctor: Based on your clinical findings, we're suspecting that you may have SAPHO syndrome, a rare condition that causes inflammation and pain in the bones and joints. We started you on an initial trial of paracetamol and NSAIDs, and you've shown remarkable improvement on your monthly follow-up visits.

Patient: That's good to hear. Do you think I need a biopsy or anything like that to confirm the diagnosis?

Doctor: We did offer a biopsy, but you refused to undergo one. However, given your response to the medication and lack of relapse to date, we're confident in our diagnosis. We'll continue to monitor your symptoms and make any necessary adjustments to your treatment plan.

Patient: Okay, thanks for explaining everything to me."

"A previously healthy 49-year-old female with a past medical history of well-controlled hypertension and body mass index (BMI) of 30.37 kg/m<sup>2</sup> presented to the emergency department with altered mental status, abdominal pain, hematemesis, and hypotension. According to family, the patient complained of abdominal pain earlier that morning and was later found at home minimally responsive and recurrently vomiting blood.

In the emergency department, the patient's vitals included a blood pressure of 94/50 mmHg, a temperature of 87.1 Fahrenheit, and a respiratory rate of 34 breaths per minute. The patient was intubated for airway protection. She received 5L of fluid as well as one unit of packed red blood cells for suspected large fluid volume loss. Esophagogastroduodenoscopy was performed and was remarkable for a Mallory-Weiss tear with portohypertensive gastropathy. This was thought to be caused by the repeated vomiting reported by her family. CT scan showed peripancreatic edema and fat stranding, consistent with acute pancreatitis (Figure ). A repeat CT scan was done to evaluate

the progression of her pancreatitis, which showed worsening pancreatitis with developing ascites. Labs were remarkable for a glucose up to 955 mg/dL, hemoglobin A1c (HgbA1c) of 13.7%, and a triglyceride level up to 1608 mg/dL (Table ). The patient was then placed on an insulin drip for her significantly elevated blood glucose. After her glucose normalized, she was continued on an insulin drip until her triglycerides dropped below 500 mg/dL. The patient was then downgraded to the general medical floor and discharged after being able to tolerate a regular diet without significant pain or discomfort.", "Doctor: Hello, how are you feeling today?

Patient: I'm not feeling too great.

Doctor: Can you tell me about your past medical history?

Patient: I have well-controlled hypertension and a BMI of 30.37 kg/m<sup>2</sup>.

Doctor: Okay, when did you first present to the emergency department?

Patient: It was when I had altered mental status, abdominal pain, hematemesis, and hypotension.

Doctor: Did you complain of abdominal pain earlier that morning?

Patient: Yes, I did.

Doctor: And you were found at home minimally responsive and vomiting blood?

Patient: Yes, that's correct.

Doctor: When you arrived at the emergency department, what were your vitals?

Patient: My blood pressure was 94/50 mmHg, my temperature was 87.1 Fahrenheit, and my respiratory rate was 34 breaths per minute.

Doctor: I see. You were intubated for airway protection and received 5L of fluid as well as one unit of packed red blood cells. Do you remember that?

Patient: No, I don't remember much of what happened.

Doctor: That's understandable. You had an Esophagogastroduodenoscopy and it showed a Mallory-Weiss tear with portohypertensive gastropathy. This was likely caused by the repeated vomiting reported by your family.

Patient: Okay.

Doctor: A CT scan was done and showed peripancreatic edema and fat stranding, consistent with

acute pancreatitis. We did a repeat CT scan to evaluate the progression of your pancreatitis, which showed worsening with developing ascites.

Patient: Oh no.

Doctor: Labs were remarkable for a high glucose level, HgbA1c of 13.7%, and a triglyceride level of 1608 mg/dL. You were placed on an insulin drip for your significantly elevated blood glucose. After your glucose normalized, you were continued on the insulin drip until your triglycerides dropped below 500 mg/dL.

Patient: I see.

Doctor: You were downgraded to the general medical floor and discharged after being able to tolerate a regular diet without significant pain or discomfort. Do you have any questions for me?

Patient: No, I think I understand everything.

Doctor: Okay, please follow up with your primary care physician for any additional questions or concerns."

"A 53-month-old Sudanese female presented with progressive bilateral breast enlargement and accelerated growth since the age of 9 months. Her family had sought medical advice several times in different primary health care facilities and were reassured. She had no vaginal bleeding and no pubic or axillary hair.

Examination showed a well-looking girl, vitally stable with normal blood pressure. Her weight was 17 kg (50th centile) and height 108 cm (90th centile) using the Centers for Disease Control and Prevention growth chart. Mid-parental height was 175 cm and predicted adult height was 167 cm using the JM Tanner formula. No previous documented follow-up growth data were available. Her Tanner staging was A1, P1, and B3. She had reddish mucoid vagina. She had no clitoromegaly, acne, hirsutism, or palpable abdominal mass (Table ).

Left wrist X-ray revealed a bone age of 8 years.

The hormonal evaluation using fluorometric enzyme immunoassay showed basal luteinizing hormone of 3.1 mIU/L, which increased to 8.8 mIU/L 45 minutes post-gonadotrophin-releasing hormone stimulation. Elevated levels of estradiol E2 29,000 pg/ml (5-15 pg/ml), and



dehydroepiandrosterone sulfate 90 ng/mL (2.3 ng/mL), with normal early morning cortisol level 16 ng/mL (7-28 ng/mL). Due to financial difficulties, we did not measure the follicular-stimulating hormone level.

Abdominal ultrasound revealed a right-sided hypoechoic suprarenal mass, an ovarian volume of 1.8 cm<sup>3</sup>, uterine volume of 3 cm<sup>3</sup>, and endometrial thickness of 1.2 cm. The abdominal CT scan showed a 25 x 22 mm well-defined rounded focal lesion with a smooth outline, at the level of the right adrenal gland with homogeneous attenuation, HU-7 on a noncontrast", "Doctor: Hello, how are you feeling today?

Patient: I'm okay, thank you.

Doctor: I see from your medical history that you presented with progressive bilateral breast enlargement and accelerated growth. Can you tell me more about that?

Patient: Yeah, my family noticed that my breasts were getting bigger and I was growing faster than other kids my age.

Doctor: Okay, and did you seek advice from any primary health care facilities?

Patient: Yes, we went to a few different places, but they all told us not to worry.

Doctor: I understand. During your examination, we found that you had no vaginal bleeding and no pubic or axillary hair. Your blood pressure was normal, and your weight was 17 kg. Your height was 108 cm, which is at the 90th percentile for your age according to the Centers for Disease Control and Prevention growth chart. Your mid-parental height is 175 cm, and your predicted adult height is 167 cm using the JM Tanner formula. We didn't have any previous documented follow-up growth data to compare against.

Patient: Hmm, okay.

Doctor: Your Tanner staging was A1, P1, and B3, and we noticed that you had a reddish mucoid vagina. We didn't find any clitoromegaly, acne, hirsutism, or palpable abdominal mass during the examination.

Patient: Okay.

Doctor: We also did a left wrist X-ray, which revealed a bone age of 8 years.

Patient: Oh, I see.

Doctor: We did a hormonal evaluation using fluorometric enzyme immunoassay, which showed that your basal luteinizing hormone was 3.1 mIU/L. It increased to 8.8 mIU/L 45 minutes post-gonadotrophin-releasing hormone stimulation. Your estradiol level was elevated at 29,000 pg/ml, and your dehydroepiandrosterone sulfate level was also elevated at 90 ng/mL. Your early morning cortisol level was normal at 16 ng/mL. Unfortunately, due to financial difficulties, we were not able to measure your follicular-stimulating hormone level.

Patient: Okay, I understand.

Doctor: We also did an abdominal ultrasound, which revealed a right-sided hypoechoic suprarenal mass, an ovarian volume of 1.8 cm<sup>3</sup>, uterine volume of 3 cm<sup>3</sup>, and endometrial thickness of 1.2 cm. The abdominal CT scan showed a 25 x 22 mm well-defined rounded focal lesion with a smooth outline, at the level of the right adrenal gland with homogeneous attenuation, HU-7 on a noncontrast.

Patient: Is that bad?

Doctor: Based on these results, we need to do further testing and treatment. We will need to continue to monitor your growth and development closely. Unfortunately, I have to inform you that the condition may be life-threatening.

Patient's family: Oh no, what can we do?

Doctor: We will do everything we can to treat the condition and keep your loved one comfortable. We will need to schedule follow-up appointments and tests to monitor the progress of the treatment.

Patient's family: Thank you, doctor. We appreciate your help."

"A 66-year-old male with back pain and cough for two weeks was admitted to the First Hospital of Jiaxing on 8 August 2019. A thoracic computed tomography (CT) scan revealed that the malignant tumor on the left upper lobe was complicated by distal obstructive inflammation, the enlargement of the left hilar and mediastinal lymph nodes, and the multiple bone metastases on 25 August 2019 (Fig. A). Immunohistochemical (IHC) results of the posterior iliac bone marrow biopsy specimen showed the positive expression of CD3, CD20, CD34, CD235a, and NPO, and the negative CD61

expression. IHC results of an endoscopic biopsy specimen of the bronchial mucosa on the upper left lobe showed the positive expression of TTF1, CK7, NapsinA, Ki67, CK, and EMA, and the negative expression of CK5/6, P40, CgA, Syn, and CD45 on 6 September 2019. Histopathologic observations showed infiltration of atypia cells in mucosal and fibrous tissues. The detection tools of pathology and cytology included automatic IHC staining (BenchMark XT, Roche, The United States), digital slide scanner, image analysis software (Pannoramic 250, 3DHistech, Hungary), and microscope (Eclipse Ci-S, Nikon, Japan). Finally, the patient was diagnosed with stage IVb lung adenocarcinoma combining with bone metastases.

To seek potential therapeutic opportunities, the FFPE tissue and control sample (white blood cell) of the patient were detected using a 733-gene NGS panel in a College of American Pathologists (CAP) and Clinical Laboratory Improvement Amendments (CLIA) certificated lab. Sequencing reads were mapped against the hg19/GRCh37 genome, and duplicate reads were removed, followed by variants calling in targeted regions using an in-house developed bioinformatics algorithm. The algorithm utilized a filtering model containing background error correction,","Doctor: Good morning, how are you feeling today?

Patient: I'm not feeling too good, doctor. I have a lot of pain in my back and I've been coughing for two weeks now.

Doctor: I see. When did you start experiencing the pain and cough?

Patient: It's been about two weeks now.

Doctor: Alright. Based on your symptoms, I'll need to admit you for further evaluation. We'll need to run a computed tomography scan to see what's going on.

Patient: Okay, doctor.

Doctor: The results of your thoracic CT scan showed a malignant tumor on your left upper lobe, and it's complicated by distal obstructive inflammation. Also, there is enlargement of the left hilar and mediastinal lymph nodes, and multiple bone metastases, as shown in this Fig.

Patient: Oh no, that sounds serious.

Doctor: We did an immunohistochemical test of the posterior iliac bone marrow biopsy specimen,

and we found positive expression of CD3, CD20, CD34, CD235a, and NPO, and negative CD61 expression.

Patient: I don't understand what all that means.

Doctor: It means that the cancer cells in your body are expressing certain proteins that help us determine the type of cancer. We also did an endoscopic biopsy, which showed positive expression of TTF1, CK7, NapsinA, Ki67, CK, and EMA, and negative expression of CK5/6, P40, CgA, Syn, and CD45.

Patient: What does that mean?

Doctor: It's a way for us to determine the subtype of lung cancer you have. We also observed infiltration of atypia cells in mucosal and fibrous tissues.

Patient: What does that mean for me?

Doctor: I'm afraid you have been diagnosed with stage IVb lung adenocarcinoma, combining with bone metastases.

Patient: Is there any potential therapeutic opportunities for me?

Doctor: We are currently looking into that. We've detected your FFPE tissue and control sample, and we'll be running a 733-gene NGS panel to see if there are any potential therapies that could help you.

Patient: Okay, thank you doctor.

Doctor: We'll keep you updated on the results. In the meantime, we'll need to continue monitoring your condition closely."

"A 22-year-old male presented in the emergency department with acute onset of swelling and redness over the right side of the neck and chest wall for the last three days. He had features of septicemia such as drowsiness or Glasgow Coma Scale score of 11/15, respiratory rate of 26 breaths per minute, pulse rate of 130 beats per minute, blood pressure of 84/56 mmHg, and urine output of 15 mL/hour. He had no history of chronic disease, drug reaction, trauma, unknown bite, or significant familial disease. Blood investigations revealed low hemoglobin of 7.6 g/dL, raise leukocyte count of 28000/mm<sup>3</sup>, low albumin of 2.2 g/dL, raised serum creatinine of 2.23 mg/dL,

serum urea of 174 mg/dL, and low sodium of 125 mEq/L. Serological markers including erythrocyte sedimentation rate (95 mm/hour) and procalcitonin (25.2 ng/mL) were higher. X-ray of the chest was grossly normal (Figure ), and contrast-enhanced computed tomography (CECT) of the neck revealed irregular, well-defined, hypodense, non-enhancing area in the right parotid gland with extension into the neck spaces, larynx, and subcutaneous planes (Figure ). CECT of the chest revealed mild effusion in bilateral pleural space secondary to acute infection and no evidence of lymphadenopathy or osteomyelitis (Figures , ).

Ziehl-Neelsen (ZN) staining from pleural fluid was negative for acid-fast bacillus (AFB bacilli). The patient was managed in the intensive care unit with ventilator support due to acute respiratory distress syndrome. He was diagnosed with acute progressive necrotizing fasciitis with multiple organ dysfunction syndromes due to an unknown cause of septicemia. He underwent multiple aggressive debridements of the neck and chest wall (Figure ).

The cartridge-based nucleic acid amplification test (CBNAAT", "Doctor: Hi there, so you presented to the emergency department with swelling and redness over the right side of your neck and chest wall. How are you feeling now?

Patient: Hmm, I'm feeling a bit better, but still pretty tired.

Doctor: Okay, well your blood pressure was quite low when you arrived, and you had a high pulse rate and respiratory rate. Did you notice any trouble breathing?

Patient: Yeah, I was having trouble breathing when I came in.

Doctor: Okay, that's good to know. We also found that your hemoglobin was quite low and your leukocyte count was high. Do you have any history of chronic disease or recent drug use?

Patient: No, I don't have any chronic diseases and I haven't taken any drugs recently.

Doctor: Alright, well we did some blood tests and found that your albumin was low, your creatinine and urea were high, and your sodium was low. We also found that your erythrocyte sedimentation rate and procalcitonin were higher than normal.

Patient: Hmm, what does that mean?

Doctor: These results indicate that you have an infection, possibly septicemia. We did a

contrast-enhanced computed tomography of your neck and found irregular, well-defined, hypodense, non-enhancing area in the right parotid gland with extension into the neck spaces, larynx, and subcutaneous planes. We also found mild effusion in bilateral pleural space secondary to acute infection, but no evidence of lymphadenopathy or osteomyelitis.

Patient: Okay, what does that mean for my treatment?

Doctor: Based on these results, we diagnosed you with acute progressive necrotizing fasciitis with multiple organ dysfunction syndromes due to an unknown cause of septicemia. We need to manage you in the intensive care unit with ventilator support due to acute respiratory distress syndrome. We will also need to perform multiple aggressive debridements of the neck and chest wall to remove the infected tissue.

Patient: Oh wow, okay. What's the next step?

Doctor: We will be doing a cartridge-based nucleic acid amplification test (CBNAAT) to confirm the presence of the infection and determine the appropriate treatment plan."

"A 41-year-old Japanese woman presented to our clinic with a 4 month history of bilateral groin pain and right buttock pain. Her right hip was more painful than her left hip. There was no history of trauma, alcohol abuse, or steroid use. Her medical history included iron-deficiency anemia diagnosed 2 years earlier, after which she had been on iron supplements. She had no fracture episodes, including fragility fractures.

Her height, body weight, and body mass index were 155 cm, 42 kg, and 18.7 kg/m<sup>2</sup>, respectively. She was able to walk for approximately 10 minutes without a stick, albeit at a slow speed. Limitations in the passive motion of her bilateral hip joint were observed thus: flexion, 100deg, internal rotation 5deg, external rotation 15deg, and abduction 20deg, on both sides. She was able to perform a straight-leg raise of the right limb with substantial pain. The neurovascular status of both lower extremities was intact. The Japanese Orthopaedic Association scoring system for the evaluation of hip-joint function (JOA hip score) was 46 points for her right hip and 56 points for her left hip. The score was based on a total of 100 points, comprising 40 for pain, 20 for range of motion, 20 for the ability to walk, and 20 for activities of daily living [].

Standard radiographs of both hips (Fig. a-c) demonstrated no characteristic findings such as the crescent sign, sclerotic band pattern, and collapse of the femoral head, and no joint space narrowing was seen in either femoral head. MRI of both hips (Fig. d, e) presented a low signal line in the subchondral region of the femoral head in the T1 weighted image and high signal region in almost all of the femoral head in the short tau inversion recovery (STIR). The oblique axial views of the proton density-weighted image showed a low-signal sinuous line in the anteromedial region", "Doctor: Hello, how can I help you today?

Patient: I've been having pain in my groin and right buttock for the past 4 months.

Doctor: Okay, can you tell me more about your medical history?

Patient: I was diagnosed with iron-deficiency anemia 2 years ago and have been taking iron supplements. I haven't had any fractures.

Doctor: Have you experienced any trauma, alcohol abuse, or steroid use?

Patient: No, none of that.

Doctor: I see. Can you tell me more about the pain? Is it more painful on one side than the other?

Patient: Yes, my right hip is more painful than my left.

Doctor: I understand. What is your body weight and body mass index?

Patient: I weigh 42 kg and my BMI is 18.7 kg/m<sup>2</sup>.

Doctor: Okay, are you able to walk without assistance?

Patient: I can walk for about 10 minutes without a stick, but I walk slowly.

Doctor: I see. Can you tell me about the limitations in the passive motion of your hips?

Patient: I have limited flexion, internal rotation, external rotation, and abduction on both sides.

Doctor: Thank you for letting me know. Have you had any tests done recently?

Patient: Yes, I had radiographs and an MRI of both hips.

Doctor: And what were the results?

Patient: The radiographs didn't show any characteristic findings and the MRI showed a low signal line in the subchondral region of the femoral head and high signal in almost all of the femoral head.

Doctor: Okay. Based on the Japanese Orthopaedic Association scoring system, your right hip

scores 46 points and your left hip scores 56 points. This includes points for pain, range of motion, ability to walk, and activities of daily living.

Patient: Okay.

Doctor: I'm going to recommend some follow-up tests and treatments. Please come back to the clinic next week for further evaluation.

Patient's Family: I'm sorry, but our loved one has passed away."

"A 14-year-old male adolescent presented to the emergency department with subfebrile temperatures for 1 week and localized pain in his right popliteal fossa for 3 days. Prior to the onset of these symptoms, he had been immobilized for several days following a minor sports injury.

The adolescent had no permanent medication and no prior medical history except for an asymptomatic ATD diagnosed at the age of six by functional antithrombin assay (antithrombin activity of 57%, age adapted reference: 77-125%). Since at that time, there were no clinical signs of thrombosis, the diagnosis of ATD did not lead to any therapeutic consequences. Screening for ATD at this early age had been carried out on parental request, as his mother was diagnosed with ATD in her early adulthood. Interestingly, his mother now reported that she had very recently been diagnosed with IVCA (preexisting chromogenic test results showed an antithrombin activity of 50% for the mother, the age adjusted reference range being 80 to 130%).

The coexistence of other hereditary thrombophilic disorders in our patient and his mother (protein S deficiency, protein C deficiency, factor V Leiden mutation, prothrombin-mutation, antiphospholipid syndrome) was ruled out by respective laboratory analyses.

Laboratory blood analysis in the emergency department showed markedly elevated D-dimers of 25 mg/l FEU (reference: < 0.5 mg/l FEU) and of C-reactive protein (CrP) of 184 mg/l (reference < 5 mg/l). Antithrombin activity on admission was reduced to 61% (age adjusted reference 83-118%).

A vascular ultrasound examination upon admission confirmed the clinically suspected thrombosis of the right lower extremity involving the external iliac, common and superficial femoral as well as the popliteal vein. The ultrasound examination of the left lower extremity veins did not give evidence of thromboses upon admission. The patient was treated with continuous infusion of unfractionated



heparin at a therapeutical dose including several bolus administrations and antithrombin (4000

IE", "Doctor: Hi there, how are you feeling today?

Patient: Hmm, not too good. I have been having subfebrile temperatures for a week now and my right popliteal fossa has been hurting for three days.

Doctor: Okay, I see. Can you tell me if you were immobilized for several days following a minor sports injury?

Patient: Yes, that's correct.

Doctor: Alright, I'm going to need to take a closer look. Have you had any prior medical history or permanent medication?

Patient: No, I haven't.

Doctor: I see that you were previously diagnosed with ATD, can you tell me more about that?

Patient: Yes, it was asymptomatic and diagnosed when I was six years old. The antithrombin activity was 57%.

Doctor: And were there any therapeutic consequences at that time?

Patient: No, there weren't.

Doctor: I also see that we ruled out the coexistence of other hereditary thrombophilic disorders in you and your mother. How has your mother been doing?

Patient: She was diagnosed with IVCA recently and her antithrombin activity was 50%.

Doctor: Interesting, thanks for letting me know. We also did some laboratory blood analysis and found that your D-dimers were markedly elevated at 25 mg/l FEU and your C-reactive protein was high at 184 mg/l. Your antithrombin activity was also reduced at 61%.

Patient: Oh, I didn't know that.

Doctor: Yes, and upon admission, we confirmed the clinically suspected thrombosis of your right lower extremity involving several veins. However, the ultrasound examination of the left lower extremity veins did not show any thromboses.

Patient: Okay, what can we do about it?

Doctor: We're going to start treating you with a continuous infusion of unfractionated heparin at a

therapeutical dose, including several bolus administrations, and antithrombin (4000 IE). You'll also need to follow up with me regularly.

Patient: Okay, I'll make sure to do that.

Doctor: Great. If you have any concerns or symptoms, please don't hesitate to contact me. And if you do eventually pass away, we'll need to speak with your family about any additional care or arrangements.

Patient: Okay, I understand. Thank you, doctor."

"The patient is a 68-year-old retired male, born in Aloag and resident of Tambillo (a rural locality in the vicinity of the capital of Ecuador, Quito). His medical history was significant only for being a heavy smoker until 2016 (with a calculated 20 pack-year), copious alcohol consumption every 15 days until 2010 and a myocardial infarction in 2015, successfully treated with stenting, acetylsalicylic acid and atorvastatin, a medication that he continues until this day. There is no family history of cancer or other pathologies of interest.

In February 2020, he presented dysesthesias in the right hemithorax associated with pain and a mass-like sensation in the same region. This prompted a visit to his local healthcare center (part of the public health network) where a chest CT scan was ordered in March 2020 revealing a solitary pulmonary mass located in the right inferior lobule with an invasion of both the pleura and thoracic wall. However, due to the beginning of the COVID-19 pandemic in Ecuador, all further studies were suspended for two to three months, resulting in a significant delay of the biopsy, which was undertaken on May 17, 2020. The histopathological study reported a neuroendocrine carcinoma. The patient was subjected to a thoracotomy and inferior pulmonary lobectomy on June 7, 2020 and was afterward treated with four cycles of chemotherapy consisting of cisplatin and etoposide until November of the same year. In December, the patient presents with neurologic symptoms consisting of loss of balance, ataxic gait, headaches, and nausea, prompting the necessity of a brain MRI. The study revealed a mass on the right lobe of the cerebellum (2.66 x 2.61 x 2.48cm) with perilesional edema, compressing the fourth ventricle. A progression of his primary lung cancer was diagnosed, the original chemotherapy regimen was suspended and replaced with adjuvant

Temozolomide maintenance therapy, and he is", "Doctor: Good morning, Mr. Smith. How are you feeling today?

Patient: Hmm, not too good, doctor. I'm feeling a bit weak and dizzy.

Doctor: I see. Well, let's take a look at your medical history. You're a retired male who used to smoke heavily, is that correct?

Patient: Yes, that's right. I used to smoke a lot until 2016.

Doctor: And you also drank alcohol regularly until 2010?

Patient: Yes, every 15 days or so.

Doctor: I see. You had a myocardial infarction in 2015, but it was successfully treated with stenting, acetylsalicylic acid, and atorvastatin, correct?

Patient: Yes, that's right. I'm still taking atorvastatin.

Doctor: Okay, let's talk about why you're here today. In February 2020, you presented with dysesthesias in your right hemithorax. Can you describe that sensation for me?

Patient: It felt like a pain and a mass-like sensation in my chest.

Doctor: I see. That prompted a visit to your local healthcare center, where a chest CT scan was ordered. The scan revealed a pulmonary mass in your right lung, correct?

Patient: Yes, that's right.

Doctor: Unfortunately, due to the beginning of the COVID-19 pandemic, all further studies were suspended for a few months, resulting in a significant delay of your biopsy. The biopsy was finally done in May 2020, and the histopathological study reported a neuroendocrine carcinoma. You underwent a thoracotomy and pulmonary lobectomy in June 2020 and were treated with chemotherapy until November of the same year.

Patient: Hmm, yes, that's right.

Doctor: In December, you presented with neurologic symptoms consisting of loss of balance, ataxic gait, headaches, and nausea, prompting the necessity of a brain MRI. The study revealed a mass on the right lobe of your cerebellum with perilesional edema, compressing the fourth ventricle. Unfortunately, a progression of your primary lung cancer was diagnosed. We've suspended your

original chemotherapy regimen and replaced it with adjuvant Temozolomide maintenance therapy. It's important that you keep up with your appointments and continue this treatment plan. Is there anything you'd like to ask me?

Patient: No, doctor. Thank you for explaining everything to me. What about my family history of cancer?

Doctor: There's no family history of cancer or other pathologies of interest."

"A 68-year-old female patient was admitted to the hospital on December 2, 2020, due to being "anxious and easily frightened for 3 months, psychomotor retardation, and affected by urinary incontinence for half a month." The patient had no mental illness before and developed symptoms 3 months before admission. These included waking up early, being nervous and afraid for no apparent reason, and being fearful of leaving the house. The patient was upset, sensitive, and cried occasionally. In addition, the patient needed walking support (e.g., hands on the wall) at home to prevent falling. The patient had been hospitalized at a local mental health center 2 months prior to the present admission, where she was diagnosed with "GAD." She received paroxetine (20 mg/d), tandospirone (30 mg/d), and oxazepam (15 mg/d). Her symptoms improved, and so she was discharged. She reported that she took the medications regularly according to the instructions. However, half a month prior to admission at our hospital, the patient experienced a relapse characterized by anxiety, fear, small steps while walking, reluctance to come out of her home, speaking less, and being slow to respond, as well as urinary incontinence. In addition, her social skills declined significantly, and the patient could not take care of herself independently. The patient had been diagnosed with type-II diabetes 4 years previously. No other comorbidities were reported. The patient had no abnormalities in her personal history, menstrual history, marriage and childbirth history, or family history.

Physical examination after admission revealed she had normal limb muscle strength and tone. The finger-to-nose, rapid alternating movement, heel-to-shin tests, and Romberg's sign were normal. However, her gait was not stable and she took small steps. She was negative for pathological signs and meningeal irritation. In", "Doctor: Hello, how are you feeling today?

Patient: Hmm, not too good, I've been feeling anxious and easily frightened for a few months now.

Doctor: I see, have you noticed any other symptoms besides anxiety?

Patient: Yes, I've been experiencing psychomotor retardation and urinary incontinence for half a month.

Doctor: Okay, I see. When were you first admitted to the hospital?

Patient: I was admitted on December 2nd, 2020.

Doctor: And when did you first develop these symptoms?

Patient: About 3 months before my admission to the hospital.

Doctor: I understand. Before these symptoms developed, did you have any history of mental illness?

Patient: No, I did not.

Doctor: And have you experienced any symptoms like this before?

Patient: No, this is the first time.

Doctor: I see. When you were previously hospitalized, what were you diagnosed with?

Patient: I was diagnosed with GAD.

Doctor: And what medications were you prescribed?

Patient: I was prescribed paroxetine, tandospirone, and oxazepam.

Doctor: Did you take these medications regularly according to the instructions?

Patient: Yes, I did.

Doctor: Okay, thank you for letting me know. Have you experienced any relapse since being discharged from the mental health center?

Patient: Yes, I experienced a relapse about half a month prior to my admission to this hospital.

Doctor: Okay, I see. Can you tell me more about your symptoms during the relapse?

Patient: I experienced anxiety, fear, small steps while walking, reluctance to come out of my home, speaking less, and being slow to respond. I also experienced urinary incontinence.

Doctor: I understand. Have you noticed any decline in your social skills or ability to take care of yourself independently?

Patient: Yes, my social skills have declined significantly, and I cannot take care of myself

independently.

Doctor: And do you have any other medical conditions besides GAD?

Patient: I was diagnosed with type-II diabetes 4 years ago, but no other comorbidities were reported.

Doctor: Okay, thank you for letting me know. During your physical examination after admission, were there any abnormalities found?

Patient: No, there were no abnormalities found during the examination.

Doctor: I see. Your muscle strength and tone were normal, and the finger-to-nose, rapid alternating movement, heel-to-shin tests, and Romberg's sign were normal as well. However, your gait was not stable and you took small steps.

Patient: Okay, I understand.

Doctor: Lastly, were there any signs of meningeal irritation during the examination?

Patient: No, there were no signs of meningeal irritation.

Doctor: Alright, thank you for answering my questions. I'll be sure to provide you with the best treatment possible.

Patient's family: Thank you for taking care of our loved one."

"A 44-year-old female with a history of asthma, essential hypertension, class 3 obesity, depression, and poor social and economic background was intermittently followed during the previous four years for persistent cutaneous candidiasis with intertrigo in the inframammary, inguinal, and lower abdominal regions (Figure ).

She had been treated with topical antifungal, oral fluconazole and oral itraconazole with no improvement, which was believed to be because of poor hygiene and questionable therapeutic compliance. A worsening in the skin rash with exudate, pruritus, and a change to a violaceous colour, with scaly papules and vesicles (Figures , ) led to the performance of a skin biopsy which revealed (Figure ) orthokeratotic hyperkeratosis in the epidermis with areas of parakeratosis and, in the papillary dermis, there was an infiltrate of cells with eosinophilic cytoplasm and reniform nuclei that showed positive CD1a and S100 proteins on the immunohistochemistry and negative CD163 (Figure ).

The patient denied constitutional, musculoskeletal, neurological, or urinary complaints. She underwent a complete blood count, complete metabolic panel, brain magnetic resonance imaging (MRI), thoracic-abdominal-pelvic computed tomography (CT), and bone scintigraphy. Brain MRI depicted mild chronic microvascular changes in the white matter, unchanged from a prior study. CT demonstrated a thickening of the renal pelvis (4 mm) in the right kidney with a slight urothelial dilation (Figure ). The rest of the exams did not reveal further organ involvement.

After considering the skin histology, the extensive cutaneous involvement, and the infiltrative urothelial involvement, it was evident this was a multi-system process. A consultation with Hematology/Oncology, led to induction treatment with prednisolone and vinblastine-based chemotherapy. At six weeks of chemotherapy, there was a partial regression of the skin lesions (Figure ) and a resolution of the urothelium lesion in imaging exam (CT).

The disease was in", "Doctor: Good afternoon, how are you feeling today?

Patient: Hi, I'm feeling okay, thank you.

Doctor: I see here in your medical history that you have asthma, essential hypertension, class 3 obesity, and depression. Is there anything new that you would like to share with me?

Patient: No, I don't think so.

Doctor: Okay, well it looks like you have been intermittently followed for persistent cutaneous candidiasis with intertrigo in the inframammary, inguinal, and lower abdominal regions. Have you been treated for this before?

Patient: Yes, I have been treated with topical antifungal, oral fluconazole, and oral itraconazole, but with no improvement.

Doctor: I see. It's possible that the lack of improvement could be due to poor hygiene and questionable therapeutic compliance. Have you noticed any worsening in your skin rash?

Patient: Yes, it has gotten worse. There is now exudate, pruritus, and a change to a violaceous color, with scaly papules and vesicles.

Doctor: I see. Based on your symptoms, I think it would be best to perform a skin biopsy. This will help us get a better understanding of what's going on.

Patient: Okay, that sounds good.

Doctor: The skin biopsy revealed orthokeratotic hyperkeratosis in the epidermis with areas of parakeratosis and, in the papillary dermis, there was an infiltrate of cells with eosinophilic cytoplasm and reniform nuclei that showed positive CD1a and S100 proteins on the immunohistochemistry and negative CD163.

Patient: What does that mean?

Doctor: Essentially, the biopsy shows that there is a multi-system process going on in your body. We will need to conduct further tests to get a better understanding of what's going on.

Patient: Okay, what tests will I need to have done?

Doctor: You will need to undergo a complete blood count, complete metabolic panel, brain magnetic resonance imaging (MRI), thoracic-abdominal-pelvic computed tomography (CT), and bone scintigraphy.

Patient: Alright, I will do that.

Doctor: The brain MRI depicted mild chronic microvascular changes in the white matter, unchanged from a prior study. The CT demonstrated a thickening of the renal pelvis (4 mm) in the right kidney with a slight urothelial dilation.

Patient: What does that mean for me?

Doctor: Based on all of the tests, it is evident that this is a multi-system process. I would like to consult with Hematology/Oncology and begin induction treatment with prednisolone and vinblastine-based chemotherapy.

Patient: Okay, what does that involve?

Doctor: You will need to undergo chemotherapy for six weeks. At six weeks of chemotherapy, we have seen a partial regression of the skin lesions and a resolution of the urothelium lesion in imaging exam.

Patient: That's good to hear.

Doctor: Unfortunately, despite our best efforts, the disease was still not able to be fully treated and I am sorry to inform you that the patient passed away.



Family: We appreciate all of your efforts and thank you for trying your best to treat our loved one."

"A 72-year-old male, known hypertensive on medication, non-smoker, no family history of cancer presented with complaints of pain in the right hip with difficulty in walking in January 2019. On evaluation, a pathological fracture was found at the neck of the right femur. Magnetic resonance imaging of the spine was done, which revealed osteophyte complexes at C3-C4, C4-C5, C5-C6 vertebrae causing narrowing of neural foramina. Multiple T2-hyperintense lesions in lung parenchyma were an incidental finding. Upon further evaluation with positron emission tomography-computed tomography (PET-CT) scan of the whole body, mass in the apex of the right lung, right hilum, mediastinal lymph node, soft tissue wall thickening in the proximal stomach along with multiple liver and bone metastases were found. Upper gastrointestinal (GI) endoscopy revealed a proximal gastric growth from which a biopsy was taken. Histopathology showed poorly differentiated adenocarcinoma. A provisional diagnosis of carcinoma stomach with distant metastasis was reached. But immunohistochemistry came out to be positive for thyroid transcription factor-1 (TTF-1) and cytokeratin-7 (CK-7), while negative for cytokeratin 20 (CK-20) (Figures -).

So, a possibility of metastasis from a lung primary was considered. It was confirmed by a biopsy from the lung mass that revealed adenocarcinoma as the histopathology. On immunohistochemistry, it was positive for TTF-1 and CK-7 while negative for CK-20 and synaptophysin. Analysis for anaplastic lymphoma kinase, epidermal growth factor receptor, and receptor tyrosine kinase 1 were all negative but programmed death ligand 1 (PD-L1) tumor proportion score (TPS) was 90%. So, the final diagnosis was adenocarcinoma lung with multiple lung, liver, femur, as well as gastric metastases.

For the pathological fracture, he underwent fixation by intramedullary nailing followed by palliative external beam radiotherapy 8 Gy in a single fraction. He received 10 three", "Doctor: Good afternoon, Mr. Johnson. How are you feeling today?

Patient: Hmm, not too good, doctor. My hip still hurts and I'm having trouble walking.

Doctor: I see. You presented with complaints of pain in your right hip, correct?

Patient: Yes, that's right.

Doctor: And you're a known hypertensive on medication, a non-smoker, and you have no family history of cancer, is that correct?

Patient: Yes, that's right.

Doctor: We did some evaluations and found a pathological fracture at the neck of your right femur. We also did a Magnetic Resonance Imaging and found osteophyte complexes at C3-C4, C4-C5, C5-C6 vertebrae causing narrowing of neural foramina. Did you experience any other symptoms?

Patient: No, just the pain and difficulty walking.

Doctor: We also found multiple T2-hyperintense lesions in your lung parenchyma, which were an incidental finding. We did further evaluation with a PET-CT scan of your whole body and found a mass in the apex of your right lung, right hilum, mediastinal lymph node, soft tissue wall thickening in the proximal stomach, along with multiple liver and bone metastases. We did an upper GI endoscopy and found a proximal gastric growth from which a biopsy was taken. Histopathology showed poorly differentiated adenocarcinoma. Did you have any other symptoms related to your stomach?

Patient: No, I didn't have any stomach problems.

Doctor: The immunohistochemistry came out to be positive for thyroid transcription factor-1 (TTF-1) and cytokeratin-7 (CK-7), while negative for cytokeratin 20 (CK-20). So, a possibility of metastasis from a lung primary was considered. It was confirmed by a biopsy from the lung mass that revealed adenocarcinoma as the histopathology. On immunohistochemistry, it was positive for TTF-1 and CK-7 while negative for CK-20 and synaptophysin. Analysis for anaplastic lymphoma kinase, epidermal growth factor receptor, and receptor tyrosine kinase 1 were all negative but programmed death ligand 1 (PD-L1) tumor proportion score (TPS) was 90%. So, the final diagnosis was adenocarcinoma lung with multiple lung, liver, femur, as well as gastric metastases.

Patient: Oh no, that's not good news.

Doctor: We understand that this is difficult news to hear, but we will do everything we can to help manage your symptoms and provide the best care possible. For the pathological fracture, you underwent fixation by intramedullary nailing followed by palliative external beam radiotherapy 8 Gy

in a single fraction. You received 10 three-minute daily fractions of external beam radiotherapy to your hip. How have you been feeling since receiving treatment?

Patient: It's been a little better, but the pain is still there.

Doctor: We understand that it can take some time for the treatment to take effect. It's important to continue to follow up with us so we can monitor your progress and make any necessary adjustments to your treatment plan. Is there anything else you'd like to discuss or any questions you have for us?

Patient: No, I think that's all for now.

Doctor: Alright, we will schedule a follow-up appointment to check on your progress. If you have any concerns or experience any new symptoms, don't hesitate to contact us. We'll be here to support you every step of the way."

"A 90-year-old male was found in his home slumped to his right side and unable to be awakened. Paramedics calculated an 8/15 Glasgow Coma Scale (GCS) score, which remained the same on admission. On presentation to the hospital, the patient had left facial droop, bilateral pinpoint pupils, and right-sided weakness. The National Institutes of Health Stroke Scale (NIHSS) score on admission was 26, suggesting a severe stroke. All other observations on admission were non-revealing, including vital signs, biochemical tests, and systems review.

The patient's neurological medical history included two previous transient ischemic attacks and suspected dementia. Other past medical history included chronic obstructive pulmonary disease, hypertension, abdominal aortic aneurysm repair, stage 3 chronic kidney disease, adult polycystic kidney disease, hypercholesterolemia, and aortic valve sclerosis. He was an ex-smoker of unknown pack-years and prior to admission was living independently.

Initial head CT performed only showed chronic small vessel disease with periventricular leukoaraiosis, consistent with his age. Thrombolysis was initiated with an intravenous tissue-plasminogen activator, however, the patient's GCS declined to 6/15 approximately 40 minutes after the start of thrombolysis. A repeat head CT was performed, again showing no acute findings. To prevent further deterioration, a decision to monitor the patient's condition conservatively was made.

Over the next few days, the patient remained very somnolent. When the patient was able to awaken, he was only capable of responding to simple commands. Speech and language therapists noted that fatigue was limiting conversations, with the patient speaking with imprecise articulation and at a low volume. Occupational therapists concurred that the patient was poorly engaged during sessions, while physiotherapists classified this patient as having limited rehabilitation potential.

Stroke was finally confirmed upon a third head CT several days after admission, which showed", "Doctor: Hello, how are you feeling today?

Patient: Hmm, not too good.

Doctor: I see. Can you tell me about any symptoms you've been experiencing lately?

Patient: Well, I've been feeling weak on my right side and my face has been drooping.

Doctor: Have you also noticed any pinpoint pupils or difficulty speaking?

Patient: Yes, I have.

Doctor: Okay, based on your symptoms and the test results from your presentation, it appears that you've had a severe stroke.

Patient: Oh no.

Doctor: Yes, unfortunately your Glasgow Coma Scale score was 8/15 on admission and your NIHSS score was 26, which are both indicators of a serious stroke.

Patient: What does that mean for me?

Doctor: Well, we started you on thrombolysis to try to dissolve the blood clot causing the stroke, but your condition declined and we had to stop the treatment. We also performed a few head CT scans, which didn't show any acute findings.

Patient: I don't remember any of that.

Doctor: That's understandable, you were quite somnolent for a few days. When you were able to awaken, you had some difficulty speaking and following commands.

Patient: Yes, I remember that.

Doctor: Our team of speech and language therapists, occupational therapists, and physiotherapists all agree that your rehabilitation potential is limited.

Patient: Oh, I see.

Doctor: Unfortunately, upon a third head CT several days after admission, we confirmed that the cause of your symptoms was indeed a stroke. At this point, we will continue to monitor your condition conservatively.

Patient's Family: Is there anything else we can do for him?

Doctor: At this point, it's important for him to rest and for us to continue monitoring his vital signs and neurological function. We will also provide supportive care and address any other medical issues that arise."

"A 47-year-old male with a past medical history notable for hypertension on metoprolol succinate, morbid obesity, and pre-diabetes presented to the emergency department (ED) with a chief complaint of generalized weakness. The patient tested positive for COVID-19 and exhibited mild unspecified respiratory symptoms. He was subsequently discharged home to recover in isolation per the CDCs COVID-19 response protocols. One week later, the patient returned to the ED for ongoing symptoms and was admitted requiring supplemental oxygen for hypoxia. Upon admission to the hospital, the patient was noted to have difficulty standing and ambulating. Two days into his inpatient stay, the patient developed urinary retention issues requiring intermittent catheterization. Three days later, he developed facial weakness and numbness. The clinical diagnosis of GBS was suspected and subsequent EDX studies reported AIDP. The patient was treated with a five-day course of intravenous immune globulin (IVIG). Three days after the completion of his IVIG treatment, the patient noted improvement with right upper extremity anti-gravity strength.

The patient was transferred to inpatient rehabilitation with significant proximal lower extremity weakness. The bilateral upper extremities demonstrated slight weakness. The bilateral lower extremities demonstrated a significant loss of strength, 1/5 dorsiflexion, and 3/5 plantar flexion bilaterally. The patient also reported diminished sensation to light touch in bilateral upper extremities in all dermatomes. His blood pressure upon rehabilitation admission was 110/73 mmHg.

Prior to hospitalization, the patient was independent with mobility and all activities of daily living. Upon evaluation in the inpatient rehabilitation, the patient was at a significant functional decline from

baseline, requiring dependent assistance with toileting hygiene, showering, upper body dressing, lower body dressing, footwear management, rolling left and right, and all transfers. The patient was unable to ambulate due to his level of impairment. In inpatient rehabilitation, the patient completed three hours total of physical, occupational, and speech therapy per day five days a week with", "Doctor: Good morning! How are you feeling today?

Patient: Hmm, not great. I've been feeling really weak lately.

Doctor: Okay. Can you tell me a bit about your past medical history?

Patient: Sure. I have hypertension and I take metoprolol succinate for it. I'm also morbidly obese and have pre-diabetes.

Doctor: I see. And when did you first present to the emergency department?

Patient: A few weeks ago. I had mild respiratory symptoms and tested positive for COVID-19.

Doctor: Okay. You were discharged home to recover in isolation, correct?

Patient: Yes, that's right.

Doctor: And when did you return to the ED?

Patient: About a week later. My symptoms were getting worse.

Doctor: You were admitted and required supplemental oxygen for hypoxia. Did you have any difficulty standing or walking at that point?

Patient: Yes, I did. It was hard for me to move around.

Doctor: Okay. And during your inpatient stay, did you develop any other symptoms?

Patient: Yeah, I had urinary retention issues and then facial weakness and numbness.

Doctor: Based on your symptoms, it's possible that you had Guillain-Barre Syndrome. Did you have any EDX studies done?

Patient: Yes, they reported AIDP.

Doctor: I see. You were treated with intravenous immune globulin. Did you notice any improvement after the treatment?

Patient: Yes, my right arm started getting stronger.

Doctor: That's good to hear. You were then transferred to inpatient rehabilitation. How is your

strength now?

Patient: My upper body is okay, but I have significant weakness in my lower extremities.

Doctor: I see. And have you noticed any loss of sensation?

Patient: Yes, I have diminished sensation in both my upper extremities.

Doctor: Okay. Your blood pressure upon admission to rehab was 110/73 mmHg. How were you doing before hospitalization with mobility and activities of daily living?

Patient: I was independent. I could do everything on my own.

Doctor: And how are you doing now with those tasks?

Patient: I need a lot of help. I can't even walk on my own.

Doctor: I see. Well, we'll be starting you on physical, occupational, and speech therapy. You'll be doing three hours per day, five days a week.

Patient: Okay.

Doctor: And we'll be monitoring your progress closely. It's important to keep up with the therapy and follow-up requirements. If you or your family notice any changes in your condition, please let us know right away.

Patient: Okay, thank you."

"This is a case of a 4-year-old male who was brought to our clinic with complaints of four-day history of constipation, dry cough, vomiting, high fever (104 degF), abdominal pain with bloating, headache, and rash. The patient's symptoms started gradually with fatigue, loss of appetite, muscle aches, cough, bloated abdomen, and poor oral intake, prior to presenting to the hospital. The parents assumed it was stomach flu, and so managed their child's symptoms with Tylenol and soups. However, the patient continued to have constipation, abdominal discomfort, and eventually maculo-papular rashes on the head, face, and extremities erupted (Figure ).

On day 1, upon admission to the hospital, IV fluid with 0.9% normal saline solution was started, due to signs of dehydration, bradycardia, and hypotension. Norepinephrine was also administered. Lab samples (stool, urine, and blood) were collected for analysis, and abdominal ultrasound was ordered which showed clumps of worms in the jejunum which explained the constipation our patient had

(Figure ).

Stool test for helminth (stained with bile) showed rounded 45-78 micrometer long thick-shelled eggs indicative of roundworm infestation (*Ascaris lumbricoides*). Blood test came back positive for typhoid DNA and increased level of eosinophils with relatively high leukocytes. The rest of the complete blood count (CBC) was normal including a chest X-ray.

Following day 2 of in-hospital admission, the patient's condition remained unstable due to high fever (102 degF), vomiting, and fatigue. Antibiotics were initiated with ceftriaxone, antipyretics, albendazole, and more IV fluids.

Finally on day 3, the patient's symptoms improved clinically, although body rashes persisted. CBC had normalized, and he was later discharged home with one", "Doctor: Hello, how are you feeling today?

Patient: I'm not feeling too well.

Doctor: Can you tell me what your complaints are?

Patient: I have a dry cough, high fever, abdominal pain with bloating, headache, and rash.

Doctor: Okay, let me take a look at your medical history. Have you experienced any symptoms prior to this?

Patient: Yes, I had fatigue, loss of appetite, muscle aches, cough, and bloated abdomen.

Doctor: It sounds like your symptoms started gradually. Did you manage your symptoms with anything?

Patient: Yes, my parents gave me Tylenol and soups.

Doctor: I see. Did your symptoms improve?

Patient: No, I continued to have constipation and abdominal discomfort. Eventually, I developed maculo-papular rashes on my head, face, and extremities.

Doctor: Okay, let's take a look at your test results. Your stool test showed roundworm infestation and your blood test came back positive for typhoid with increased levels of eosinophils. Your CBC was normal including a chest X-ray.

Patient: What does that mean?



Doctor: It means you have a parasitic infection and a bacterial infection. We need to treat both infections.

Patient: How will you treat it?

Doctor: We will start you on antibiotics, antipyretics, and albendazole. We will also give you IV fluids with normal saline solution to treat your dehydration, bradycardia, and hypotension.

Patient: Will I need to stay in the hospital?

Doctor: Yes, we will need to monitor your condition closely. We will also order an abdominal ultrasound to see if there are any clumps of worms in your jejunum.

Patient: Okay, thank you.

Doctor: Don't worry, we will take good care of you."

"The patient was a 31-year-old male, a right-hand-dominant construction worker who was referred to our plastic surgery unit from a local minor injuries unit. He complained of pain in his left ring finger, following an inadvertent injury with a spray gun containing Newton 103-S (a type of liquid cement). The patient had been wearing protective gloves at the time of injury. He had no past medical history, took no regular medications, and had no allergies.

The patient had been given tetanus immunisation by the referring hospital. He had a plastic surgery review approximately three hours post-injury. On examination, his left ring finger was swollen, erythematous with necrotic skin on the volar aspect of the finger (Figure ). There was no evidence of distal vascular compromise and the dorsal skin was well-perfused. He had a complete loss of sensation in the distribution of the ulnar digital nerve; however, the radial digital nerve was clinically intact. There was decreased range of movement at both the proximal interphalangeal joint (PIPJ) and distal interphalangeal joint (DIPJ). The palmar skin was not involved.

Blood results and observations were within normal ranges. No X-rays were taken at the time of presentation. Broad-spectrum IV antibiotics were commenced, and the patient was taken to theatre for urgent debridement and washout under general anaesthetic.

The initial surgical approach consisted of Bruner incisions. Significantly hardened concrete was identified in the subcutaneous tissues (Figure ). It was evident that skin and subcutaneous tissues

were non-viable and were debrided, improving access. The pH of the wound was 8.5, in keeping with the alkaline substance injected; irrigation continued until pH returned to 7. The ulnar digital artery was thrombosed, but the radial digital artery was patent. The concrete had penetrated the flexor sheath, surrounding both flexor tendons. Subsequent flexor sheath washout from A1 to A5 confirmed that", "Doctor: Hello, how are you feeling today?

Patient: I'm in a lot of pain.

Doctor: I see. Can you tell me about the injury you sustained?

Patient: I'm a construction worker and I accidentally sprayed my left ring finger with Newton 103-S while wearing protective gloves.

Doctor: I understand. Were you referred to us from a minor injuries unit?

Patient: Yes, that's correct.

Doctor: Okay, let's take a look at your finger. On examination, your finger is swollen and erythematous with necrotic skin on the volar aspect.

Patient: Yes, that's where the spray hit me.

Doctor: I see. There is no evidence of distal vascular compromise and the dorsal skin is well-perfused. However, you have a complete loss of sensation in the distribution of the ulnar digital nerve.

Patient: Yes, that's right.

Doctor: Additionally, there is decreased range of movement at both the proximal interphalangeal joint and distal interphalangeal joint.

Patient: Yes, my finger feels stiff.

Doctor: The palmar skin is not involved. Blood results and observations were within normal ranges. No X-rays were taken at the time of presentation. Broad-spectrum IV antibiotics were commenced, and the patient was taken to theatre for urgent debridement and washout under general anaesthetic.

Patient: Okay, what does that mean?

Doctor: We needed to remove the damaged tissue and clean the wound thoroughly. During the surgery, we discovered hardened concrete in the subcutaneous tissues.

Patient: That sounds painful.

Doctor: It was, but we needed to do it to prevent further damage. The pH of the wound was 8.5, in keeping with the alkaline substance injected. We continued to irrigate until the pH returned to 7.

Patient: Does that mean the substance is out of my body?

Doctor: Yes, we removed as much of it as we could. The ulnar digital artery was thrombosed, but the radial digital artery was patent. The concrete had penetrated the flexor sheath, surrounding both flexor tendons. Subsequent flexor sheath washout from A1 to A5 confirmed that we removed all of the concrete.

Patient: Thank you for taking care of me.

Doctor: Of course, it's our job to make sure you're healthy. Is there anything else you're concerned about?

Patient: No, I just hope I can recover from this soon.

Doctor: We'll make sure to follow up with you and monitor your progress. If you have any concerns, don't hesitate to contact us."

"A 46-year-old male patient was admitted to the hospital with intermittent back pain and chest tightness for 2 weeks. The patient works in ozone disinfection. Prior to symptom onset, he had a history of acute ozone inhalation. He recalled smelling something more pungent than usual for several days. Before coming to our hospital, he had not undergone any treatment. In addition, he denied any history of chest trauma. He had suffered from hypertension for over a decade and was treated with oral nifedipine and metoprolol. However, medication poorly controlled his blood pressure. The highest recorded systolic blood pressure with treatment was 180 mmHg. His blood pressure upon admission was 148/91 mmHg.

An echocardiogram revealed a left SVA that ruptured into the left-ventricular myocardium, forming an echo-lucent cavity (). The left-ventricular wall had thickened resulting in uncoordinated motion and reduced systolic function. Moreover, moderate eccentric aortic regurgitation was also noted. Furthermore, CT angiograms better captured a large, left-ventricular, IPA arising from a small perforation in the left SVA (). The adjacent left ventricle and interventricular septum were

compressed. With CMR examination, late gadolinium enhancement (LGE) clearly demonstrated the left-ventricular IPA with distal thrombus and a linear enhancement of the IPA wall, compatible with myocardial fibrosis ().

Subsequently, the patient underwent surgery where the perforation was sutured and repaired, and the left aortic valve was lengthened with pericardial patches. Three weeks after surgery, a follow-up echocardiogram demonstrated the cessation of the abnormal blood flow in the left sinus of Valsalva ().", "Doctor: Good morning, Mr. Smith. I see that you were admitted to the hospital recently. How are you feeling now?

Patient: Hmm, not too good. I've been having intermittent back pain and chest tightness for about 2 weeks now.

Doctor: I see. Can you tell me more about your work? You mentioned something about ozone disinfection?

Patient: Yes, that's right. I work with ozone disinfection. Before my symptoms started, I remember smelling something more pungent than usual for several days.

Doctor: Okay, that's helpful information. Do you have any history of chest trauma?

Patient: No, I don't.

Doctor: And have you had any treatment for your symptoms prior to coming to our hospital?

Patient: No, I haven't.

Doctor: I see that you've suffered from hypertension for over a decade. How has it been treated?

Patient: I've been taking oral nifedipine and metoprolol, but it hasn't been controlling my blood pressure very well.

Doctor: I see. The highest recorded systolic blood pressure with treatment was 180 mmHg. And what was your blood pressure upon admission?

Patient: It was 148/91 mmHg.

Doctor: Okay. After conducting an echocardiogram, we found that a left sinus of Valsalva had ruptured into the left-ventricular myocardium, forming an echo-lucent cavity. Additionally, the left-ventricular wall had thickened, resulting in uncoordinated motion and reduced systolic function.

Moderate eccentric aortic regurgitation was also noted.

Patient: I see.

Doctor: We also conducted CT angiograms which better captured a large, left-ventricular, IPA arising from a small perforation in the left SVA. The adjacent left ventricle and interventricular septum were compressed. With CMR examination, late gadolinium enhancement (LGE) clearly demonstrated the left-ventricular IPA with distal thrombus and a linear enhancement of the IPA wall, compatible with myocardial fibrosis.

Patient: Okay...

Doctor: As a result of these findings, you underwent surgery where the perforation was sutured and repaired, and the left aortic valve was lengthened with pericardial patches. Three weeks after surgery, a follow-up echocardiogram demonstrated the cessation of the abnormal blood flow in the left sinus of Valsalva.

Patient: Okay, thank you for explaining everything to me.

Doctor: Of course. It's important that you continue to monitor your blood pressure and follow-up with any recommended treatments or medications. We'll schedule regular check-ups to monitor your progress. Is there anyone from your family that I can speak to about your condition and treatment?

Patient: Yes, my wife would be the best person to speak to."

Patient 1: A 64-year-old man with a left inferior visual field deficit and headache. The CT angiography showed a left superior carotid-ophthalmic aneurysm (4 x 5 mm) ().,"Doctor: Good morning, how are you feeling today?

Patient: I'm not feeling too well, Doctor. I have a headache and I'm experiencing difficulty with my left visual field.

Doctor: I see. How long has this been going on?

Patient: It's been a few days now, Doctor.

Doctor: Alright. Based on your symptoms, I would like to recommend a CT angiography to get a clearer picture of what's going on. Have you had one before?

Patient: No, I haven't.

Doctor: Okay. The CT angiography results showed a left superior carotid-ophthalmic aneurysm that measures 4 by 5 millimeters.

Patient: What does that mean, Doctor?

Doctor: An aneurysm is a bulge in a blood vessel that can potentially rupture and cause bleeding in the brain. In your case, the aneurysm is located in the left superior carotid-ophthalmic region, which is why you're experiencing a deficit in your left visual field. The size of the aneurysm is 4 by 5 millimeters, which means it's relatively small at this stage.

Patient: What are my treatment options, Doctor?

Doctor: We can either monitor the aneurysm over time and wait for it to grow before considering surgery, or we can perform a coiling procedure to prevent the aneurysm from rupturing.

Patient: What do you recommend, Doctor?

Doctor: Based on the size and location of the aneurysm, I would recommend monitoring it for now and scheduling regular follow-up appointments to keep an eye on any changes. If the aneurysm grows or if you experience any worsening symptoms, we can revisit the option of surgery.

Patient: Okay, that sounds good. What should I expect in terms of follow-up appointments?

Doctor: We'll need to do another CT angiography in about six months to see if there have been any changes to the aneurysm. In the meantime, I'll prescribe some medication to help manage your headache and monitor your blood pressure to make sure it's stable.

Patient: Thank you, Doctor. Is there anything else I need to know?

Doctor: Just make sure to follow up with me regularly and let me know if you experience any new symptoms or if your headache worsens. If anything urgent comes up, don't hesitate to contact me or seek emergency medical attention."

"Patient 2: A 43-year-old woman with subarachnoid hemorrhage, classified as Fisher I, Hunt, and Hess II. In the digital 3D angiographic reconstruction multiple aneurysms are observed: a right M1 aneurysm and a right superior carotid-ophthalmic aneurysm ()." "Doctor: Good morning, how are you feeling today?

Patient: Not so good, my head still hurts a lot.

Doctor: I see. Can you tell me more about your symptoms?

Patient: Well, I had a really bad headache and then suddenly felt a sharp pain in my head.

Doctor: Okay, I need to tell you that you have a subarachnoid hemorrhage. That means that there was bleeding in the space between your brain and the tissues that cover it.

Patient: Oh no, is it serious?

Doctor: It can be. In your case, we also found multiple aneurysms in a digital 3D angiographic reconstruction, specifically a right M1 aneurysm and a right superior carotid-ophthalmic aneurysm.

Patient: What does that mean?

Doctor: It means that there are bulges in the walls of some of your blood vessels, which can cause bleeding and put you at risk for stroke or other complications. We need to monitor these aneurysms closely and may need to perform surgery to fix them.

Patient: Okay, what do I need to do now?

Doctor: Right now, we need to keep you in the hospital for observation and further tests. We may need to perform a digital angiographic reconstruction to get a better idea of what's going on. In the meantime, we'll manage your pain and keep you comfortable.

Patient: Thank you, doctor.

Doctor: Of course. Do you have any other questions for me?

Patient: No, I think that covers it.

Doctor: Okay. We'll keep you updated on your condition and what we find in the tests. If you have any concerns or questions, don't hesitate to ask.

Patient: Okay, thank you.

(If the patient eventually dies, a family member may enter the conversation at this point.)

Family member: Doctor, what happened to our loved one?

Doctor: I'm sorry to tell you this, but despite our best efforts, your loved one passed away due to complications from the subarachnoid hemorrhage and aneurysms. We did everything we could to manage their pain and keep them comfortable. Please accept our condolences.

Family member: Thank you, doctor. We appreciate everything you did for them."

"A 77-year-old woman was hospitalized in the cardiology department due to atrial fibrillation. Contraindications were excluded, and atrial fibrillation (AF) ablation was performed on an optional schedule. However, abdominal contrast-enhanced computed tomography (CT) scan found a circular and low-density lesion in the Segment 4 of the liver with unclear border, approximately 15 mmx 12 mm in size, which was mildly progressive enhanced in the arterial phase and portal phase. HCC was suspected, but no hepatic cirrhosis and history of hepatitis (). Tumor markers, including CEA, CA199, CA125, AFP, were within normal range, hepatitis panel was negative, and hepatic function was normal.

To confirm the diagnosis, the patient underwent further examinations. Abdominal magnetic resonance imaging (MRI) disclosed one nodule in the segment 7, one nodule in the segment 5, and two nodules in the segment 4 of the liver (4, 6, 17, and 6 mm in diameter), respectively. The larger one was located in the segment 4 of liver, with hypointense on T1-weighted images (T1WI) and hyperintense on T2-weighted images (T2WI), which showed significant enhancement on the arterial phase and slight washout on the portal phase. In the delayed phase, the edge of the tumor was underscored as a circular enhancement which is unsimilar to the enhancement method of dynamic CT. It showed a significant restriction of diffusion on diffusion weighted images (DWI) and apparent diffusion coefficient (ADC). Other lesions in segments 7 and 5 showed the same hemodynamic characteristics as the tumor in segment 4 (). Based on MRI findings, it is considered as tumorous lesions of the liver.

For further differential diagnosis, the patient underwent positron emission tomography-computer tomography (PET-CT) examination, founding that the segment 4 of liver had a slightly low-density lesion with increased uptake of <sup>18</sup>F-fluoro-deoxy-glucose (FDG), and SUVmax of early and", "Doctor: Good morning, Mrs. Smith. How are you feeling today?

Patient: I'm feeling okay, thank you.

Doctor: I see from your medical records that you were hospitalized in the cardiology department due to atrial fibrillation. Is that correct?

Patient: Yes, that's correct.



Doctor: Were any contraindications excluded before the AF ablation was performed?

Patient: Yes, they were.

Doctor: That's good to know. However, during your abdominal contrast-enhanced computed tomography (CT) scan, a circular and low-density lesion was found in Segment 4 of your liver with an unclear border. Did you experience any symptoms related to this?

Patient: No, I didn't feel anything unusual.

Doctor: That's interesting. The lesion was approximately 15 mm x 12 mm in size and progressively enhanced in the arterial phase and portal phase. Hepatocellular carcinoma (HCC) was suspected, but no hepatic cirrhosis or history of hepatitis was found. Your tumor markers, including CEA, CA199, CA125, AFP, were within the normal range, hepatitis panel was negative, and hepatic function was normal. We wanted to confirm the diagnosis, so you underwent further examinations.

Patient: Yes, I remember.

Doctor: Your abdominal magnetic resonance imaging (MRI) disclosed one nodule in segment 7, one nodule in segment 5, and two nodules in segment 4 of the liver (4, 6, 17, and 6 mm in diameter), respectively. The larger one was located in segment 4 of the liver, with hypointense on T1WI and hyperintense on T2WI, which showed significant enhancement on the arterial phase and slight washout on the portal phase. In the delayed phase, the edge of the tumor was underscored as a circular enhancement which is unsimilar to the enhancement method of dynamic CT. It showed a significant restriction of diffusion on diffusion weighted images (DWI) and apparent diffusion coefficient (ADC). Other lesions in segments 7 and 5 showed the same hemodynamic characteristics as the tumor in segment 4. Based on MRI findings, it is considered as tumorous lesions of the liver.

Patient: I see.

Doctor: For further differential diagnosis, you underwent positron emission tomography-computer tomography (PET-CT) examination, founding that the segment 4 of liver had a slightly low-density lesion with increased uptake of <sup>18</sup>F-fluoro-deoxy-glucose (FDG), and SUVmax of early and delayed images were 3.7 and 3.6, respectively. I'm sorry to say that after considering all of these findings, it's

highly likely that you have liver cancer.

Patient: Oh no, that's terrible news.

Doctor: I understand how you feel. We will discuss the best treatment options for you moving forward. In the meantime, we will need to monitor your condition closely. Please come back for regular check-ups and follow-up examinations.

Patient: Okay, I will.

Doctor: Is there anyone in your family we can contact to provide support during this difficult time?

Patient: Yes, please contact my daughter. Her number is XXX-XXX-XXXX.

Doctor: Thank you, we will do that. Please take care of yourself, Mrs. Smith.

Patient: Thank you, doctor."

"Patient 1 was a 45-year-old right-handed woman, who sought treatment for a depressive episode. The current episode onset was placed after a switch from sertraline to vortioxetine due to unbearable side effects (nausea and headache). She suffered from her first depressive episode at the age of 25, then alternating depressive and hypomanic episodes, which led clinicians to a diagnosis of BD-II.

The patient has also been suffering from EDs since her adolescence: she was diagnosed with anorexia nervosa at the age of 13; she then shifted to a bulimic eating pattern, with binge episodes followed by purging behaviors. This phase lasted for 10 years, followed by a complete remission until the age of 38. At this age she developed BED. Once a week or more she used to wake up at night and eat everything she could find in the fridge, including raw food. After these episodes she used to feel guilty and nauseated, but she did not show purging behavior anymore. She felt very uncomfortable due to either the loss of control or her weight gain. Her private psychiatrist then diagnosed her with BED, but apparently, she did not receive any psychological or pharmacological specific support. In the following years she had alternating periods of remission with periods of active disease. She denied alcohol or other psychoactive substances consumption. In the 2 months previous to our study, she had gained 12 kg, with 3-4 binge episodes per week on average. She denied medical comorbidities. When she first came to our attention, her therapy was the following:

lamotrigine (150 mg daily), vortioxetine (20 mg daily). She was suffering from a depressive episode defined as mild according to the Hamilton Rating Scale for Depression (HAMD) and moderate according to the Montgomery-Asberg Depression Rating Scale (MADRS) ().", "Doctor: Hello, how are you feeling today?

Patient: I'm not feeling very well, doctor.

Doctor: I see. Can you tell me more about what's been going on?

Patient: Well, I've been feeling really down and I think I might be having another depressive episode.

Doctor: I understand. It says here in your medical history that you've suffered from depressive episodes before. When did this one start?

Patient: It started after I switched from sertraline to vortioxetine because of some side effects I was experiencing, like nausea and headaches.

Doctor: I see. And you've also had hypomanic episodes in the past, correct?

Patient: Yes, that's right.

Doctor: It's important that we treat both the depressive and hypomanic episodes. In addition to the vortioxetine, you are also taking lamotrigine. How has that been working for you?

Patient: It's been helping a bit, but I still feel pretty low.

Doctor: I understand. It's also noted here that you've been struggling with eating disorders since your adolescence. Can you tell me more about that?

Patient: Yes, I was diagnosed with anorexia nervosa when I was 13, and then later shifted to a bulimic eating pattern with binge episodes followed by purging behaviors. After that phase ended, I had a complete remission until I was 38 and then I developed BED.

Doctor: I see. And how often are you experiencing binge episodes now?

Patient: About 3-4 times a week on average.

Doctor: That's a lot. Have you noticed any medical comorbidities?

Patient: No, I haven't noticed anything else.

Doctor: Alright, we'll keep an eye on that. In the meantime, I want you to continue taking your medication as prescribed and we'll also schedule some follow-up appointments to monitor your

progress."

"The second patient we are reporting is a 28-year-old right-handed woman, who came to our attention for a severe depressive episode. Her psychopathological onset is placed 10 years ago; she developed her first depressive episode with comorbid panic attacks. From that moment the patient has alternated phases of depression with sporadic episodes of elation, thus a sign of hypomanic episodes, which led clinicians to a diagnosis of BD-II. Her depressive phases used to have a seasonal pattern, with autumn or winter worsening. When she came to our attention (November 2020), the current episode had been lasting for 3 months, according to her seasonal pattern. She reported low consumption of alcohol in social circumstances and sporadic use of cannabis in her adolescence.

Regarding her ED, binge behaviors were reported to happen from the first diagnosis of depression, with various degrees of intensity and severity, and appeared to be more intense in depressive phases. Binge eating episodes during depressive phases used to be daily. No compensatory behaviors were ever observed. Notably, her first BED diagnosis was given in our center during her last depressive episode, as she had always been trying to hide her eating behaviors, even with physicians. Along with the current depression, she referred almost daily binge eating: after her dinner she used to go out and then buy and rapidly eat large amounts of high-fat food. This used to cause both physical and psychological distress.

In her past pharmacological history, many pharmacological therapies had been prescribed (i.e., valproate, fluoxetine, citalopram, venlafaxine, and bupropione) and when she came to our attention her therapy was clomipramine (150 mg daily) and pregabalin (225 mg daily). Her depressive symptoms at baseline were severe according to both MADRS and HAMD ( ).", "Doctor: Hello there, how are you feeling today?

Patient: I'm not feeling too great, I've been having a severe depressive episode.

Doctor: I see. According to your medical history, you developed your first depressive episode with comorbid panic attacks about 10 years ago.

Patient: Yes, that's correct.

Doctor: And you've been experiencing sporadic episodes of elation, which is a sign of hypomanic episodes, leading to a diagnosis of BD-II. Your depressive phases used to have a seasonal pattern, with autumn or winter worsening.

Patient: That's right.

Doctor: I also see that you've reported low consumption of alcohol in social circumstances and sporadic use of cannabis in your adolescence. Is that still the case?

Patient: Yes, I don't drink too much and I don't use cannabis anymore.

Doctor: Okay, thank you for letting me know. Now, regarding your eating behaviors, it has been reported that you've had binge behaviors from the first diagnosis of depression. Can you tell me more about that?

Patient: Yes, I tend to binge eat when I'm feeling depressed. It used to happen daily during my depressive phases.

Doctor: I understand. And during this current episode, you've referred to almost daily binge eating, particularly after dinner when you go out and buy and rapidly eat large amounts of high-fat food, causing both physical and psychological distress. Is that correct?

Patient: Yes, that's exactly what's been happening.

Doctor: I see. In terms of your pharmacological history, you've been prescribed many therapies in the past, including valproate, fluoxetine, citalopram, venlafaxine, and bupropione. Currently, your therapy is clomipramine and pregabalin, which you've been taking daily. Is that still the case?

Patient: Yes, I'm still taking those medications.

Doctor: I understand. Your depressive symptoms at baseline were severe according to both MADRS and HAMD. It's important that you continue to take your medication as prescribed and follow up with me regularly."

"Patient 1: A 65-year-old male was diagnosed with AML in January 2020 with the manifestation of leukocytosis, thrombocytopenia and anaemia. BM aspiration revealed a hypercellular BM with 50% blasts. Flow cytometry showed the immunophenotype of myeloid blasts. Cytogenetics revealed a complex karyotype, and a molecular panel identified aberrations in ASXL1, CEBPA, JAK2, and

RUNX1. None of the 41 gene fusions were detected by using multiple RT-PCR assay (). Therefore, AML with adverse risk was diagnosed according to genetic risk stratification (). After one course of induction treatment with the IA regimen [idarubicin 12 mg/m<sup>2</sup> day1-3, cytarabine 100 mg/m<sup>2</sup> continuous infusion day1-7.], the patient achieved complete remission with minimal residual disease as low as 5.8x10<sup>-4</sup> by flow cytometry analysis. Genetic analyses showed that all gene mutations were negative. Subsequently, the patient refused bone marrow transplant for financial reasons. He received one course of the IA regimen and 3 courses of the high-dose Ara-c (HiDAC) regimen [cytarabine 2 g/m<sup>2</sup> over 3 h every 12 h on day1-3.] as consolidation therapies. However, the remission duration only lasted for 11 months. In November 2020, relapsed BM morphology was detected, with 17.5% blasts concurrent with molecular aberration recurrence. Therefore, relapsed AML was diagnosed. Initially, venetoclax combined with azacitidine [VA, venetoclax once daily (100 mg day1, 200 mg day2, 400 mg day3-28) and azacitidine 75 mg/m<sup>2</sup> day1-7.] was administered as a salvage therapy, an effective regimen recommended for the treatment of R/R AML patients who are ineligible for intensive salvage chemotherapy, but progressive disease was observed. Then, his treatment plan switched to a chidamide combined with venetoclax plus azacitidine", "Doctor: Hi, how are you feeling today?

Patient: Not great, doctor. I've been feeling really weak and tired lately.

Doctor: I see. Well, according to your clinical notes, you were diagnosed with AML earlier this year. Can you tell me more about the symptoms you experienced?

Patient: Yes, I had leukocytosis, thrombocytopenia, and anemia.

Doctor: And did you have any tests done to confirm the diagnosis?

Patient: Yes, I had a BM aspiration that showed a hypercellular BM with 50% blasts. Flow cytometry revealed the immunophenotype of myeloid blasts, and cytogenetics showed a complex karyotype with molecular aberrations in ASXL1, CEBPA, JAK2, and RUNX1.

Doctor: I see. And none of the 41 gene fusions were detected by using multiple RT-PCR assay, so AML with adverse risk was diagnosed according to genetic risk stratification. After one course of induction treatment with the IA regimen, you achieved complete remission with minimal residual

disease as low as  $5.8 \times 10^{-4}$  by flow cytometry analysis. Genetic analyses showed that all gene mutations were negative.

Patient: Yes, that's correct.

Doctor: Subsequently, you refused bone marrow transplant for financial reasons and received one course of the IA regimen and 3 courses of the high-dose Ara-c regimen as consolidation therapies. However, the remission duration only lasted for 11 months. In November 2020, relapsed AML was diagnosed.

Patient: Yes, that's right.

Doctor: Initially, venetoclax combined with azacitidine was administered as a salvage therapy, but progressive disease was observed. Then, your treatment plan switched to chidamide combined with venetoclax plus azacitidine.

Patient: Okay, I understand. What are the next steps?

Doctor: We need to closely monitor your progress and adjust your treatment plan as necessary. It's important to keep up with all your appointments and lab tests. Do you have any questions?

Patient: No, I think I understand everything. Thank you, doctor.

Doctor: Of course. And if you have any concerns or experience any new symptoms, don't hesitate to reach out. We're here to help."

"Patient 2: A 57-year-old male was diagnosed with AML in July 2016. Investigation revealed a pancytopenia. BM examination showed a hypercellular marrow with 65% myeloid blasts. Flow cytometry analysis showed the immunophenotype of myeloid blasts. Cytogenetics revealed del (1)(q22q36), and a molecular panel identified aberrations in DNMT3A and IDH2. The patient achieved CR after 1 cycle of the IA regimen [idarubicin 12 mg/m<sup>2</sup> day1-3, cytarabine 100 mg/m<sup>2</sup> continuous infusion day1-7.] and received 6 courses of the HiDAC regimen [cytarabine 2 g/m<sup>2</sup> over 3 h every 12 h on day1-3.] as consolidation therapies while not adopting allogeneic haematopoietic stem cell transplantation. The patient experienced his first relapse 2 years after first remission with a 9% immature cell level in the BM and was treated with the CAG [cytarabine 10 mg/m<sup>2</sup> every 12 h, day1-14; aclarubicin 5-7 mg/m<sup>2</sup>, daily on day1-8; and concurrent use of G-CSF 200 ug/m<sup>2</sup>/day.]

regimen for 3 cycles, resulting in a second CR in March 2019. A second relapse occurred 20 months later. The patient began the VA regimen [venetoclax once daily (100 mg day1, 200 mg day2, 400 mg day3-28) and azacitidine 75 mg/m<sup>2</sup> day1-7.], but no response was observed after 2 courses of therapies. Finally, the patient received a chidamide combined with venetoclax plus azacitidine regimen [chidamide 5 mg daily day1-7, venetoclax 100 mg day1, 200 mg day2, 400 mg day3-21; azacitidine 75 mg/m<sup>2</sup> daily day1-7.] as salvage therapy as described above. The patient achieved his third CR.", "Doctor: Good morning, how are you feeling today?

Patient: I'm feeling okay, thanks.

Doctor: So, you were diagnosed with AML?

Patient: Yes, back in July 2016.

Doctor: And what were your symptoms at the time?

Patient: I was experiencing pancytopenia.

Doctor: I see, and what did the examination reveal?

Patient: A hypercellular marrow with 65% myeloid blasts.

Doctor: Okay, and what did the flow cytometry analysis show?

Patient: The immunophenotype of myeloid blasts.

Doctor: And what about the Cytogenetics results?

Patient: They revealed del ( ) (q22q36), and a molecular panel identified aberrations in DNMT3A and IDH2.

Doctor: I see. So, you achieved CR after 1 cycle of the IA regimen?

Patient: Yes, that's correct.

Doctor: And then you received 6 courses of the HiDAC regimen as consolidation therapies while not adopting allogeneic haematopoietic stem cell transplantation?

Patient: Yes, that's right.

Doctor: Okay, and you experienced your first relapse 2 years after first remission, correct?

Patient: Yes, that's correct.

Doctor: And you were treated with the CAG regimen for 3 cycles, resulting in a second CR in March



2019?

Patient: Yes, that's right.

Doctor: And a second relapse occurred 20 months later?

Patient: Yes, unfortunately.

Doctor: And you began the VA regimen, but no response was observed after 2 courses of therapies?

Patient: Yes, that's correct.

Doctor: Okay, and finally, you received a chidamide combined with venetoclax plus azacitidine regimen as salvage therapy?

Patient: Yes, and thankfully, I achieved my third CR.

Doctor: That's great news. I'll need to schedule some follow-up appointments to monitor your progress."

"Patient 3: A 60-year-old female was diagnosed with AML in December 2020. BM examination showed a hypercellular marrow with 32% myeloid blasts. A molecular panel identified aberrations in RUNX1. Karyotype was normal. All patient baseline characteristics at diagnosis and treatment characteristics are shown in . For induction therapy, the patient received the VA [venetoclax once daily (100 mg day1, 200 mg day2, 400 mg day3-28) and azacitidine 75 mg/m<sup>2</sup> day1-7.] regimen and achieved CR after one course. Subsequently, she continued two courses of VA as consolidation therapy, but progressive disease was observed during the second course, with 67% blasts in BM. Then, a chidamide combined with venetoclax plus azacitidine regimen [chidamide 5 mg daily day1-7, venetoclax 100 mg day1, 200 mg day2, 400 mg day3-21; azacitidine 75 mg/m<sup>2</sup> daily day1-7.] was given. After one course, the patient obtained CR. Treatment process is shown in . During the whole course, no severe adverse events occurred. After 1 month of follow-up, the patient remains in CR at the time of writing.", "Doctor: Hello, how are you feeling today?

Patient: I'm okay, thank you.

Doctor: I see from your medical record that you were diagnosed with AML in December 2020. Can you tell me more about your symptoms at the time?

Patient: I was feeling very tired and weak, and I had some unusual bruising.

Doctor: I see. And did you undergo a BM examination?

Patient: Yes, I did.

Doctor: And what were the results of the examination?

Patient: The examination showed a hypercellular marrow with 32% myeloid blasts.

Doctor: I see. And a molecular panel was also performed, correct?

Patient: Yes, that's right.

Doctor: And the molecular panel identified aberrations in RUNX1. The Karyotype was normal, correct?

Patient: Yes, that's correct.

Doctor: Okay. Based on your baseline characteristics at diagnosis, we started you on induction therapy with the VA regimen, which includes venetoclax and azacitidine. You achieved CR after one course. How did you feel during the induction therapy?

Patient: I felt okay, a bit tired, but no severe adverse events occurred.

Doctor: I'm glad to hear that. After induction therapy, we continued with two courses of VA as consolidation therapy, but unfortunately, progressive disease was observed during the second course, with 67% blasts in BM. So, we started you on a new regimen, which includes chidamide combined with venetoclax and azacitidine. How did you feel during this treatment?

Patient: I felt okay, a bit tired, but no severe adverse events occurred.

Doctor: I'm glad to hear that. After one course of the new regimen, you obtained CR. After 1 month of follow-up, you remain in CR at the time of writing. Do you have any questions or concerns?

Patient: No, I don't have any questions or concerns at the moment."

"A 54-year-old Caucasian male patient was referred to our institution, initially with the diagnosis of a T-cell lymphoma, not otherwise specified, which was refractory to two courses of chemotherapy (CHOEP: cyclophosphamide, doxorubicine, vincristine, etoposide and prednisolone). At presentation an erythroderma involving >90% of the integument was predominant (). Computer tomography (CT) scans showed enlarged axillary, inguinal and cervical lymph nodes. The complete blood counts

showed a leukocytosis of 24,300/ul. Flow cytometry of the pb revealed 11,664 Sezary cells/ul with CD4+CD7- phenotype and with a CD4:CD8 ratio of 85.5. Flow cytometry of the bone marrow aspirate confirmed CD30 positivity with expression of 7% in Sezary cells. Polymerase chain reaction of pb confirmed the clonality in T-cell receptor beta and gamma showing monoclonal Vb-b2 and two clonal Vg1-8-Jg1.1 and 2.1 rearrangements. While conventional cytogenetics showed a normal male karyotype, fluorescent in situ hybridization (FISH) detected the deletion of chromosome 17p in 22 of 200 interphases with deletion of TP53 gene. Immunohistochemistry of both trephine biopsy ( ) and skin histology revealed infiltrations with Sezary cells ( ). The skin histology also confirmed CD30 positivity with 5-10%, and the diagnosis was revised to SS.

The diagnosis was thus revised to Sezary Syndrome in Stage IVA (pT4 Nx M0 B2) according to the updated classification of International Society for Cutaneous Lymphomas (ISCL) and the European Organization of Research and Treatment (EORTC) ( ).

Subsequently, successive therapies with 3,000,000 IU interferon alpha three times weekly for 6 months, combined with 10 mg/m<sup>2</sup> methotrexate (MTX) and 19 courses ECP including bex", "Doctor: Good morning, Mr. Smith. How are you feeling today?

Patient: I'm feeling okay, doctor. Thank you.

Doctor: I see you were referred to our institution with a diagnosis of T-cell lymphoma, not otherwise specified. Is that correct?

Patient: Yes, that's right.

Doctor: I understand that you received two courses of chemotherapy with cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisolone, but unfortunately, it was refractory. Is that correct?

Patient: Yes, that's correct.

Doctor: At presentation, you had an erythroderma involving over 90% of the integument, and computer tomography scans showed enlarged axillary, inguinal, and cervical lymph nodes. Did you experience any other symptoms at that time?

Patient: I was feeling very fatigued and had night sweats.

Doctor: I see. The complete blood counts showed a leukocytosis of 24,300/ul. We also performed flow cytometry, which revealed 11,664 Sezary cells/ul with a CD4+CD7- phenotype and a CD4:CD8 ratio of 85.5.

Patient: I don't understand what that means.

Doctor: Essentially, it means that the cancer cells were present in your blood and had a certain phenotype and ratio. We also confirmed the clonality of the T-cell receptor beta and gamma by polymerase chain reaction and detected the deletion of chromosome 17p in 22 of 200 interphases with deletion of TP53 gene by fluorescent in situ hybridization.

Patient: Okay, I see.

Doctor: Immunohistochemistry of both trephine biopsy and skin histology revealed infiltrations with Sezary cells and CD30 positivity with 5-10%, and the diagnosis was revised to Sezary Syndrome. You are in Stage IVA.

Patient: Is that bad?

Doctor: It's a serious diagnosis, but we have treatment options available. You have already received interferon alpha, methotrexate, and extracorporeal photopheresis (ECP). How have you been responding to those treatments?

Patient: I think I've been responding well.

Doctor: That's good to hear. We will need to continue monitoring your response to treatment and possibly adjust your therapy as needed. Do you have any questions for me?

Patient: No, not at the moment.

Doctor: Alright then. We will schedule a follow-up appointment for you and make sure to keep monitoring your progress. If you have any concerns or side effects, please don't hesitate to reach out to us."

"The first case was that of a 37-year-old man. At admission, the patient was diagnosed with septic shock, previous total cystectomy with ileal bladder replacement, urinary retention with pyuria, chronic renal insufficiency stage V, and neurogenic bladder. In addition, the patient's vital signs were unstable, and noradrenaline and phenylephrine were required to maintain blood pressure after fluid

resuscitation. Blood culture analyses were negative. *Escherichia coli* [extended spectrum beta-lactamase (ESBL) +], *Enterococcus avium*, and *Enterococcus faecium* were detected in the drainage fluid of the ileostomy. The antibiotic regimen at admission was 1000 mg meropenem q12 h ivgtt combined with vancomycin (loading dose on D1 of 1500 mg and maintenance dose of 1000 mg on D2). CVVH was also administered. From D7, the patient's condition tended to be stable, and the CVVH frequency was reduced to every other day. On D9, puncture and catheterization of left subphrenic effusions were conducted under the guidance of B-ultrasound. *Escherichia coli* (ESBL+) and *Enterococcus avium* were identified in the drainage fluid. The intra-abdominal infection improved and the function of organs other than the kidney returned to normal. On D22, the culture of drainage fluid was negative, thus vancomycin and meropenem were stopped. On D26, the patient was transferred out of the intensive care unit and resumed routine hemodialysis.", "Doctor: Good morning, how are you feeling today?

Patient: I'm feeling a little better, but still weak.

Doctor: I see, well let's go over your medical history. You were admitted with septic shock, a previous total cystectomy with ileal bladder replacement, and urinary retention with pyuria.

Patient: Yes, that's correct.

Doctor: Your vital signs were unstable at admission, and we had to use noradrenaline and phenylephrine to maintain your blood pressure after fluid resuscitation.

Patient: I remember feeling very weak and dizzy.

Doctor: We also did blood culture analyses, which turned out negative. However, we did detect *Escherichia coli* (ESBL+), *Enterococcus avium*, and *Enterococcus faecium* in the drainage fluid of your ileostomy.

Patient: I see.

Doctor: At admission, we started you on an antibiotic regimen of 1000 mg meropenem q12 h ivgtt combined with vancomycin. We also administered CVVH.

Patient: What's CVVH?

Doctor: It stands for continuous venovenous hemofiltration, which is a type of dialysis that helps

remove excess fluids and waste from your blood.

Patient: Okay.

Doctor: From D7, your condition started to stabilize, and we were able to reduce the frequency of CVVH to every other day.

Patient: That's good to hear.

Doctor: On D9, we had to do a puncture and catheterization of your left subphrenic effusions under the guidance of B-ultrasound. We found *Escherichia coli* (ESBL+) and *Enterococcus avium* in the drainage fluid.

Patient: Was that serious?

Doctor: It was concerning, but we were able to treat it with antibiotics and the intra-abdominal infection improved. Your other organs also returned to normal function.

Patient: That's a relief.

Doctor: On D22, we found that the culture of the drainage fluid was negative, so we stopped the vancomycin and meropenem. And on D26, you were transferred out of the intensive care unit and resumed routine hemodialysis.

Patient: Thank you for explaining everything to me."

"The second case was that of a 93-year-old woman. Her diagnosis at admission included a gallstone, acute attack of chronic cholecystitis, biliary pancreatitis, septic shock, and multiple organ dysfunction syndrome. The surgeons performed endoscopic retrograde cholangiopancreatography to relieve the biliary obstruction. The growth of *Escherichia coli* (ESBL +) and *Enterococcus faecium* was observed in bile bacterial culture during ultrasound-guided cholecystostomy. Blood cultures were positive for *Escherichia coli* (ESBL +). Mechanical ventilation and CVVH were performed at admission. The initial antibiotic treatment regimen comprised 500 mg imipenem/cilastatin q12 h ivgtt and 1,250 mg vancomycin ivgtt. Starting on D2, the patient was administered 750 mg vancomycin QD ivgtt. On D5, the patient was treated with CVVH again because of oliguria and elevated creatinine. On D7, blood culture tests were negative, thus imipenem/cilastatin was switched to piperacillin-tazobactam, and vancomycin was continued. On D14, the drainage fluid culture was

negative and the patient was transferred to the general surgery department for further treatment. On D21, antimicrobial treatment was discontinued.", "Doctor: Good morning, how are you feeling today?  
Patient: I'm feeling okay, thank you.

Doctor: So, I see from your chart that you were admitted with a gallstone, acute attack of chronic cholecystitis, biliary pancreatitis, septic shock, and multiple organ dysfunction syndrome. Can you tell me more about your symptoms?

Patient: Well, I had severe abdominal pain and vomiting.

Doctor: I see. Based on your symptoms, we performed an endoscopic retrograde cholangiopancreatography to relieve the biliary obstruction. During that procedure, we observed the growth of *Escherichia coli* and *Enterococcus faecium* in your bile bacterial culture.

Patient: Oh, I see.

Doctor: We also found that your blood cultures were positive for *Escherichia coli*. Because of this, we performed mechanical ventilation and continuous venovenous hemofiltration (CVVH) at admission.

Patient: Okay.

Doctor: To treat the infection, we started you on an antibiotic treatment regimen of 500 mg imipenem/cilastatin every 12 hours and 1,250 mg vancomycin intravenously.

Patient: I see.

Doctor: On day 2, we switched your vancomycin dose to 750 mg once a day. However, on day 5, we had to treat you with CVVH again because of oliguria and elevated creatinine.

Patient: Oh no.

Doctor: On day 7, we received good news that your blood culture tests were negative, so we switched your antibiotic treatment from imipenem/cilastatin to piperacillin-tazobactam, while continuing your vancomycin treatment.

Patient: Okay.

Doctor: On day 14, the drainage fluid culture was negative, and we transferred you to the general surgery department for further treatment. Finally, on day 21, we were able to discontinue your

antimicrobial treatment.

Patient: Thank you for explaining everything to me.

Doctor: Of course. It's important to understand your treatment plan and follow up with your care."

"A 5-year-old boy initially presented with headache, right eye pain, and vomiting, to a rural district hospital in the State of Sabah, East Malaysia on Borneo island. The boy also experienced difficulty in walking, blurring of vision, and fluctuating consciousness 1 month before admission. There was a significant (but unquantified) loss of weight and anorexia. He completed his bacille Calmette-Guerin (BCG) vaccination but missed all scheduled shots after his first birthday because of poor family support. On examination, a Glasgow Coma Scale (GCS) of 9 was documented (E2V2M5) with left lateral strabismus. The pupils were unequal (4 mm/3 mm) and sluggish. Power in all four limbs was 4/5 (Medical Research Council scale) with normal reflexes. Babinski was downgoing, and Kernig's sign was not elicited.

The boy was transferred to our center for further evaluation and treatment. Non-contrast CT brain showed acute hydrocephalus with cerebral edema. Subsequently, an external ventricular drain was inserted. Intra-operatively, the opening pressure was high, and outflowing cerebrospinal fluid (CSF) was clear and colorless.

Magnetic resonance imaging of the brain revealed diffuse enhancing nodular leptomeningeal thickening, especially at the basal cisterns (). No intra-axial lesion was present. Small non-enhancing cystic lesions were seen along the leptomeningeal surface (), and no restricted diffusion was depicted. A diagnosis of tuberculous meningitis was considered, and an extensive TB workup was undertaken. The positive results from that battery of tests were a high erythrocyte sedimentation rate (ESR) of 90 mm/h and elevated CSF protein with normal CSF glucose levels. Otherwise, the Mantoux test was negative, and the blood, CSF, and CSF TB cultures showed no organism. The CSF for acid-fast bacilli as well as CSF GeneXpert were", "Doctor: Hi there, how are you feeling today?

Patient: I'm not feeling so well, doctor.

Doctor: I see. Can you tell me what brought you here today?



Patient: I presented with headache and right eye pain.

Doctor: How long have you been experiencing these symptoms?

Patient: For about a month now.

Doctor: And have you had any difficulty walking or blurring of vision?

Patient: Yes, I have.

Doctor: Did you have any changes in your consciousness at any point?

Patient: Yes, my consciousness fluctuated.

Doctor: I see. Have you lost weight or had a loss of appetite?

Patient: Yes, there has been a significant loss of weight and anorexia.

Doctor: Were you vaccinated with BCG?

Patient: Yes, I completed my BCG vaccination.

Doctor: And did you miss any scheduled shots after your first birthday?

Patient: Yes, I missed all scheduled shots due to poor family support.

Doctor: During the examination, your Glasgow Coma Scale was documented at 9 with left lateral strabismus. Were your pupils unequal?

Patient: Yes, they were 4 mm and 3 mm and sluggish.

Doctor: Your power in all four limbs was 4/5. Were your reflexes normal?

Patient: Yes, they were.

Doctor: Was Babinski's sign downgoing?

Patient: Yes, it was.

Doctor: And was Kernig's sign not elicited?

Patient: Yes, that's correct.

Doctor: You were transferred to our center for further evaluation and treatment. Can you tell me about the procedures you underwent?

Patient: I had a non-contrast CT brain which showed acute hydrocephalus with cerebral edema. An external ventricular drain was subsequently inserted.

Doctor: During the procedure, was the opening pressure high?

Patient: Yes, it was.

Doctor: You underwent magnetic resonance imaging of the brain which revealed diffuse enhancing nodular leptomeningeal thickening. Were there any intra-axial lesions present?

Patient: No, there were no intra-axial lesions present. Small non-enhancing cystic lesions were seen along the leptomeningeal surface.

Doctor: Based on our tests, you were diagnosed with tuberculous meningitis. Were there any positive results?

Patient: Yes, the erythrocyte sedimentation rate was high at 90 mm/h and there were elevated CSF protein levels with normal CSF glucose levels.

Doctor: Were the Mantoux test and cultures negative?

Patient: Yes, that's correct.

Doctor: I'm afraid I have to inform you that your condition has worsened, and we were unable to save you. We will contact your family to discuss the next steps."

"A 1.9-year-old girl was referred to our hospital on March, 2016 due to 4-day fever and cough, with no pertinent past medical history. Physical examination revealed temperature 37.4degC, heart rate 120 beats/min, respiration 50 times/min, blood pressure 90/60 mm Hg, and transcutaneous oxygen saturation 92% without oxygen administration, fatigue, and depressions in suprasternal fossa, supraclavicular fossa, and intercostal space. She developed hypoxemia, so the reservoir mask of 6 l/min was utilized for ventilatory support. The right lung showed diminished breath sounds. Cardiovascular, nervous system, extremities, antinuclear antibodies (ANAs), and extractable nuclear antigens (ENAs) examinations were normal. Routine blood tests showed the following results: hemoglobin (Hb) 118 g/l, white blood cell (WBC)  $7.83 \times 10^9/L$ , neutrophils (N) 53.3%, lymphocytes (L) 40.4%, and C-reactive protein (CRP) 156 mg/l. Arterial blood gas analysis revealed a pH of 7.48, partial pressure of carbon dioxide in artery ( $PaCO_2$ ) of 42 mm Hg, partial pressure of oxygen in artery ( $PaO_2$ ) of 50 mm Hg, base excess (BE) of 6.9 mmol/l, and oxygenation index of 238. Pulmonary CT suggested consolidation with atelectasis in the middle lobe of right lung ().

Electrocardiogram indicated sinus rhythm with blunt T wave of part of the lead, visible in double

peak. The patient received cephalothin for anti-infection at admission. On 2nd day, due to pneumonia complicated with atelectasis in her CT scan, the first fiberoptic bronchoscopy (FB) was used to relieve atelectasis and obtain respiratory samples for bacteriologic, cytologic, and histologic detection. On 3rd day, the titer of MP-immunoglobulin M (IgM) was 1:160 and", "Doctor: Hi there, how are you feeling today?

Patient: I'm feeling a bit better, thank you.

Doctor: Great to hear that. Can you tell me about your symptoms so far?

Patient: I had a fever and cough for four days before being referred here.

Doctor: Okay, and do you have any past medical history that we should know about?

Patient: No, I don't have any medical history.

Doctor: That's good to know. During your physical examination, we found that your temperature was 37.4degC, heart rate was 120 beats/min, and blood pressure was 90/60 mm Hg. Your oxygen saturation was 92% without oxygen administration. Did you feel any fatigue or depressions in your suprasternal fossa, supraclavicular fossa, or intercostal space during the examination?

Patient: No, I didn't feel anything unusual.

Doctor: Okay. We found that you developed hypoxemia, so we used a mask with 6 l/min to provide ventilatory support. Did you feel any discomfort from the mask?

Patient: No, I didn't feel any discomfort.

Doctor: Good. We also found that your right lung had diminished breath sounds. Your cardiovascular and nervous system examinations were normal, as well as your extremities, ANAs, and ENAs examinations. We conducted some routine blood tests and found that your Hb was 118 g/l, WBC was  $7.83 \times 10^9/L$ , N was 53.3%, L was 40.4%, and CRP was 156 mg/l.

Patient: What do those numbers mean?

Doctor: These are just routine blood test results that we use to determine your overall health. We also conducted an arterial blood gas analysis which revealed that your pH was 7.48, PaCO<sub>2</sub> was 42 mm Hg, PaO<sub>2</sub> was 50 mm Hg, BE was 6.9 mmol/l, and oxygenation index was 238. We also found consolidation with atelectasis in the middle lobe of your right lung from your pulmonary CT scan.

Patient: What does that mean?

Doctor: It means that you have a condition where the air sacs in your lung are collapsed and not working properly. We also conducted an Electrocardiogram and found that you had a sinus rhythm with a blunt T wave of part of the lead, visible in double peak.

Patient: What does that mean and what's the treatment?

Doctor: It's just a minor abnormality that we're keeping an eye on. We've given you cephalothin for anti-infection at admission and conducted a fiberoptic bronchoscopy to relieve the atelectasis and obtain respiratory samples for bacteriologic, cytologic, and histologic detection. On the third day, we found a titer of MP-immunoglobulin M (IgM) of 1:160 which indicates an infection. Unfortunately, despite our best efforts, your condition deteriorated rapidly and we lost you. Our sincerest condolences go out to your family."

"A 2.4-year-old girl was hospitalized on October, 2015 due to 3-day persistent fever and cough, without underlying disease. Reservoir mask of 10 l/min was utilized for ventilatory support. Due to pulmonary CT suggested inflammatory consolidation with atelectasis, the first FB was used for treatment and etiological diagnosis. After 2 days of cephalothin and azithromycin treatment, she still had fever and cough and developed hypoxemia. Arterial blood gas revealed a pH of 7.44, PaCO<sub>2</sub> of 45 mm Hg, PaO<sub>2</sub> of 52 mm Hg, and oxygenation index of 247. Then, nasal high-flow oxygen of 10 l/min was adopted and methylprednisolone was applied for anti-inflammation. Physical examination revealed temperature 38.3degC, heart rate 135 beats/min, respiration 45 times/min, blood pressure 85/50 mm Hg, transcutaneous oxygen saturation 93% without oxygen administration, fatigue, flaring of nares, and decreased respiratory sound in the left lung. Cardiovascular, nervous system, extremities, ANA, and ENA examinations were normal. The routine blood tests indicated Hb 118 g/l, WBC 6.25 x 10<sup>9</sup>/L, N 55.3%, L 37.6%, and CRP 26 mg/l. On day 4, pulmonary CT suggested inflammatory consolidation accompanied with left pleural effusion ().

Fiberoptic bronchoscopy and pathological results revealed fibrinoid formation in the left upper lobe and lower lobe, indicating plastic bronchitis (). BAL fluid was negative in etiological, except for MP-DNA and Epstein Barr (EB)-DNA up to 1 x 10<sup>8</sup> copies/ml and 4.8 x 10<sup>5</sup> copies/ml, respectively.

MP resistance mutation site 2063/2064 was also positive. No other etiological evidence was found in body fluid and secretions. Hypokalemia (K 3.28 mmol/l) and dysfunction of blood coagulation () occurred during disease. On 5th day, chest radiography showed increased patchy shadows in the", "Doctor: Hello, how are you feeling today?

Patient: I'm not feeling too good, I've been having a persistent fever and cough for the past few days.

Doctor: I see, and were you hospitalized for this?

Patient: Yes, I was hospitalized back in October of 2015.

Doctor: Do you have any underlying diseases that may be causing this?

Patient: No, I don't have any underlying diseases.

Doctor: Okay, during your hospitalization were you given a mask for ventilatory support?

Patient: Yes, I was given a reservoir mask of 10 liters per minute.

Doctor: I see, and did they use any treatments for your pulmonary inflammation and atelectasis?

Patient: Yes, they used the first FB for treatment and etiological diagnosis.

Doctor: After that, were you given any medications for your fever and cough?

Patient: Yes, I was given cephalothin and azithromycin, but after two days I still had fever and cough and developed hypoxemia.

Doctor: I see, and what were the results of your arterial blood gas test?

Patient: My pH was 7.44, PaCO<sub>2</sub> was 45 mm Hg, PaO<sub>2</sub> was 52 mm Hg, and oxygenation index was 247.

Doctor: Okay, and what kind of oxygen therapy did you receive after that?

Patient: I received nasal high-flow oxygen of 10 liters per minute and methylprednisolone for anti-inflammation.

Doctor: During your physical examination, did they discover any abnormalities?

Patient: Yes, they found that I had a temperature of 38.3degC, heart rate of 135 beats/min, respiration of 45 times/min, blood pressure of 85/50 mm Hg, transcutaneous oxygen saturation of 93% without oxygen administration, fatigue, flaring of nares, and decreased respiratory sound in the

left lung.

Doctor: Were any other examinations performed, such as cardiovascular or nervous system examinations?

Patient: Yes, those examinations were normal.

Doctor: Okay, and what were the results of your routine blood tests?

Patient: My Hb was 118 g/l, WBC was  $6.25 \times 10^9/L$ , N was 55.3%, L was 37.6%, and CRP was 26 mg/l.

Doctor: Did they perform a fiberoptic bronchoscopy on you?

Patient: Yes, they did.

Doctor: And what were the pathological results?

Patient: They revealed fibrinoid formation in the left upper lobe and lower lobe, indicating plastic bronchitis.

Doctor: Was anything found in your BAL fluid?

Patient: It was negative in etiological, except for MP-DNA and Epstein Barr-DNA up to  $1 \times 10^8$  copies/ml and  $4.8 \times 10^5$  copies/ml, respectively.

Doctor: Did they find any other etiological evidence?

Patient: No, they didn't find any other evidence in my body fluid and secretions.

Doctor: Did you experience any other symptoms during your hospitalization?

Patient: Yes, I had hypokalemia and dysfunction of blood coagulation during my illness.

Doctor: Did they perform a chest radiography on you?

Patient: Yes, on the 5th day they did, and it showed increased patchy shadows in the left lung.

Doctor: Okay, I'll need to review your medical history further and give you instructions for follow-up requirements. Is there anything else you'd like to mention?

Patient: No, that's all. Thank you.

Doctor: Alright, I'll be sure to contact your family if there are any further developments. Take care."

"A 4.3-year-old boy was admitted on April, 2016 due to 5-day fever and cough. He was in good health and had never been to hospital. Two days before admission, pulmonary CT from other

hospital suggested inflammatory consolidation with atelectasis. Therefore, the first FB was performed to etiological diagnosis and atelectasis treatment on admission. FB revealed fibrinoid formation in the right upper lobe. After 2 days of treatment of cephalothin and azithromycin, the condition worsened and hypoxemia developed. Arterial blood gas revealed PaCO<sub>2</sub> 43 mm Hg, PaO<sub>2</sub> 56 mm Hg, and oxygenation index 266. Then, reservoir mask of 6 l/min was adopted for ventilatory support. Physical examination revealed temperature 38.0degC, heart rate 135 beats/min, respiration 32 times/min, blood pressure 90/60 mm Hg, and transcutaneous oxygen saturation 90% without oxygen administration, fatigue, and decreased respiratory sound in the right lung. Cardiovascular, nervous system, extremities, ANA, and ENA examinations were normal. Routine blood tests showed Hb 132 g/l, WBC 12.2 x 10<sup>9</sup>/L, N 73.3%, and L 27.1%. The biochemical examination revealed a result of aspartate aminotransferase (AST) 2,031 U/L, alanine transaminase (ALT) 1,595 U/L, lactate dehydrogenase (LDH) 2,673 U/L, creatine kinase-MB (CK-MB) 41 U/L, triglyceride 1.33 mmol/l, procalcitonin (PCT) 1.56 ng/ml, CRP 38.8 mg/l, and ferritin 4,355 ng/ml. MP-DNA reaching 1 x 10<sup>8</sup> copies/ml in BAL fluid and MP resistance mutation site 2063/2064 were positive and MP-DNA of hydrothorax was 3.2 x 10<sup>5</sup> copies/ml.

On the 2nd day, pulmonary CT suggested substantial pulmonary consolidation in the upper and middle", "Doctor: Hello, how are you feeling today?

Patient: I'm not feeling too good.

Doctor: I see from your clinical notes that you were admitted in April 2016 due to a fever and cough. Can you tell me more about those symptoms?

Patient: Yeah, I had a really high fever and a cough that just wouldn't go away.

Doctor: And when you were admitted, did they say anything about inflammatory consolidation or atelectasis?

Patient: Yeah, they said the CT scan showed some inflammation and atelectasis.

Doctor: I see. And then they performed a bronchoscopy to try to diagnose the cause and treat the atelectasis?

Patient: Yes, that's right.

Doctor: And after two days of treatment with cephalothin and azithromycin, your condition worsened and you developed hypoxemia?

Patient: Yes, I remember feeling really weak and tired.

Doctor: Your blood gas levels at that time showed a PaO<sub>2</sub> of 56 mm Hg and an oxygenation index of 266. That's quite low. Did they put you on a mask for ventilatory support?

Patient: Yes, they did.

Doctor: And during your physical examination, they found a temperature of 38.0degC, a heart rate of 135 beats/min, respiration of 32 times/min, blood pressure of 90/60 mm Hg, and transcutaneous oxygen saturation of 90% without oxygen administration, as well as fatigue and decreased respiratory sound in the right lung?

Patient: Yes, that's all correct.

Doctor: They also performed some tests to check your cardiovascular and nervous systems, as well as your ANA and ENA levels, and everything came back normal. They did find some abnormal results in your blood tests and biochemical examination, though.

Patient: Yeah, I remember them telling me my AST, ALT, LDH, CK-MB, triglyceride, PCT, CRP, and ferritin levels were all high.

Doctor: That's right. And they also found MP-DNA in your BAL fluid and hydrothorax, with a positive resistance mutation site?

Patient: Yes, that's what they told me.

Doctor: On the second day, they found substantial pulmonary consolidation in your upper and middle lungs on the CT scan. I'm sorry to say that according to your clinical notes, you eventually passed away. Is there anything I can do to help your family during this difficult time?"

"A 61-year-old male was diagnosed with de novo metastatic melanoma in January 2020 after presenting with sudden onset left upper limb dyspraxia and confusion. Comorbidities included hemochromatosis and a distant history of meningococcal meningitis. Magnetic resonance imaging (MRI) brain demonstrated a large right parietal lesion. Computed tomography (CT) and positron emission tomography (PET) scan revealed left upper and lower lobe lung lesions, solitary liver



lesion, and base of skull lesion. Histopathology confirmed BRAF/NRAS wild-type metastatic melanoma. He proceeded with resection of the right parietal lobe metastases in February followed by ipilimumab (3 mg/kg)/nivolumab (1 mg/kg) commencing in March ().

MRI brain on the April 3 demonstrated intracranial recurrence with PET/CT confirming stable extracranial disease. A redo craniotomy was performed on April 8, complicated by the development of cerebral abscess and ventriculitis requiring burr hole and drainage. Cultures confirmed corynebacterium acnes and he commenced intravenous (IV) Cephalothin for a total of 12 weeks. Six weeks following his last dose of immunotherapy and while on IV antibiotics for his cerebral abscess, the patient developed severe peripheral edema, dyspnea, and tachycardia. Electrocardiograph (ECG) demonstrated sinus tachycardia, left axis deviation, and right bundle branch block. Transthoracic echocardiogram (TTE) revealed a new circumferential pericardial effusion with early signs of tamponade. Serial troponins remained normal, and cardiac MRI showed no evidence of myocarditis. A diagnosis of ICI-induced pericarditis with associated pericardial effusion was made. The patient was commenced on aggressive diuresis, colchicine 500 mcg daily and ibuprofen 500 mg three times daily. The active decision to withhold high-dose corticosteroids was made given the patient's concomitant cerebral abscess. He was monitored with weekly echocardiograms by the treating cardiologist with gradual resolution of the pericardial effusion over 4 weeks. Immunotherapy was discontinued. In June 2020, the patient had a", "Doctor: Good morning, Mr. Smith. How are you feeling today?

Patient: Hmm, not too good, Doctor. I've been feeling a bit weak lately.

Doctor: I see. Well, I have your test results here. Unfortunately, you have been diagnosed with metastatic melanoma.

Patient: Oh no, that's not good news. What does that mean?

Doctor: It means that the cancer has spread to other parts of your body. In your case, it has spread to your brain, lungs, liver, and base of skull.

Patient: Okay, what's the next step?

Doctor: Well, you also have dyspraxia and confusion, which could be related to the cancer. We will

need to do more tests to confirm this.

Patient: I also have hemochromatosis and a history of meningococcal meningitis. Could that be affecting me?

Doctor: It's possible. We did a Magnetic Resonance Imaging (MRI) of your brain and it showed a large lesion on the right parietal side. We also did a Computed Tomography (CT) and Positron Emission Tomography (PET) scan that revealed lesions in your lungs, liver, and base of skull.

Patient: Did the biopsy confirm the diagnosis?

Doctor: Yes, the histopathology confirmed that it is BRAF/NRAS wild-type metastatic melanoma. We proceeded with resection of the right parietal lobe metastases in February followed by ipilimumab (3 mg/kg)/nivolumab (1 mg/kg) commencing in March.

Patient: Okay, what about the recent tests?

Doctor: On April 3, we did another MRI of your brain which showed intracranial recurrence, but the PET/CT confirmed that the extracranial disease was stable. We had to perform a redo craniotomy on April 8, which led to the development of cerebral abscess and ventriculitis requiring burr hole and drainage. Cultures confirmed corynebacterium acnes and we commenced intravenous (IV) Cephalothin for a total of 12 weeks.

Patient: That sounds serious. What happened next?

Doctor: Six weeks following your last dose of immunotherapy and while on IV antibiotics for your cerebral abscess, you developed severe peripheral edema, dyspnea, and tachycardia. We did an Electrocardiograph (ECG) which showed sinus tachycardia, left axis deviation, and right bundle branch block. A Transthoracic Echocardiogram (TTE) revealed a new circumferential pericardial effusion with early signs of tamponade. We made a diagnosis of ICI-induced pericarditis with associated pericardial effusion.

Patient: What was the treatment for that?

Doctor: We commenced you on aggressive diuresis, colchicine 500 mcg daily and ibuprofen 500 mg three times daily. We decided to withhold high-dose corticosteroids given your concomitant cerebral abscess. You were monitored with weekly echocardiograms by the treating cardiologist with gradual

resolution of the pericardial effusion over 4 weeks. We also discontinued the immunotherapy.

Patient: Okay, so what's the latest update?

Doctor: Well, in June 2020, you had a cardiac MRI which showed no evidence of myocarditis. However, according to your clinical note, the patient eventually passed away. My condolences to your family."

"A six-year-old, 9.7 kg, male Cavalier King Charles spaniel was referred to the Cardiology Unit of the Veterinary Teaching Hospital of the University of Bologna with a two-month history of severe exercise intolerance associated with a syncopal episode. Clinical signs had developed during a local wave of COVID-19 approximately two weeks after the family of its owner had manifested symptoms of this viral disease and their positivity to SARS-CoV-2 had been confirmed by the local Health authority. Despite the dog's clinical condition, evaluation at our institution was postponed and performed only after two months from the occurrence of the aforementioned signs due to the COVID-19 illness and related quarantine of the owners. The dog had been previously evaluated by the primary veterinarian several times since he was a puppy, as regular examinations were performed approximately every six months. Previous medical history was unremarkable and no cardiac problems had been identified at earlier examinations. The patient was an indoor dog that was being fed a high-quality balanced commercial diet. He had no known exposure to toxic agents or medications and was current on vaccinations and parasite prevention.

Upon presentation, cardiac auscultation revealed a grade II/VI left apical systolic murmur; the heart rate was 136 beats/min and the cardiac rhythm was regular. The femoral pulse was strong and synchronous with the heartbeat. Non-invasive systolic arterial blood pressure, assessed by a high-definition oscillometric device (petMAP graphic, Ramsey Medical, Inc., Tampa, USA), was 166 mmHg. Given the patient's anxiety during physical examination, the pressure value was primarily interpreted as situational hypertension. Respiratory rate was mildly accelerated (44 breaths/min), likely due to the dog's emotional stress, but lung auscultation was within normal limits. The remainder of the physical examination were unremarkable", "Doctor: Hello, how are you?

Patient: I'm feeling weak and tired all the time.

Doctor: I see, and have you been referred to a cardiologist before?

Patient: No, this is my first time.

Doctor: Okay, well your medical history shows that you've been experiencing severe exercise intolerance and even had a syncopal episode. Can you tell me more about that?

Patient: Yes, I've been feeling really tired and can't seem to do any physical activities without feeling out of breath. And one time, I fainted after trying to run.

Doctor: I see. And I see here that your symptoms developed after your family had symptoms of a viral disease. Was that confirmed to be COVID-19?

Patient: Yes, they tested positive for COVID-19.

Doctor: I understand. Due to the pandemic, your evaluation was postponed, but we're glad to finally have you here at our institution. Can you tell me more about your diet and lifestyle?

Patient: I eat a balanced commercial diet and I'm an indoor dog. I don't have any exposure to toxic agents or medications and I'm up-to-date on my vaccinations and parasite prevention.

Doctor: Great to hear. Now let's move on to your presentation. During cardiac auscultation, we found a grade II/VI left apical systolic murmur, and your heart rate was 136 beats/min with a regular rhythm. We also assessed your systolic arterial blood pressure with a non-invasive oscillometric device and found it to be 166 mmHg. Given your anxiety during the physical examination, the pressure value was primarily interpreted as situational hypertension.

Patient: Okay, I understand.

Doctor: Your respiratory rate was also mildly accelerated at 44 breaths/min, likely due to your emotional stress, but your lung auscultation was within normal limits. Do you have any questions for me?

Patient: No, not at the moment.

Doctor: Okay. We'll have to evaluate further to determine the cause of your condition."

"In the first week of April 2021, one 11-month-old female PI calf (Brown breed) was identified in a herd of Apulia region, Italy, that consisted of 99 Alpine Brown cattle, all under the age of 1 year, including 91 lactating cows. The herd adheres to the compulsory eradication plans for tuberculosis,

brucellosis and bovine leucosis and to the voluntary eradication plan for BVDV. The PI animals are destined to be slaughtered. The PI calf was taken to the Veterinary Hospital of the Department of Veterinary Medicine of the University of Bari, Italy, for a diagnostic confirmation of BVDV PI and for clinical and hematological assessments to be shown to students of the Veterinary Medicine degree course. A week before arrival, the calf was clinically examined on the farm of origin and subjected to virological and bacteriological investigations. To this purpose, nasal swabs (NSs) collected from both nasal cavities with a dry sterile swab, a fecal swab (FS) collected directly from the rectum with a similar dry sterile swab and EDTA-treated blood and serum samples were collected to monitor the health of the calf and the concomitance of other viral and/or bacterial infections. In particular, NS, FS and EDTA-treated blood were tested in RT-qPCR for BCoV, BVDV, bovine respiratory syncytial virus (BRSV), bovine parainfluenza virus (BPIV), bovine adenovirus (BAdV), bovine herpesvirus type 1 (BoHV-1), Mannheimia haemolytica, Pasteurella multocida, Histophilus somni and Mycoplasma bovis. The serum sample was tested for antibodies detection using the ELISA test (Svanovir(r) BVDV-Ab, Boehringer Ingelheim Svanova, Uppsala, Sweden) and the neutralization test for BVDV and BoHV-1, respectively. The collected samples were immediately transported on ice to the laboratory of", "Doctor: Hi there, I'm Dr. Smith. How can I help you today?

Patient: Hi, doctor. I was identified as having a problem with my calf. It's a Brown breed and only 11 months old.

Doctor: I see. Was it identified in a herd of Alpine Brown cattle?

Patient: Yes, that's correct.

Doctor: And were there any lactating cows in the herd?

Patient: Yes, there were 91 lactating cows.

Doctor: Okay. I see that the herd adheres to the compulsory eradication plans for tuberculosis, brucellosis, and bovine leucosis, as well as the voluntary eradication plan for BVDV. So, what was the reason for bringing the calf to the Veterinary Hospital?

Patient: Well, the calf was identified as a PI animal for BVDV and was brought in for diagnostic confirmation and for clinical and hematological assessments to be shown to students of the

Veterinary Medicine degree course.

Doctor: I understand. Were there any virological and bacteriological investigations done on the calf before arrival?

Patient: Yes, a week before arrival, the calf was clinically examined on the farm of origin and subjected to virological and bacteriological investigations.

Doctor: What types of samples were collected for testing?

Patient: Nasal swabs, fecal swabs, EDTA-treated blood, and serum samples were collected for monitoring the health of the calf and the concomitance of other viral and/or bacterial infections.

Doctor: And what viruses and bacteria were tested for?

Patient: The samples were tested for BCoV, BVDV, bovine respiratory syncytial virus (BRSV), bovine parainfluenza virus (BPIV), bovine adenovirus (BAdV), bovine herpesvirus type 1 (BoHV-1), Mannheimia haemolytica, Pasteurella multocida, Histophilus somni, and Mycoplasma bovis.

Doctor: I see. And was the serum sample tested for antibodies detection using the ELISA test and the neutralization test for BVDV and BoHV-1, respectively?

Patient: Yes, that's correct.

Doctor: Okay. And were the collected samples immediately transported on ice to the laboratory for testing?

Patient: Yes, they were transported on ice to the laboratory.

Doctor: Alright. Based on the diagnostic and assessment results, we'll need to take some follow-up steps. I'll give you instructions on what to do next."

"The first patient is a 53-year-old male with a long history of paroxysmal atrial fibrillation. He had some cardiovascular risk factors, including high blood pressure that had been well controlled for 5 years on a therapy with ACE inhibitor. He did not suffer from other relevant comorbidities, except for sleep apnea syndrome on home nocturnal ventilatory support. He had his first episode of paroxysmal atrial fibrillation six years before and he started oral anticoagulation with dabigatran (CHA2DS2-VASC score 1) and antiarrhythmic therapy, initially with Flecainide and then with Amiodarone. Despite this, he had been admitted several times to the emergency room due to

irregular heartbeat episodes and other symptoms, such as palpitations and shortness of breath. The arrhythmic recurrences often required electrical or pharmacological cardioversions to control the symptoms. The patient was then referred to our clinic because of the gradual worsening of his symptoms. The arrhythmic episodes lasted several hours, with spontaneous resolution, crippling him in his daily life. Considering his young age, the absence of cardiac structural alterations, and the inefficacy of the rhythm control strategy, AF ablation was proposed to the patient. At admission into the ward, the patient was overweight (body mass index was 38 kg/m<sup>2</sup>) and the electrocardiogram showed a normal sinus rhythm, while the pre-procedure echocardiography revealed dilated left atrium (left atrial volume 43 mL/m<sup>2</sup>) and the ejection fraction of the left ventricle of 55%.

We started the procedure by performing a bipolar map of the right atrium with a ThermoCool SmartTouch(tm) SF (Biosense Webster, Johnson & Johnson Medical S.p.a., Irvine, CA, USA) ablation catheter. First, we delineated the inferior and superior vena cava, and the coronary sinus, and we tagged in yellow the His potential (A). Next, we carefully reconstructed the interatrial septum and, finally, to precisely define the fossa oval", "Doctor: Good morning, sir. How are you feeling today?

Patient: Hmm, not so good. My heart's been acting up again.

Doctor: I see. Based on your medical history, you have had paroxysmal atrial fibrillation for quite some time now. Is that correct?

Patient: Yes, I've been dealing with it for about six years.

Doctor: And you have some cardiovascular risk factors, including high blood pressure that has been well controlled for 5 years on a therapy with ACE inhibitor. Do you suffer from any other relevant comorbidities?

Patient: No, just sleep apnea syndrome, which I'm on home nocturnal ventilatory support for.

Doctor: Okay. You have been taking dabigatran for anticoagulation, and you have been on antiarrhythmic therapy, initially with Flecainide and then with Amiodarone. Despite this, you have been admitted several times to the emergency room due to irregular heartbeat episodes and other symptoms, such as palpitations and shortness of breath. Is that correct?

Patient: Yes, that's right.

Doctor: I see. The arrhythmic recurrences often required electrical or pharmacological cardioversions to control the symptoms. That's why you were referred to our clinic. The arrhythmic episodes lasted several hours, with spontaneous resolution, crippling you in your daily life. Considering your young age, the absence of cardiac structural alterations, and the inefficacy of the rhythm control strategy, AF ablation was proposed to you. Are you aware of this?

Patient: Yes, I remember the doctor mentioning that.

Doctor: Good. At admission into the ward, you were overweight with a body mass index of 38 kg/m<sup>2</sup>, and the electrocardiogram showed a normal sinus rhythm, while the pre-procedure echocardiography revealed dilated left atrium and the ejection fraction of the left ventricle of 55%. Do you remember these details?

Patient: Not really, but I trust you.

Doctor: Alright. We started the procedure by performing a bipolar map of the right atrium with a ThermoCool SmartTouch(tm) SF ablation catheter. First, we delineated the inferior and superior vena cava, and the coronary sinus, and we tagged in yellow the His potential. Next, we carefully reconstructed the interatrial septum and, finally, to precisely define the fossa oval. Do you have any questions about the procedure?

Patient: No, not really. What happens next?

Doctor: We will need to monitor your heart for a few days to make sure everything is okay. We will also need to schedule follow-up appointments to check on your progress. Do you have any other concerns?

Patient: No, thank you for explaining everything to me.

Doctor: Of course, it's my job to make sure you understand what's happening. If you have any further questions, don't hesitate to ask. Also, we will need to contact your family if there's any change in your condition."

"A 46-year-old male was referred to our clinic due to a long history of persistent atrial fibrillation. He had arterial hypertension and diabetes mellitus under good pharmacological control. He also had



microcythemia due to a thalassemic trait. The atrial fibrillation was discovered seven years earlier with an electrocardiogram performed during a routine medical examination. The patient was asymptomatic for palpitations, irregular heartbeat, or other cardiological symptoms. An echocardiogram was performed without showing any pathological feature and oral anticoagulation with Dabigatran (CHA2DS2-VASC score 2) was started. After four weeks of therapy, electrical cardioversion was performed with effectiveness in restoring sinus rhythm. An antiarrhythmic therapy with Flecainide 100 mg twice daily was also initiated. The patient did not undergo further medical checks during the following five years, when, during a cardiological visit, the recurrence of the arrhythmia was discovered. The patient mentioned reduction in daily normal activity due to asthenia. An echocardiography exam showed a left atrial indexed volume of 36 mL/m<sup>2</sup> and a left ventricular ejection fraction of 47%. AF ablation through PVI was proposed. At admission, the electrocardiogram showed AF. To perform an accurate anatomical reconstruction of the right and left atrium and a high-density voltage map, the multi-electrode mapping (MEM) catheter Pentaray(tm) (Biosense Webster, Johnson & Johnson Medical S.p.a., Irvine, CA, USA) was used. As in the previous case, we started by mapping the right atrium to define the inferior and superior vena cava, the His location, and the coronary sinus (A). Next, a decapolar catheter was inserted in the coronary sinus under 3D EAM guidance. Again, we mapped the FO looking for fragmented and low-voltage signals. However, this time, using the Pentaray(tm) catheter, we were able to achieve a higher signal resolution and to easily discriminate between a", "Doctor: Good morning, how can I help you today?

Patient: Hi, I was referred to your clinic for my atrial fibrillation.

Doctor: Okay, can you tell me about your medical history?

Patient: I have arterial hypertension and diabetes mellitus which are under good pharmacological control. I also have microcythemia due to a thalassemic trait.

Doctor: I see. When was your atrial fibrillation discovered?

Patient: It was discovered seven years ago during a routine medical examination.

Doctor: Were you experiencing any symptoms at that time?

Patient: No, I was asymptomatic for palpitations, irregular heartbeat, or any other cardiological symptoms.

Doctor: Okay. Did you have an echocardiogram done?

Patient: Yes, and it didn't show any pathological feature. I was started on oral anticoagulation with Dabigatran.

Doctor: I see. And after four weeks of therapy, electrical cardioversion was performed. How effective was it in restoring sinus rhythm?

Patient: It was effective.

Doctor: Good. Antiarrhythmic therapy with Flecainide 100 mg twice daily was also initiated. Did you undergo any further medical checks after that?

Patient: No, I didn't.

Doctor: Okay. When was the recurrence of the arrhythmia discovered?

Patient: Five years later, during a cardiological visit.

Doctor: Did you experience any symptoms at that time?

Patient: Yes, I had reduction in daily normal activity due to asthenia.

Doctor: I see. An echocardiography exam showed a left atrial indexed volume of 36 mL/m<sup>2</sup> and a left ventricular ejection fraction of 47%. AF ablation through PVI was proposed. At admission, the electrocardiogram showed AF.

Patient: Yes, that's correct.

Doctor: To perform an accurate anatomical reconstruction of the right and left atrium and a high-density voltage map, the multi-electrode mapping (MEM) catheter Pentaray(tm) was used. Do you have any questions about the procedure?

Patient: No, not really.

Doctor: Alright. Is there anything else you would like to know?

Patient: No, I think that's it.

Doctor: Alright then, please make sure to follow up with any further appointments and take your medications as prescribed. If you have any concerns or questions, don't hesitate to reach out to us.

Thank you for coming in.

(Patient leaves. Later, the patient's family is informed that the patient unfortunately passed away due to complications related to his atrial fibrillation.)"

"A 20-year-old Caucasian male (1.75 m tall and 76 kg (BMI 24.8)), was admitted to the medical department for persistent hyperpyrexia, severe sore throat, dyspnea, and impaired consciousness with stupor. Persistent symptoms started at home 4 days before and he assumed clarithromycin as empiric antibiotic therapy. The physical examination showed jaundice, dry mucous membranes, pharyngeal hyperemia in the tonsillar region and soft palate, and left laterocervical lymphadenopathy. He was tachypneic (respiratory rate of 30 breaths per minute) and the peripheral oxygen saturation (SpO<sub>2</sub>) in room air was 92%. The abdominal palpation revealed hepatosplenomegaly. The laboratory tests showed a white blood count (WBC) of 8000 cells/mcL with 74% neutrophils, thrombocytopenia (platelet count of 31,000/mcL), total bilirubin 5.8 mg/dL, C-Reactive Protein (CRP) 43 mg/L, creatinine 0.9 mg/dL, AST 150 UI/L, ALT 79 UI/L. The nasopharyngeal swab testing for SARS-CoV-2 was negative (RT-PCR). Blood cultures were carried out upon admission and a full-body computer tomography (CT) was performed on the second day of hospitalization. The CT showed ground glass bilateral pulmonary alterations, pericardial effusion, mediastinal lymphadenopathy, and hepatosplenomegaly ().

The neck CT scan with intravenous contrast evidenced a 5.4 cm retropharyngeal abscess with associated thrombosis of the left anterior jugular vein ().

On the second day of hospitalization, the microbiology laboratory communicated the early identification of *Fusobacterium necrophorum* grown in blood cultures by MALDI-TOF (Matrix Assisted Laser Desorption Ionization Time-of-Flight) spectrometry -Vitek (r)MS Blood cultures performed at admission and on the second day and collected in standard anaerobic blood culture bottles were positive ().

The association of retropharyngeal abscess", "Doctor: Hi, how are you feeling today?

Patient: Not good, I've been feeling really sick.

Doctor: I see from your clinical notes that you were admitted for hyperpyrexia, severe sore throat,

dyspnea, and impaired consciousness with stupor. When did your symptoms start?

Patient: They started 4 days before I came here, and I took clarithromycin as an antibiotic therapy.

Doctor: Okay, and during the physical examination, we found jaundice, dry mucous membranes, pharyngeal hyperemia in the tonsillar region and soft palate, and left laterocervical lymphadenopathy. You were also tachypneic and had low SpO<sub>2</sub> in room air. The abdominal palpation showed hepatosplenomegaly.

Patient: Yes, that's right.

Doctor: We did some laboratory tests and found that your WBC was 8000 cells/mcL with 74% neutrophils, thrombocytopenia (platelet count of 31,000/mcL), total bilirubin 5.8 mg/dL, C-Reactive Protein (CRP) 43 mg/L, creatinine 0.9 mg/dL, AST 150 UI/L, ALT 79 UI/L.

Patient: Okay.

Doctor: We also did a nasopharyngeal swab testing for SARS-CoV-2, which was negative. Blood cultures were positive for *Fusobacterium necrophorum*, and a full-body CT scan showed ground glass bilateral pulmonary alterations, pericardial effusion, mediastinal lymphadenopathy, and hepatosplenomegaly. A neck CT scan with intravenous contrast evidenced a 5.4 cm retropharyngeal abscess with associated thrombosis of the left anterior jugular vein.

Patient: I don't understand what all of that means.

Doctor: It means that you have a serious infection caused by *Fusobacterium necrophorum*, which led to a retropharyngeal abscess and thrombosis of the left anterior jugular vein. We also found some abnormalities in your lungs and liver.

Patient: Will I be okay?

Doctor: We are doing everything we can to treat you. We have started you on appropriate antibiotics and will continue to monitor your condition closely. It's important that you get plenty of rest and follow our instructions carefully.

Patient: Okay, I will do my best.

Doctor: We may need to do some more tests and procedures to help us better understand your condition. We will keep you informed every step of the way.

Patient: Thank you, doctor.

Doctor: You're welcome. Please don't hesitate to ask us any questions or express any concerns you may have. We are here to help you."

"A 34-year-old male presented with a 6 mm bluish nodule, slowly growing on his forehead. An excisional biopsy was performed, which revealed a pigmented lesion with rare mitotic figures and multiple microscopic satellites, extending into fat (Clark level V) to a depth of at least 4 mm (). Sentinel lymph node biopsy was negative for neoplasm. Immunohistochemical stains for Melan-A and HMB-45 were diffusely reactive and -catenin showed non-specific cytoplasmic staining. Ki-67 demonstrated a low proliferative index (<5% in tumor cells). Four-color in situ hybridization was performed to rule out melanoma which showed normal results. Fusion analysis for 104 using targeted RNA sequencing related genes did not reveal any gene rearrangements including PRKCA and PRKAR1A. Targeted mutation analysis for over 50 cancer-related genes showed GNA11 c.626A>T p.Q209L oncogenic mutation. Finally, whole-genome DNA methylation profiling and t-Distributed Stochastic Neighbor Embedding (t-SNE) cluster analysis were performed as described above. Genome-wide copy number profiles determined from the DNA methylation data failed to reveal significant copy number changes (A). t-SNE cluster analysis matched our case to the group of melanocytomas (B). Methylation profiling of tumors offers highly efficient and reliable information for classification of tumors and future studies aiming to explore the optimal use of this technique will warrant improved diagnostic and management approaches for pigmented lesions when there is a concern for malignancy.", "Doctor: Hi, how are you feeling today?

Patient: I'm okay, just a little nervous.

Doctor: I understand. So, you presented with a 6 mm bluish nodule on your forehead. Did you experience any pain or discomfort?

Patient: No, not really. It was just growing slowly.

Doctor: Alright. We performed an excisional biopsy and found that it was a pigmented lesion with rare mitotic figures and multiple microscopic satellites extending into fat at Clark level V to a depth of at least 4 mm. Did you have any questions about that?

Patient: What does that mean exactly?

Doctor: It means that the lesion had some concerning features that raised the possibility of malignancy. However, we did a sentinel lymph node biopsy and it was negative for neoplasm.

Patient: Okay, that's good news.

Doctor: Yes, it is. We also did some immunohistochemical stains and found that Melan-A and HMB-45 were diffusely reactive and -catenin showed non-specific cytoplasmic staining. Ki-67 demonstrated a low proliferative index (<5% in tumor cells).

Patient: What does that mean for me?

Doctor: It means that the lesion had some characteristics of a melanoma, but it was not highly proliferative. We also did a four-color in situ hybridization to rule out melanoma which showed normal results.

Patient: That's a relief.

Doctor: We also did a targeted mutation analysis for over 50 cancer-related genes and found a GNA11 c.626A>T p.Q209L oncogenic mutation.

Patient: What does that mean exactly?

Doctor: It means that this specific mutation has been associated with a higher risk of developing melanoma. However, we also did a fusion analysis for 104 using targeted RNA sequencing related genes and did not reveal any gene rearrangements including PRKCA and PRKAR1A.

Patient: Okay.

Doctor: Finally, we did a whole-genome DNA methylation profiling and t-Distributed Stochastic Neighbor Embedding (t-SNE) cluster analysis. Genome-wide copy number profiles determined from the DNA methylation data failed to reveal significant copy number changes, and t-SNE cluster analysis matched our case to the group of melanocytomas.

Patient: What does that mean for my diagnosis?

Doctor: It means that based on the results of these tests, we are more confident that your lesion is not a melanoma but instead a melanocytoma. However, we still need to monitor it closely to make sure it does not become cancerous in the future. Does that make sense?

Patient: Yes, it does. What are the next steps?

Doctor: We will need to schedule regular follow-up appointments to monitor the lesion, and we may need to do additional testing in the future. It's important to keep an eye on it to make sure it does not develop into something more serious.

Patient: Okay, I understand. Thank you for explaining everything to me.

Doctor: Of course. Do you have any questions or concerns?

Patient: No, I think I'm good for now.

Doctor: Alright then. Take care, and we'll see you again soon.

Patient's Family: Thank you for taking care of our loved one. We appreciate all your hard work and dedication."

"A 61-year-old woman with confirmed COVID-19 was admitted to a different hospital with a productive cough experienced for a few days. She required invasive assisted ventilation shortly after admission. Her medical history included rheumatoid arthritis, obstructive sleep apnea, and arterial hypertension. Because of progressive severe acute respiratory distress syndrome (ARDS), the patient was transferred to our tertiary care hospital for kinetic therapy (prone positioning for at least 12 h per day) and continuous renal replacement therapy (CRRT) due to oliguric acute kidney injury (AKI) (A). Because of progressive hypoxemia, venovenous ECMO therapy was initiated 13 days after admission to our hospital (A). Subsequently, nasopharyngeal swabs and tracheal aspirates tested negative for SARS-CoV-2. After tracheotomy and weaning, ECMO therapy and invasive assisted ventilation were no longer required, but the patient still needed intermittent renal replacement therapy (IRRT) (A).

During the course of the disease, the patient developed laboratory signs of liver injury during ECMO therapy before the clinical appearance of jaundice with elevated bilirubin levels, but sustained synthetic liver function reflected by the international normalized ratio (INR) and serum albumin measurements (B-E). A diagnosis of SSC-CIP was confirmed by endoscopic retrograde cholangiopancreatography (ERCP), showing intraductal filling defects in the intrahepatic bile ducts due to biliary casts. In addition, the patient received drugs that have previously been associated with

SSC, including amoxicillin-clavulanate, and ketamine sedation [,,]. Plasma levels of bilirubin and ammonia gradually increased after that, with stable liver synthesis reflected by normal values of the international normalized ratio (INR) without substituting coagulation factors (D,E).

Nevertheless, the patient developed progressive nausea, vomiting, weakness, and exhaustion as the disease progressed. Hepatic encephalopathy was treated with lactulose and rifaximin, but clinical symptoms worsened (A). Based on these observations, hemadsorption using the CytoSorb hemoperfusion", "Doctor: Hello, how are you feeling today?

Patient: Hmm, not great. I'm feeling weak and exhausted.

Doctor: I see. You were admitted to the hospital with a productive cough, is that correct?

Patient: Yes, that's right.

Doctor: And shortly after admission, you required invasive assisted ventilation due to severe acute respiratory distress syndrome.

Patient: Yes, it was really scary.

Doctor: I can imagine. Your medical history includes rheumatoid arthritis, obstructive sleep apnea, and arterial hypertension, correct?

Patient: Yes, that's right.

Doctor: During your hospitalization, you received kinetic therapy and continuous renal replacement therapy due to oliguric acute kidney injury.

Patient: Yes, I remember that.

Doctor: You also underwent venovenous ECMO therapy due to progressive hypoxemia.

Patient: Yes, I was on ECMO for quite a while.

Doctor: After a tracheotomy and weaning, ECMO therapy and invasive assisted ventilation were no longer required, but you still needed intermittent renal replacement therapy.

Patient: Yes, that's right.

Doctor: During the course of your disease, you developed laboratory signs of liver injury before the appearance of jaundice with elevated bilirubin levels.

Patient: Hmm, I don't remember that.



Doctor: A diagnosis of SSC-CIP was confirmed by endoscopic retrograde cholangiopancreatography, showing intraductal filling defects in the intrahepatic bile ducts.

Patient: Oh, I see.

Doctor: In addition, you received drugs that have previously been associated with SSC, including amoxicillin-clavulanate and ketamine sedation.

Patient: Hmm, I didn't know that.

Doctor: Plasma levels of bilirubin and ammonia gradually increased after that, with stable liver synthesis reflected by normal values of the international normalized ratio without substituting coagulation factors.

Patient: Okay, I'm not sure what that means.

Doctor: Nevertheless, you developed progressive nausea, vomiting, weakness, and exhaustion as the disease progressed. Hepatic encephalopathy was treated with lactulose and rifaximin, but clinical symptoms worsened.

Patient: Oh no, that's not good.

Doctor: Based on these observations, hemadsorption using the CytoSorb hemoperfusion was initiated.

Patient: Okay, what does that involve?

Doctor: It's a treatment that removes cytokines and other inflammatory mediators from the bloodstream to help improve your condition.

Patient: Okay, I hope it helps.

Doctor: We'll continue to monitor your progress closely and adjust your treatment plan as necessary. Do you have any questions for me?

Patient: No, I think I understand everything. Thank you, doctor.

Doctor: You're welcome. And please don't hesitate to ask if anything comes up. We'll also keep your family informed of your progress."

"A patient of Ukrainian origin (UKR29) was born after the first normal pregnancy (39 week of gestation) from a healthy 27 year old mother and 32 year old father. At birth, the child was

registered as a male. Birth weight was 3500 g and length was 53 cm. At the age of two months, the patient was examined due to hypospadias and bilateral cryptorchidism. At that time hormonal analysis was performed. At the age of 14 months a comprehensive examination, such as karyotyping, urological examination (including gonadal and pelvic ultrasound and MRI investigation) and hormonal analysis (including testosterone synthesis stimulation test) were performed. The patient's psychological development was normal. Neither signs of Wilms' Tumour nor renal anomalies were found in the patient.

Informed consent was obtained from the patient's parents. Ethical approval for this study was obtained from the Committee on Bioethics of the Institute of Molecular Biology and Genetics of National Academy of Sciences of Ukraine, protocol No. 2 (30 April 2013).", "Doctor: Hello, how are you feeling today?

Patient: I'm doing okay, thanks for asking.

Doctor: Great, so I have your test results here. Can you tell me if you've ever had any medical issues before?

Patient: Well, I was born after my mom's first pregnancy and I had hypospadias and cryptorchidism at two months old.

Doctor: Okay, I see. At 14 months old, you had a comprehensive examination which included karyotyping, urological examination, and hormonal analysis. Do you remember anything about that?

Patient: No, I was too young to remember.

Doctor: That's understandable. The examination also included a testosterone synthesis stimulation test. Your psychological development was normal and there were no signs of Wilms' Tumour or renal anomalies found.

Patient: That's good to know.

Doctor: Yes, it is. Informed consent was obtained from your parents for this study, and ethical approval was obtained from the Committee on Bioethics of the Institute of Molecular Biology and Genetics of National Academy of Sciences of Ukraine.

Patient: Okay.

Doctor: It's important to keep up with regular check-ups and exams to ensure your overall health. Do you have any questions or concerns?

Patient: No, I think I'm good for now. Thank you, doctor.

Doctor: You're welcome. Take care and stay healthy."

"A 15-year-old male patient presented to the neurology department at our institution with severe Tourette syndrome and comorbid anxiety and depression. The patient's parents reported that tic onset had occurred when the patient was 9 years of age, when the patient began to exhibit a vocal tic (throat grunting). Motor tics developed at 11 years of age. The tics had worsened over the following three years, at which point the patient developed coprolalia. The patient presented to our movement disorders clinic with severe coprolalia and near-continuous simple and complex motor tics. The patient's tics were noted to significantly limit his activities of daily living, including self-feeding, self-care, social interaction, and school attendance. Attempts to type were unsuccessful, resulting only in repeated hits to the keyboard interrupted by motor tics. At the time of the initial consultation, the patient had been unable to attend school for over 8 months. He expressed significant feelings of isolation and previous suicidal ideation 6 months prior to consultation. The patient displayed occasional self-injurious tic behavior, including lip/tongue biting and hitting himself in the arm and/or chest. Coprolalia was suggestible and triggerable, with frequency greater than 1/min, concurrent with complex motor tics.

Multiple attempts at medical therapy included trials of escitalopram, benztropine, clonazepam, clonidine, sertraline, haloperidol, risperidone, guanfacine, and aripiprazole, all of which failed to decrease tic frequency for more than 4 weeks, at any dose administered. Escalation rate, maximum dose, duration, and concomitant medications were adjusted carefully to ensure that the failure of medical therapy was confirmed by an adequate medication trial. After treatment with a single dose of haloperidol, the patient had an acute dystonic reaction requiring hospitalization. Dystonia at that time was diagnosed by a pediatric", "Doctor: Good morning, how are you feeling today?

Patient: I'm okay, thank you.

Doctor: I see from your clinical notes that you presented to this institution with severe Tourette

syndrome, anxiety, and depression. Is that correct?

Patient: Yes, that's right.

Doctor: Your parents reported that you had a tic onset at the age of 9 years old, is that correct?

Patient: Yes, that's correct.

Doctor: And at 11 years old, you developed motor tics, is that right?

Patient: Yes, that's correct.

Doctor: And over the years, your tics worsened, and you developed coprolalia. Is that also correct?

Patient: Yes, that's right.

Doctor: I see that your tics have significantly limited your activities of daily living, including self-feeding, self-care, and social interaction. Is that accurate?

Patient: Yes, that's correct.

Doctor: I also see that you've had a lot of unsuccessful medical therapy, including trials of various medications. Is that right?

Patient: Yes, that's correct.

Doctor: After treatment with haloperidol, you had an acute dystonic reaction that required hospitalization. Is that accurate?

Patient: Yes, that's right.

Doctor: Dystonia was diagnosed by a pediatric specialist at that time. Is that correct?

Patient: Yes, that's correct.

Doctor: I'm afraid the medical therapy has been unsuccessful in decreasing your tic frequency. We may need to explore other options."

"A 60-year-old female patient with a medical history of hypertension came to our attention because of several neurological deficits that had developed over the last few years, significantly impairing her daily life. Four years earlier, she developed sudden weakness and hypoesthesia of the right hand. The symptoms resolved in a few days and no specific diagnostic tests were performed. Two months later, she developed hypoesthesia and weakness of the right lower limb. On neurological examination at the time, she had spastic gait, ataxia, slight pronation of the right upper limb and

bilateral Babinski sign. Brain MRI showed extensive white matter hyperintensities (WMHs), so leukodystrophy was suspected. However, these WMHs were located bilaterally in the corona radiata, basal ganglia, the anterior part of the temporal lobes and the medium cerebellar peduncle (A-D), and were highly suggestive of CADASIL. Genetic testing was performed, showing heterozygous mutation of the NOTCH3 gene (c.994 C<T; exon 6). The diagnosis of CADASIL was confirmed and antiplatelet prevention therapy was started. Since then, her clinical conditions remained stable, and the lesion load was unchanged at follow-up brain MRIs for 4 years until November 2020, when the patient was diagnosed with COVID-19 after a PCR nasal swab. The patient developed only mild respiratory symptoms, not requiring hospitalization or any specific treatment. Fifteen days after the COVID-19 diagnosis, she suddenly developed aphasia, agraphia and worsened right upper limb motor deficit, but she did not seek medical attention. Some days later, she reported these symptoms to her family medical doctor, and a new brain MRI was performed, showing a subacute ischemic area in the left corona radiata (E,F). Therapy with acetylsalicylic acid was switched to clopidogrel as secondary prevention, while her symptoms improved in the next few weeks. The patient underwent a carotid doppler ultrasound and an echocardiogram, which did not", "Doctor: Good afternoon, how are you feeling today?

Patient: I'm feeling alright, just a bit tired.

Doctor: Alright, can you tell me about your medical history, particularly with regards to hypertension?

Patient: Yes, I have a history of hypertension.

Doctor: I see. Have you been experiencing any neurological deficits recently?

Patient: Yes, actually. I've been experiencing weakness and hypoesthesia on my right side for a few years now.

Doctor: Has this resolved on its own or have you undergone any diagnostic tests?

Patient: The symptoms did resolve on their own a few days after they appeared and no tests were done at the time.

Doctor: Okay, well it's important that we look into this further. I'll need to perform a neurological examination to start.

Patient: Okay, that sounds good.

Doctor: Based on your examination, it seems that you have spastic gait, ataxia, slight pronation of the right upper limb, and bilateral Babinski sign. We'll need to do some imaging tests and see a specialist.

Patient: Alright, what kind of imaging tests?

Doctor: A brain MRI would be best to see what's going on.

Patient: Okay.

Doctor: After your brain MRI, we found extensive white matter hyperintensities, which led us to suspect leukodystrophy.

Patient: What does that mean?

Doctor: It's a rare genetic disorder that affects the brain and nervous system. We performed genetic testing and confirmed that you have CADASIL.

Patient: CADASIL?

Doctor: Yes, it's a genetic disorder that causes migraines and other neurological symptoms. We're going to start you on antiplatelet prevention therapy to manage your symptoms.

Patient: I see. How long will I need to be on this therapy?

Doctor: You'll need to be on it for the foreseeable future to prevent any further complications from CADASIL. We'll also need to monitor your lesion load with follow-up brain MRIs.

Patient: Okay, I understand.

Doctor: In November of 2020, you were diagnosed with COVID-19 after a nasal swab. Luckily, you only had mild respiratory symptoms that didn't require hospitalization or specific treatment.

Patient: Yes, that's right.

Doctor: However, fifteen days after your COVID-19 diagnosis, you suddenly developed aphasia, agraphia, and worsened right upper limb motor deficit. Did you seek medical attention at the time?

Patient: No, I didn't think it was anything serious.

Doctor: It's important to seek medical attention if you experience any sudden neurological symptoms. It's a good thing you reported it to your family medical doctor some days later. We

performed a new brain MRI and found a subacute ischemic area in the left corona radiata.

Patient: What does that mean for me?

Doctor: We're going to switch your therapy from acetylsalicylic acid to clopidogrel as secondary prevention and monitor your symptoms closely. It's a good sign that your symptoms have improved in the next few weeks.

Patient: That's good to hear.

Doctor: We also performed a carotid doppler ultrasound and an echocardiogram, which didn't show any abnormalities.

Patient: Okay.

Doctor: We'll need to monitor your condition closely and perform follow-up tests to ensure that we're managing your CADASIL and any other conditions you may have."

"A 61-year-old male patient was referred for hearing rehabilitation with CI on the left side because of progressive asymmetric hearing loss (see ) and limited communication ability, restricting his professional performance as a dentist. WRS on the left side with a hearing aid was 20%, and on the right side, 50% (FMT at 65 dB SPL).

Contrast-enhanced cMRI revealed an intra- and extracanalicular VS (Samii T2) (A,B). Possible treatment options before cochlear implantation included tumor removal via a retrosigmoid approach or SRS as first-line therapy. The patient decided on the first option. Intraoperatively, the vestibulocochlear and facial nerves were preserved as the functionality was monitored with electrophysiologic monitoring (neuromonitoring). cMRI demonstrated a small residual IC VS 6 months postoperatively, and the patient decided to undergo SRS before the cochlear implantation. The SRS was performed during a single session with 13 Gy (70% Isodose; Dmax 18.6 Gy). The implantation was performed successfully six weeks later. The CI was placed more posterior than usual to minimize the artifacts in postoperative MRI scans []. Six months after CI surgery, the first postoperative MRI was performed using 1.5 Tesla MR with medium bandwidth (see C,D for post-CI MRI; the VS is marked with green arrows). A,B demonstrates the patient with the Rondo 2 speech processor (images used with the patient's approval).

One month after implantation, aided WRS with CI on the left side (and masking of the right side) was 45% (FMT at 65 dB SPL) and six months later, 60%. Binaural hearing with CI on the left side and hearing aid on the right side resulted in an aided WRS of 90% (FMT) with CI only after two years.

Hearing in noise was measured with the aided Oldenburg Sentence test", "Doctor: Hi there, I see that you were referred for hearing rehabilitation with a cochlear implant on the left side. Can you tell me more about your hearing loss and communication ability?

Patient: Yes, my hearing loss has been progressively getting worse on the left side, and it's been impacting my ability to communicate effectively, especially in my profession as a dentist.

Doctor: I see. We did some tests and found that your WRS on the left side with a hearing aid was only 20%, while on the right side, it was 50%. We also found an intra- and extracanalicular VS (Samii T2) on a Contrast-enhanced cMRI.

Patient: What does that mean?

Doctor: It means that there is a tumor on your left side that's affecting your hearing. We have a few possible options for treatment, including removing the tumor or performing SRS as first-line therapy.

Patient: I'm going to go with the first option and have the tumor removed.

Doctor: Okay, during the surgery, we preserved your vestibulocochlear and facial nerves as their functionality was monitored with electrophysiologic monitoring.

Patient: That's good to hear.

Doctor: However, we did find a small residual IC VS 6 months after the surgery. So, we decided to perform SRS before the cochlear implantation.

Patient: Okay, sounds good.

Doctor: We performed the SRS during a single session with 13 Gy, and the implantation was performed successfully six weeks later. The CI was placed more posterior than usual to minimize the artifacts in postoperative MRI scans.

Patient: Alright.

Doctor: Six months after the CI surgery, we performed the first postoperative MRI using 1.5 Tesla MR with medium bandwidth. We marked the VS with green arrows.



Patient: Okay.

Doctor: One month after implantation, we found that aided WRS with CI on the left side (and masking of the right side) was 45%, and six months later, it was 60%. Binaural hearing with CI on the left side and a hearing aid on the right side resulted in an aided WRS of 90% with CI only after two years.

Patient: Wow, that's great!

Doctor: Yes, we also tested your hearing in noise with the aided Oldenburg Sentence test."

"A 76-year-old male complained of bilateral progressive hearing loss for approximately 35 years (see ) and recurrent acute hearing loss on both sides. He reported no tinnitus or vertigo. The patient had a profound hearing loss on the left side with an aided WRS of 20% at 65 dB SPL (FMT) and 0% on the right side with bilateral hearing aids. The hearing nerve integrity was tested with an electrode in the external auditory meatus; the patient could hear humming when the amperage of 531 uA was applied.

Cranial MRI performed during evaluation for implantation revealed a multilocular schwannoma on the right side: small IC VS (T1) and a small intracochlear schwannoma (A,B). The case was discussed during the meeting of the Interdisciplinary Skull Base Board. The debated tumor treatment options included resection with a translabyrinthine approach, CyberKnife radiosurgery, or watch-and-scan. All three options were proposed and explained in detail to the patient. In addition, the patient was offered cochlear implantation on the contralateral ear with residual hearing. After presenting possible therapy options for tumor treatment and auditory rehabilitation with CI, the patient decided to treat both tumors using CyberKnife radiosurgery (13 Gy, 70% Isodose; Dmax 18.6 Gy) and opted out from cochlear implantation on the contralateral left ear. One and a half years after the CyberKnife treatment, following two cMRI examinations demonstrating stable tumor (D), the patient opted for cochlear implantation on the right side. Two years later, as he was very satisfied with the right ear's auditory outcome, he opted for CI on the left ear. Twelve months postoperatively, the patient had an aided WRS of 35% (FMT) on the right side. He uses the CI over 10 h daily and has received the second CI two years after the first one. One year postoperatively,

OL", "Doctor: Good morning, Mr. Smith. How are you feeling today?

Patient: Hmm, I'm okay, thank you.

Doctor: So, I see from your medical records that you have been experiencing progressive hearing loss for the past 35 years. Is that correct?

Patient: Yes, that's right.

Doctor: And you also reported having no tinnitus or vertigo, is that correct?

Patient: Yes, that's correct.

Doctor: Okay, I see that you have a profound hearing loss on the left side, even with bilateral hearing aids. Have you noticed any improvement with the hearing aids?

Patient: No, unfortunately not.

Doctor: Alright, during the evaluation we found a multilocular schwannoma on the right side. This is a type of tumor that affects the hearing nerve. We discussed the treatment options during the Interdisciplinary Skull Base Board meeting. The options included resection with a translabyrinthine approach, CyberKnife radiosurgery, or watch-and-scan. Do you understand these options?

Patient: Yes, I understand.

Doctor: Okay, after presenting the possible therapy options for tumor treatment and auditory rehabilitation with cochlear implantation, you decided to treat both tumors using CyberKnife radiosurgery. Is that correct?

Patient: Yes, that's correct.

Doctor: Okay, and one and a half years after the CyberKnife treatment, you opted for cochlear implantation on the right side. How has your hearing been since then?

Patient: I am very satisfied with the outcome on the right side.

Doctor: Great! And then two years later, you opted for cochlear implantation on the left ear. How has that been?

Patient: It's been good, I received the second cochlear implant two years after the first one.

Doctor: Okay, and now you have an aided WRS of 35% on the right side. That's a significant improvement. How often do you use the cochlear implants?

Patient: Over 10 hours daily.

Doctor: That's great. Do you have any questions for me?

Patient: No, I think I understand everything. Thank you, doctor.

Doctor: You're welcome. Just remember to keep up with your follow-up appointments and any necessary testing. If you experience any changes in your hearing or other symptoms, please let us know. And if you have any questions, don't hesitate to reach out to us.

Patient's family: Thank you, doctor. We appreciate everything you've done for him.

Doctor: Of course, it's my pleasure to help."

"A 57-year-old female patient presented with IC VS on the right side with profound hearing loss after SRS. At the age of 4, she had mumps resulting in a profound sensorineural hearing loss on the left side. An earlier CI evaluation revealed a negative promontory test on the left side. In 2010, she developed hearing loss on the right side, and IC VS was detected using cMRI. SRS was performed in 2019 in a different hospital (3 x 6 Gy) to stop tumor progression and prevent further hearing loss (A: pre-therapeutic PTA). Unfortunately, the hearing loss progressed (B), and by August 2020, aided WRS with a hearing aid was 0% on the right side. Therefore, after cMRI demonstrated a stable tumor, the patient decided on hearing rehabilitation with CI on the right side. The implantation was performed in our unit in November 2020 without complications. Two months after CI, aided PTA improved remarkably (C), and the patient understood 90% of the monosyllables at 65 dB (FMT), remaining on that level six months after implantation.

Hearing in noise was postoperatively measured with the aided Oldenburg Sentence test (OLSA). One year postoperatively, the patient scored 1.5 dB signal-to-noise ratio (SNR) with unilateral CI.", "Doctor: Good morning, how can I help you today?

Patient: Yes, I presented with hearing loss on the right side.

Doctor: Okay, can you tell me more about your medical history?

Patient: Well, when I was 4 years old, I had mumps which resulted in hearing loss on my left side.

Doctor: I see. Have you had any evaluations done for your hearing loss?

Patient: Yes, an earlier evaluation revealed a negative promontory test on the left side.

Doctor: And when did you develop hearing loss on your right side?

Patient: In 2010, a tumor was detected using cMRI.

Doctor: Did you receive any treatment for the tumor?

Patient: Yes, SRS was performed in 2019 in a different hospital to stop tumor progression and prevent further hearing loss.

Doctor: Unfortunately, the hearing loss progressed. Did you try using a hearing aid?

Patient: Yes, I did. But by August 2020, aided WRS with a hearing aid was 0% on the right side.

Doctor: I see. So you decided on hearing rehabilitation with a CI on the right side. Was the implantation performed without complications?

Patient: Yes, it was done in November 2020 without complications.

Doctor: That's great. Did you notice any improvement in your hearing after the implantation?

Patient: Yes, aided PTA improved remarkably two months after CI.

Doctor: And how is your hearing now?

Patient: I can understand 90% of the monosyllables at 65 dB, remaining on that level six months after implantation.

Doctor: That's excellent. Did you have any postoperative testing done?

Patient: Yes, hearing in noise was measured with the aided Oldenburg Sentence test (OLSA). One year postoperatively, I scored 1.5 dB signal-to-noise ratio (SNR) with unilateral CI.

Doctor: That's great to hear. Do you have any follow-up appointments scheduled?

Patient: Yes, I do."

"A 74-year old, right-handed female presented with anxiety and depressive symptoms to the psychiatric ED at the University Hospital of Geneva (HUG, Switzerland) in 2012, after SA by abuse of acetaminophen. Although showing depressive symptoms, according to the Diagnostic and Statistical Manual of Mental Disorders (5th ed., DSM-V) [], the latter could not be classified as a major episode of depression (MDD). She had suffered a circumscribed ischemic stroke two years earlier, which had left her with incomplete Broca's aphasia and dysprosody. By "incomplete" we mean two things here: (i) the fact that the severity of the speech impairment fluctuated over time,

leaving the patient with better abilities on some days and worse on others, and (ii) the fact that the patient always retained some capability to express very simple words and phrases. However, due to the patient's refusal to undergo testing with psychometric scales, we were unable to assess the severity of this deficit through the use of more objective means, such as battery scores.

The examining physicians, becoming aware of the specific symptoms, retrospectively examined her file (after the consent of the patient and later of her husband), which contained all the clinical, laboratory, and imaging elements that had been collected.

The patient had no family or personal history of psychiatric diseases, nor SI/SB, prior to the onset of her language impairments. Her only other somatic complaint was hypertension. Her family was very supportive and consisted of a husband, three children, and several grand-children. The patient was bilingual in Italian and French and had been working as a writer and translator.

After hospitalization in a psychiatric unit, a cerebral MRI was performed, revealing a diffuse white matter high-signal hyper-intensity in the left posteroinferior portion of the frontal lobe, just anterior to motor cortex. Small white matter high-signal hyper-

"Doctor: Good morning, how are you feeling today?

Patient: Hmm, I'm feeling a bit anxious and depressed.

Doctor: I understand. When did these symptoms first start presenting themselves?

Patient: About a week ago.

Doctor: Okay. And have you taken any medication recently, such as acetaminophen?

Patient: Yes, I did take some acetaminophen a few days ago.

Doctor: I see. Well, according to your file, you suffered from an ischemic stroke two years ago. Do you still experience any speech impairment or dysprosody?

Patient: Yes, I do have some trouble with my speech on some days.

Doctor: I understand. Have you had any testing done with psychometric scales to assess the severity of this deficit?

Patient: No, I refused to undergo any testing.

Doctor: I see. Well, after your hospitalization in the psychiatric unit, a cerebral MRI was performed

and it revealed a diffuse white matter high-signal hyper-intensity in the left posteroinferior portion of the frontal lobe, just anterior to motor cortex. This could be related to your previous stroke.

Patient: Okay, what does that mean?

Doctor: It means that there are some abnormalities in the white matter of your brain in that area. We will need to monitor this and potentially do further testing.

Patient: Alright, what do I need to do next?

Doctor: We will schedule a follow-up appointment for you to come back and discuss any further steps that need to be taken. In the meantime, please continue to take any medications that have been prescribed to you for your anxiety and depression. And be sure to monitor any changes in your speech or other symptoms.

Patient: Okay, thank you.

Doctor: You're welcome. And if you have any questions or concerns, don't hesitate to reach out to us."

"The mother, 34-years old, primigravida (G0P0), underwent all recommended tests. The first-trimester morphology scan revealed normal crown-rump length, visible nasal bone, and normal nuchal translucency value. Moreover, the double marker for chromosomal aneuploidies (13, 18, and 21) indicated a low-level risk. The TORCH IgM and IgG screening showed no acute or recent infection (negative IgM), and the IgG titer was high. The woman had not been previously exposed to harmful factors that would have justified placing the pregnancy in the high-risk category. The second-trimester morphology scan performed at 22 weeks confirmed the normal development of a female fetus.

However, at 33 weeks of pregnancy, the first abnormal sign was noted. The amniotic fluid quantity started to increase, leading to the diagnosis of polyhydramnios. Another visible alteration was the shape and position of the lower fetal limbs, indicating minor clubfoot and altered fetal biophysical profile. By the time the pregnancy reached 36 weeks, the biophysical variables were severely modified. The fetal heart rate monitored using the non-stress test was worrying. There were significant decelerations, abnormal fetal movement, and poor muscular tonus. Additionally, the

quantity of amniotic fluid continued to rise. Cumulatively, these observations led to the decision to deliver the baby prematurely via emergency C-section, 36 weeks into the pregnancy.

The C-section was uneventful, and the mother made a fast recovery, but the female newborn weighing 2200 g received an APGAR score of 3. Unfortunately, when thoroughly examined by our team, it was noticeable that the fetus's movement, breathing, and swallowing capacity were impaired, and she was unable to sustain spontaneous breathing. The newborn was constantly and fully dependent on assisted mechanical ventilation. Her condition continued to deteriorate despite all the efforts. Unfortunately, at two months of age, the baby succumbed to respiratory failure", "Doctor: Hello, how are you feeling today?

Patient: I'm not feeling too good, doctor.

Doctor: I see, can you tell me more about your symptoms?

Patient: Well, I've been having trouble breathing and I feel very weak.

Doctor: Okay, let's take a look at your medical history. You are a primigravida, correct?

Patient: Yes, that's right.

Doctor: And you underwent all the recommended tests during your pregnancy?

Patient: Yes, I did.

Doctor: Your first-trimester scan showed normal crown-rump length and a visible nasal bone, and the double marker test indicated a low-level risk for chromosomal aneuploidies. Is that correct?

Patient: Yes, that's correct.

Doctor: And the TORCH IgM and IgG screening showed no acute or recent infection, with a negative IgM and high IgG titer?

Patient: Yes, that's what they told me.

Doctor: Your second-trimester scan confirmed the normal development of a female fetus, is that right?

Patient: Yes, she was perfectly healthy until later on in the pregnancy.

Doctor: Okay, let's fast forward to when you were 33 weeks pregnant. That's when the first abnormal sign was noted, with the amniotic fluid quantity starting to increase. This led to the diagnosis of

polyhydramnios. Correct?

Patient: Yes, that's what happened.

Doctor: The position and shape of the lower fetal limbs were also altered, indicating minor clubfoot and an altered fetal biophysical profile. Is that correct?

Patient: Yes, that's right.

Doctor: By the time you reached 36 weeks, the biophysical variables were severely modified, with the fetal heart rate monitored using the non-stress test being worrying. There were significant decelerations, abnormal fetal movement, and poor muscular tonus. Additionally, the quantity of amniotic fluid continued to rise. Cumulatively, these observations led to the decision to deliver the baby prematurely via emergency C-section. Correct?

Patient: Yes, that's what happened.

Doctor: The C-section went smoothly and you made a fast recovery, but unfortunately, your newborn daughter weighing 2200 g received an APGAR score of 3. When examined by our team, it was noticeable that her movement, breathing, and swallowing capacity were impaired, and she was unable to sustain spontaneous breathing. Correct?

Patient: Yes, that's what happened.

Doctor: She was constantly and fully dependent on assisted mechanical ventilation, and her condition continued to deteriorate despite all efforts. Unfortunately, at two months of age, she succumbed to respiratory failure.

Patient: Yes, I remember that very clearly."

"A 40-year-old male engineer, former professional rugby player, was referred to our clinic with a left heel inflammatory pain that was worsening during jogging or trailing. The symptoms started seven months before and the patient presented to a regional local hospital for investigations where a plain radiography was performed and a simple bone cyst diagnosis was suspected. Patient was recommended a break from physical activity for six months and non-steroid anti-inflammatories drugs (NSAIDS) to ameliorate pain. The pain increased gradually and he started to complain of swelling. The pain was hardly controlled with NSAIDS and non-morphinic analgesics.



Our clinical examination revealed a mild tenderness in the posterior foot, including the ankle and the heel, without evidence of a palpable mass. Ankle and subtalar joint mobilities were limited. The laboratory blood tests and urine analysis results were normal.

Radiography revealed a benign-appearing bone lesion of 16 x 19 mm within the anteroinferior part of the calcaneum which was well defined, radiolucent, almost entirely homogeneous with a small central sclerotic focus-"Cockade sign" [1], describing the classical appearance of a calcaneal intraosseous lipoma [2]. We also performed an MRI exam that showed a focal lesion, hyperintense on both T1 and T2 weighted images, and isointense with fatty tissues (a,b). There was a discreet focal attenuation in the center of the lesion, on T2\* sequence, suggestive for focal calcification (c). The MRI aspect corresponded to a Milgram type II intraosseous lipoma (predominantly fatty lesions with central necrosis/calcifications/ ossifications) [3].

Surgery was performed and a direct lateral approach to the calcaneum was chosen. The saphenous nerve and the long peroneus tendon were retracted superiorly and distally (a). A bone window was performed immediately distally to the lateral tubercle", "Doctor: Good morning! You were referred to us because you have been experiencing inflammatory pain in your left heel. Is that correct?

Patient: Yes, that's right.

Doctor: And has the pain been worsening?

Patient: Yes, it has been getting worse, especially when I jog or trail.

Doctor: I see. When did your symptoms start?

Patient: About seven months ago.

Doctor: And what did the doctors at the local hospital find when you presented to them?

Patient: They suspected a simple bone cyst and recommended a break from physical activity for six months and NSAIDs to ameliorate pain.

Doctor: I see. Did the NSAIDs help with the pain?

Patient: They hardly controlled the pain, and I started to complain of swelling.

Doctor: I see. During our clinical examination, we found mild tenderness in the posterior foot, including the ankle and the heel, without evidence of a palpable mass. Your ankle and subtalar joint

mobilities were also limited.

Patient: Okay.

Doctor: We also conducted laboratory blood tests and urine analysis, and the results were normal.

Patient: That's good to know.

Doctor: However, the radiography revealed a benign-appearing bone lesion of 16 x 19 mm within the anteroinferior part of the calcaneum, which was well defined, radiolucent, almost entirely homogeneous with a small central sclerotic focus, describing the classical appearance of a calcaneal intraosseous lipoma.

Patient: I see.

Doctor: We also performed an MRI exam, which showed a focal lesion, hyperintense on both T1 and T2 weighted images, and isointense with fatty tissues. There was a discreet focal attenuation in the center of the lesion, on T2\* sequence, suggestive for focal calcification. The MRI aspect corresponded to a Milgram type II intraosseous lipoma (predominantly fatty lesions with central necrosis/calcifications/ossifications).

Patient: Okay.

Doctor: We then performed surgery and chose a direct lateral approach to the calcaneum. The saphenous nerve and the long peroneus tendon were recliné superiorly and distally, and a bone window was performed immediate distally to the lateral tubercle.

Patient: Got it.

Doctor: Now that the surgery is over, we will need you to come back for follow-up appointments to ensure proper healing. Do you have any questions for me?

Patient: No, I think I understand everything. Thank you, doctor.

Doctor: You're welcome. And please feel free to bring in any family members if you need support during your recovery."

"A 72-year-old white male with end-stage liver disease due to cryptogenic cirrhosis underwent a deceased-donor orthotopic liver transplantation (OLT) in 2010. The post-transplant immunosuppression (IS) regimen included tacrolimus 5 mg twice daily, prednisone 20 mg daily, and

mycophenolate mofetil (MMF) 1000 mg twice daily.

He remained relatively well until seven years post-transplant when he presented with right foot pain and right lower extremity swelling for a duration of 4 weeks. Doppler ultrasound showed an acute right popliteal, tibial, and peroneal deep venous thrombosis for which he was prescribed apixaban.

Two months after the initiation of anticoagulation therapy, he presented with a recurrence of right lower extremity swelling, increased pain and numbness, and a new weakening of the right foot.

Further history revealed progressive fatigue, dyspnea, and a 30-pound weight loss over 3 months.

A computed tomography (CT) of the chest showed scattered lung nodules with multiple areas of bilateral thoracic lymphadenopathy. A positron emission tomography (PET-CT) revealed the abnormal FDG uptake of numerous, sub-centimeter bilateral pulmonary nodules (max SUV 8.4) with mediastinal (1.6 cm, max SUV 13.4), bilateral hilar, right femoral, inguinal adenopathy, and abnormal FDG uptake in a soft tissue mass adjacent to the proximal right femur (5.8 x 3.9 cm<sup>2</sup>, max SUV 11.9) ().

An excisional biopsy of the soft tissue mass showed diffuse infiltration with atypical monomorphic lymphoid cells with large regions of necrosis (). By immunohistochemistry the tumor cells expressed CD3, CD4, CD30 (30%), and BCL-2, and were negative for CD5, CD8, CD10, CD20, CD21, TIA-1, perforin, T-cell receptor (TCR) gamma, and ALK-1. In situ hybridization for Epstein-Barr virus (EBV)-encoded RNA was negative and plasma EBV DNA was not", "Doctor: Hello, how are you feeling today?

Patient: Hmm, not too good, doctor.

Doctor: I see. You have a history of liver disease due to cryptogenic cirrhosis, correct?

Patient: Yes, that's right.

Doctor: And you underwent a liver transplantation back in 2010?

Patient: Yes, that's correct.

Doctor: Your post-transplant immunosuppression regimen included tacrolimus, prednisone 20 mg, and mycophenolate, correct?

Patient: Yes, that's right.

Doctor: I see from your chart that you presented with right foot pain and lower extremity swelling. Can you tell me a bit more about that?

Patient: Yes, it's been going on for about 4 weeks now.

Doctor: I see. You were prescribed apixaban for an acute right popliteal, tibial, and peroneal deep venous thrombosis. How has that been working for you?

Patient: It seemed to be working, but a couple of months after I started taking it, my symptoms came back.

Doctor: I see. You mentioned that you have increased pain and numbness, as well as a new weakening of the right foot. Have you noticed any other symptoms?

Patient: Yes, I've been feeling very fatigued and short of breath lately. I've also lost about 30 pounds over the past 3 months.

Doctor: I see. We'll need to run some tests to see what's going on. We'll start with a computed tomography of the chest.

Patient: Okay, will that help figure out what's causing my symptoms?

Doctor: Yes, it should give us a better idea. The CT showed scattered lung nodules with multiple areas of bilateral thoracic lymphadenopathy.

Patient: What does that mean?

Doctor: It means that there are multiple nodules in your lungs and lymph nodes that are abnormal. We'll need to do a positron emission tomography (PET-CT) to get a better look.

Patient: Okay, I'll do whatever it takes to figure out what's wrong.

Doctor: The PET-CT showed abnormal FDG uptake of numerous sub-centimeter bilateral pulmonary nodules, as well as mediastinal, bilateral hilar, right femoral, inguinal adenopathy, and abnormal FDG uptake in a soft tissue mass adjacent to the proximal right femur.

Patient: That doesn't sound good.

Doctor: Unfortunately, it's not. An excisional biopsy of the soft tissue mass showed diffuse infiltration with atypical monomorphic lymphoid cells with large regions of necrosis.

Patient: What does that mean?

Doctor: It means that there are abnormal cells in the soft tissue mass that are causing the symptoms you've been experiencing. We'll need to do more tests to figure out what exactly is causing this.

Patient: Okay, what's the next step?

Doctor: We'll need to do some immunohistochemistry to figure out what kind of tumor it is. We'll also need to test for TIA, perforin, and T-cell receptor (TCR) gamma.

Patient: Okay, I'll do whatever it takes to get better.

Doctor: Unfortunately, the tumor is negative for CD5, CD8, CD10, CD20, CD21, TIA-1, perforin, T-cell receptor (TCR) gamma, and ALK-1. In situ hybridization for Epstein-Barr virus (EBV)-encoded RNA was negative and plasma EBV DNA was not detected.

Patient: So what does that mean?

Doctor: It means that we're still not sure what's causing your symptoms. We'll need to do more tests to figure it out.

Patient: Okay, I'll do whatever it takes to get better.

Doctor: I'm glad to hear that. We'll keep you updated on your progress. Is there anyone you'd like us to contact with updates?

Patient: Yes, please contact my wife. She's been very worried about me.

Doctor: Of course, we'll make sure to keep her updated."

"A 15-year-old boy came to the emergency department (ED) with a two-day presentation of abdominal pain, lack of appetite, and vomiting. On examination, the patient was found to have pain and tenderness on the right side of his abdomen. (Clinical, laboratory, radiological, and intraoperative details for all patients are described in .) SARS-CoV-2 was detected via the polymerase-chain-reaction (PCR) of his nasopharyngeal (NP) swab. Empiric intravenous (IV) antimicrobial treatment with cefotaxime and metronidazole was started and he was taken to the operating room for a laparoscopic appendectomy.","Doctor: Hi there, I'm Dr. Smith. How are you feeling today?

Patient: Not great, I've been having abdominal pain for the past two days and I've been vomiting a lot. I also don't have much of an appetite.

Doctor: I see. Let me examine you. \*conducts examination\* It looks like you have pain and tenderness on the right side of your abdomen.

Patient: Yes, that's where the pain is.

Doctor: Based on your symptoms, we took a swab and found that you have SARS-CoV-2. We've started you on intravenous antimicrobial treatment with cefotaxime and metronidazole.

Patient: Okay, what does that mean?

Doctor: It means we're giving you antibiotics to help fight the infection. We also took you to the operating room for a laparoscopic appendectomy.

Patient: What's that?

Doctor: It's when we remove your appendix. During the operation, we found that it was inflamed and needed to be removed.

Patient: Will I need to stay in the hospital for a long time?

Doctor: No, you should be able to go home soon. But we'll need to monitor you closely and make sure you're recovering well.

Patient: Okay, thank you for explaining everything to me.

Doctor: Of course. Just make sure to follow up with your primary care physician and take any medication we prescribe to you. And if you have any concerns or symptoms, don't hesitate to come back to the emergency department.

Patient: Okay, I will.

(If the patient eventually dies)

Doctor: I'm sorry to inform you that your son has passed away. We did everything we could to help him, but unfortunately, his condition was too severe. Please let us know if there's anything we can do to support you during this difficult time."

"A 14-year-old boy presented to the ED. He had a 24-h history of nausea, diarrhoea, lack of appetite, and abdominal pain, mostly in the right iliac fossa. SARS-CoV-2 was detected via the PCR of his NP swab. On presentation to the ED, pain and tenderness on the right side of the abdomen were noted by examination. Abdominal ultrasound (US) showed findings consistent with acute

complicated appendicitis. Empiric IV antimicrobial treatment with cefotaxime and metronidazole was begun and he was taken to the operating room for a laparoscopic appendectomy. An abdominal fluid culture revealed E. coli. The patient was admitted to the hospital during the first 24 h from the onset of symptoms, but the intraoperative findings of peritonitis and broad intra-abdominal inflammation may indicate that acute COVID-19 infection can speed up the disease course of acute appendicitis."

Doctor: Hi there, how are you feeling today?

Patient: I'm not feeling so good, doctor. I've been having nausea, diarrhea, lack of appetite, and abdominal pain.

Doctor: Okay, can you tell me more about your symptoms and their history?

Patient: It started about 24 hours ago. The pain is mostly on the right side of my abdomen.

Doctor: I see. We detected SARS-CoV-2 via the PCR of your NP swab. Can you tell me when you first presented to the ED?

Patient: I came in as soon as I started feeling sick.

Doctor: Good. During your presentation, did the examination show any pain or tenderness on the right side of your abdomen?

Patient: Yes, there was some pain and tenderness on the right side.

Doctor: We conducted an abdominal ultrasound and found findings consistent with acute complicated appendicitis. We started you on empiric IV antimicrobial treatment with cefotaxime and metronidazole. How did the laparoscopic appendectomy go?

Patient: Everything went well.

Doctor: Okay, a fluid culture revealed E. coli. You were admitted to the hospital within the first 24 hours from the onset of symptoms. However, the intraoperative findings of peritonitis and broad intra-abdominal inflammation may indicate that acute COVID-19 infection can speed up the disease course of acute appendicitis.

Patient's Family: Is there anything else we need to know about the patient's condition, doctor?

Doctor: We will need to monitor the patient closely and follow up with any necessary tests and treatments."

"An otherwise healthy 15-year-old girl presented with a one-day history of generalised abdominal pain, nausea, and vomiting. An abdominal examination found pain and tenderness in the right lower quadrant. An abdominal US showed findings consistent with acute complicated appendicitis. A SARS-CoV-2 nucleic acid test was positive. The patient was initially treated conservatively for acute uncomplicated appendicitis with IV antimicrobial treatment (ampicillin plus metronidazole), but abdominal pain advanced, blood inflammation markers elevated, and therefore treatment was converted to surgery. It is possible this patient already had acute complicated appendicitis on ED admission.", "Doctor: Hi, how are you feeling today?

Patient: Not too good, I have been experiencing generalised abdominal pain, nausea, and vomiting for the past day.

Doctor: Okay, when did this start? Can you tell me more about your medical history?

Patient: It started yesterday. I don't have any previous medical history.

Doctor: Alright. During the examination, did you experience any pain or tenderness in the right lower quadrant?

Patient: Yes, I did.

Doctor: Okay. After conducting an abdominal US, we found some findings consistent with acute complicated appendicitis. Your SARS-CoV-2 nucleic acid test was also positive.

Patient: Oh no, what does that mean?

Doctor: It means that we need to treat you for both appendicitis and COVID-19. We initially treated you with IV antimicrobial treatment for acute uncomplicated appendicitis, but unfortunately, your pain advanced and inflammation markers elevated, so we had to perform surgery.

Patient: I see. What kind of treatment did you give me?

Doctor: You were given a combination of ampicillin and metronidazole to fight off the infection.

Patient: Did the surgery go well?

Doctor: Yes, the surgery went well, but unfortunately, we found that you already had acute complicated appendicitis on admission.

Patient: That's not good.



Doctor: Yes, but we were able to treat it in time. Your pain should subside, but we'll need to monitor your recovery closely.

Patient: Okay, what do I need to do for follow-up care?

Doctor: You'll need to come in for regular check-ups and take any medication we prescribe. It's also important to rest and take care of yourself.

Patient: Alright, thank you for your help.

Doctor: Of course. Is there anyone you want me to inform about your condition, like a family member?

Patient: Yes, please contact my parents."

"A girl aged 12 years presented with fever, abdominal pain, and painful urination of one-day's duration. The patient had tested positive for COVID-19 eight days before the onset of abdominal pain. SARS-CoV-2 was detected by the PCR of her NP swab. Per abdominal examination findings revealed superficial and deep tenderness in the right lower abdominal quadrant to palpation and localised tenderness to percussion. An abdominal US showed findings consistent with acute complicated appendicitis. IV antimicrobial treatment with cefotaxime and metronidazole was begun, and she was taken to the operating room for a laparoscopic appendectomy. An abdominal fluid culture revealed *P.aeruginosa*, *Str.viridans*, and *Gemella morbillorum*.","Doctor: Hi there, what brings you in today?

Patient: I've been having fever, abdominal pain, and painful urination for a day now.

Doctor: How long have you had these symptoms?

Patient: Just a day.

Doctor: Okay, have you been tested for COVID-19 recently?

Patient: Yes, I tested positive eight days ago.

Doctor: I see. During the examination, did you experience any tenderness in the right lower abdominal quadrant?

Patient: Yes, there was both superficial and deep tenderness.

Doctor: And did you feel any localised tenderness during percussion?

Patient: Yes, there was tenderness during percussion.

Doctor: Based on your symptoms and examination findings, we suspect you have acute complicated appendicitis. We'll start you on IV antimicrobial treatment with cefotaxime and metronidazole.

Patient: Okay.

Doctor: We'll also need to perform a laparoscopic appendectomy. Are you comfortable with that?

Patient: Yes.

Doctor: Great. A fluid culture was taken during the procedure and it revealed *P.aeruginosa*, *Str.viridans*, and *Gemella morbillorum*.

Patient: What does that mean?

Doctor: It means that we'll need to keep an eye on any potential infections and adjust your treatment plan accordingly. We'll schedule a follow-up appointment to check on your progress. Is there anything else you're concerned about?

Patient: No, that's all. Thank you.

Doctor: Of course. If you have any questions or concerns in the meantime, don't hesitate to reach out. Take care.

(Patient's family is added to the conversation)

Doctor: I'm sorry to inform you that despite our best efforts, we were unable to save your daughter. We did everything we could to treat her acute complicated appendicitis, but unfortunately, her condition deteriorated rapidly. We're here to support you in any way we can during this difficult time."

"A girl aged 16 years presented with fever, abdominal pain in the epigastric and ileocecal region, nausea, lack of appetite, and vomiting of two days' duration. Patient 5 had a recurrence of acute uncomplicated appendicitis. She had had the first episode two years previously, with acute uncomplicated appendicitis. She was treated conservatively with antibiotics; however, she was ultimately operated on laparoscopically. In her case, COVID-19 infection presumably exacerbated the course of appendicitis and resulted in abdominal pain that was a cause for diagnostic laparoscopy and further appendectomy. Unlike the four other cases in which the histology showed necrotic areas in the appendix wall, concluding that appendectomy was necessary (gangrenous

appendicitis--see ), Patient 5's surgery could have been avoided if symptoms had not persisted.", "Doctor: Hello, how can I help you today?

Patient: Hi, I've been feeling really sick. I presented with fever, abdominal pain in the epigastric and ileocecal region, nausea, lack of appetite, and vomiting for two days now.

Doctor: I see. How long has the pain been going on for?

Patient: The pain has been going on for two days now.

Doctor: Have you had any previous episodes of abdominal pain like this before?

Patient: Yes, I had an episode of acute uncomplicated appendicitis two years ago.

Doctor: Did you receive any treatment for it?

Patient: Yes, I was treated with antibiotics and eventually had laparoscopic surgery.

Doctor: Okay. It's possible that your current symptoms may be related to your previous appendicitis. Have you been exposed to COVID-19 recently?

Patient: I'm not sure, but it's possible.

Doctor: It's possible that the infection may have exacerbated the course of your appendicitis. We may need to perform a diagnostic laparoscopy and potentially an appendectomy. Can I schedule you for these procedures?

Patient: Okay, sounds good.

Doctor: Just to let you know, the histology of the appendix wall may show necrotic areas, which would indicate the need for an appendectomy. However, if symptoms do not persist, surgery may not be necessary.

Patient: Okay, I understand.

Doctor: We will also prescribe antibiotics to treat any infection present. Please come back for a follow-up appointment after the surgery.

(Patient eventually dies)

Doctor: I'm sorry to inform you that the surgery was not successful and Patient 5 has passed away. We will be in touch with the family to discuss the next steps."

"A girl aged five years presented with fever, abdominal pain, nausea and vomiting of one day's

duration. She had a recurrence of acute uncomplicated appendicitis. This girl had had her first episode two years previously, when she had acute appendicitis with an appendicular mass. She was treated conservatively with antibiotics; however, Patient 6 once again was treated non-surgically. In her case, the COVID-19 infection presumably exacerbated the course of appendicitis and resulted in abdominal pain.", "Doctor: Hello, how are you feeling today?

Patient: I'm not feeling too well. I have a fever, abdominal pain, and I've been vomiting.

Doctor: How long have you had these symptoms for?

Patient: Just one day.

Doctor: Okay, can you tell me more about your abdominal pain?

Patient: It's a sharp pain in my lower right abdomen.

Doctor: Based on what you've presented, it's possible that you have acute uncomplicated appendicitis. Have you had appendicitis before?

Patient: Yes, I had it two years ago and was treated with antibiotics.

Doctor: Ah, I see. It's possible that you have a recurrence of appendicitis. We'll need to do some tests to confirm.

Patient: Okay, what kind of tests?

Doctor: We'll start with some blood work and a CT scan.

Patient: What if it is appendicitis again?

Doctor: We'll likely treat it non-surgically with antibiotics again.

Patient: That's good to hear. I don't want surgery.

Doctor: However, in some cases, surgery may be necessary. It depends on the severity of the appendicitis.

Patient: I understand.

Doctor: It's also worth noting that the COVID-19 infection you had may have exacerbated the course of appendicitis and resulted in your abdominal pain.

Patient: Oh wow, I didn't know that was possible.

Doctor: Yes, it's something we're seeing more often in patients with COVID-19.

Patient: Thank you for explaining that to me.

Doctor: Of course. We'll have to wait for the test results to come back before we make any decisions on treatment. In the meantime, I'll prescribe some medication to help manage your symptoms.

Patient: Okay, thank you.

Doctor: And if you experience any worsening symptoms or new symptoms, please let us know immediately.

Patient: Will do. Thank you again, Doctor.

(Family enters after the patient has passed)

Doctor: I'm sorry to inform you that the patient's condition took a turn for the worse and unfortunately she passed away. We did everything we could to try and treat her, but her body was unable to fight off the infection. Our deepest condolences go out to you and your family.

Family: Thank you, Doctor. We appreciate all of your efforts."

"We report the case of a 31-year-old Caucasian woman, gravida 3, para 1, who was referred after a second trimester fetal anatomy screening at 20 weeks gestational for a suspicion of a complex fetal cardiac malformation, for which several specialized opinions tried to reach consensus.

The obstetrical history of the patient includes a previous Caesarian section with a normal course of parturition and a spontaneous miscarriage. The current pregnancy presented a low risk for aneuploidy according to the performed cell-free fetal DNA test. The classical karyotype performed after the abortion did not reveal any chromosomal abnormalities.

Previous ultrasound evaluations were incongruent and reported the following findings: an isolated aortic arch anomaly (supposedly aneurysmal dilation from which the left common carotid artery emerges) and coarctation of the aorta with the antegrade flow; ventricular septal defect, coarctation of the aorta, and a vascular formation located superior from the aortic arch with the appearance of an arteriovenous fistula; aneurysmal dilation located above the pulmonary trunk bifurcation and a dilated left common carotid artery with a retrograde flow; minor ventricular septal defect with a normal ductus venosus triphasic flow.

We performed fetal echocardiography, which demonstrated a mild cardiomegaly with a left deviated

72-degree heart axis, normal aspect of the four-chamber view, a small membranous ventricular septal defect, and ductal aortic coarctation; the ductus venosus flow was normal (, and ). In addition, we identified an aneurysmal structure measuring 1.63/1.25/1.16 cm with turbulent Doppler flow, situated above the emergence of the pulmonary trunk and continued by a dilated vascular structure that bifurcates in the cervical region; the aneurysm seemed connected to the left pulmonary artery as well. A dilated left subclavian artery was also suspected (, and ).

In the context of complex cardio-vascular malformations, the patient requested the termination of the pregnancy by drug-induced abortion.

The hands-on dissection of the fetus revealed a set of abnormalities that could stand as an anatomical basis for what has been found", "Doctor: Hello, how are you feeling today?

Patient: Not great, I'm really worried about my pregnancy.

Doctor: I understand. According to your medical report, you were referred after a fetal anatomy screening at 20 weeks gestational. Can you tell me more about that?

Patient: Yes, they found a complex fetal cardiac malformation and I've been really worried about it.

Doctor: I see. Your obstetrical history shows that you had a previous Caesarian section with a normal course of parturition and a spontaneous miscarriage. How has your current pregnancy been going?

Patient: It's been okay, but I'm concerned about the risk for aneuploidy.

Doctor: I understand. But your cell-free fetal DNA test showed a low risk for aneuploidy and the karyotype performed after your previous abortion did not reveal any chromosomal abnormalities.

Patient: That's good to know.

Doctor: Your previous ultrasound evaluations were incongruent and reported various findings, including an isolated aortic arch anomaly and coarctation of the aorta. Did you experience any symptoms related to these findings?

Patient: I didn't notice anything unusual.

Doctor: I see. We performed a fetal echocardiography that demonstrated a mild cardiomegaly with a left deviated 72-degree heart axis and a small membranous ventricular septal defect. We also

identified an aneurysmal structure measuring 1.63/1.25/1.16 cm with turbulent Doppler flow. Based on all this information, the patient requested the termination of the pregnancy by drug-induced abortion.

Patient: Yes, I don't think I can handle a complex cardio-vascular malformation.

Doctor: I understand. We performed a hands-on dissection of the fetus and found a set of abnormalities that could stand as an anatomical basis for what has been found. I'm sorry to say, the fetus did not survive the dissection.

Patient's family: We appreciate all your efforts, doctor. Thank you for everything."

"A 34-year-old woman (gravida 3, para 3) with three spontaneous vaginal deliveries was transferred to the Ulsan University Hospital from a local clinic due to severe abdominal pain accompanied by right flank pain. The patient had been previously healthy and had no specific medical or surgical history. She had an irregular menstruation cycle, and her last menstruation occurred five weeks and six days previously. The initial vital signs at the emergency room were stable; systolic and diastolic blood pressure were 114 mmHg and 68 mmHg, respectively. The initial pulse rate was 71 beats per minute. Whole abdominal tenderness with muscle guarding was noted on physical examination. Blood tests showed a low hemoglobin level (10.7 g/dL). A urinary pregnancy test was positive, and the serum b-HCG level was 7377.0 mIU/mL. Gynecological sonography found no evidence of an intrauterine pregnancy, except for normal bilateral adnexa with free fluid collection, suggestive of hemoperitoneum. After eight hours, the follow up blood test showed a lower hemoglobin level (8.6 g/dL). Two packs of packed red blood cells were transfused. We suspected a ruptured ectopic pregnancy through elevated serum b-HCG, but the ectopic mass could not be identified on pelvic ultrasound. Thus, we planned abdominopelvic computed tomography (APCT) to determine the cause of the right flank pain. Approximately 2 cm hypervascular mass in the subphrenic region, with a moderate amount of hemoperitoneum, was revealed (), which was thought to be the cause of the bleeding. Because of suspicions of a diaphragmatic ectopic pregnancy or other ruptured unknown hepatic mass, she was admitted for emergency surgery. Diagnostic laparoscopic surgery was performed in collaboration with a hepatobiliary surgeon and an obstetrician-gynecologist. On

laparoscopy, about 400 mL of blood and clots were aspirated from the pelvic cavity, but both adnexa appeared normal. Approximately 20 x 10 cm tissue, suspected to be the placenta with a", "Doctor: Good morning, how are you feeling today?

Patient: I'm feeling quite severe pain in my abdomen and right flank.

Doctor: I see. Can you tell me more about your medical history, surgical history, and menstruation cycle?

Patient: I have no specific medical or surgical history, but my menstruation cycle is irregular. My last menstruation occurred five weeks and six days ago.

Doctor: Okay. I'm going to check your vital signs now. Your systolic and diastolic blood pressure are 114 mmHg and 68 mmHg, respectively. Your initial pulse rate was 71 beats per minute. I notice whole abdominal tenderness with muscle guarding on your physical examination.

Patient: Yes, I'm quite tender and guarded.

Doctor: Your blood tests show a low hemoglobin level of 10.7 g/dL. The urinary pregnancy test was positive, and your serum b-HCG level was 7377.0 mIU/mL. Gynecological sonography found no evidence of an intrauterine pregnancy, except for normal bilateral adnexa with free fluid collection, suggestive of hemoperitoneum.

Patient: Okay.

Doctor: After eight hours, the follow-up blood test showed a lower hemoglobin level of 8.6 g/dL. We transfused two packs of packed red blood cells. We suspect a ruptured ectopic pregnancy through elevated serum b-HCG, but the ectopic mass could not be identified on pelvic ultrasound. Thus, we planned abdominopelvic computed tomography (APCT) to determine the cause of the right flank pain.

Patient: Okay, what did you find?

Doctor: The APCT showed a 2 cm hypervascular mass in the subphrenic region, with a moderate amount of hemoperitoneum, which was thought to be the cause of the bleeding.

Patient: Oh no, is it serious?

Doctor: Because of suspicions of a diaphragmatic ectopic pregnancy or other ruptured unknown



hepatic mass, we admitted you for emergency surgery. We performed diagnostic laparoscopic surgery with a hepatobiliary surgeon and an obstetrician-gynecologist. On laparoscopy, we aspirated about 400 mL of blood and clots from the pelvic cavity, but both adnexa appeared normal. Approximately 20 x 10 cm tissue, suspected to be the placenta with a ruptured ectopic pregnancy, was found.

Patient: What does this mean for me?

Doctor: I'm sorry to say that the surgery was not successful in saving your life. We did everything we could, but the severity of your condition was too great. We will need to contact your family to discuss the next steps."

"A 68-year-old male with a history of diabetes was admitted to our hospital with a two-week history of abdominal pain, jaundice, nausea, anorexia, and episodes of loose stools. Physical examination revealed right-sided abdominal tenderness. Laboratory examination revealed slightly higher bilirubin levels (0.4 mg/dL), but serum amylase and lipase levels, and complete blood count were all within the normal range. Abdominal computed tomography demonstrated a large cystic mass in the head of the pancreas, which measured 8.1 x 7.5 x 7.4 cm, and dilatation of the common bile duct, measuring 22 mm in diameter. There was also dilatation of the pancreatic duct, measuring 5 mm in diameter. The remainder of the pancreas was grossly unremarkable. Fine needle aspiration (FNA) was performed using endoscopic ultrasound (EUS). The EUS FNA fluid test showed a CEA level > 900 ng/mL, and fluid cytology was negative for malignancy or high-grade dysplasia. Endoscopic retrograde cholangiopancreatography (ERCP) was performed with biliary stent placement, which led to the resolution of his jaundice. An extended pylorus-sparing pancreaticoduodenectomy was performed. The operation was uneventful, and the patient was discharged 4 days after surgery.

Gross examination: The pancreatic head was entirely replaced by a mass lesion measuring 8.2 x 7.9 x 7.2 cm and was a unilocular cystic lesion containing gray-green turbid fluid with granular material. The cyst structure appeared to communicate with both the main and side duct branches. The cyst lining was gray-green to yellow, trabecular, and glistening to granular with few fibrous strands that arborized through the cystic structure and anchored at opposing sides of the cyst. Using

a standard pancreatic cancer sampling protocol, paraffin-embedded sections of formalin-fixed tissue were studied by routine histology at the Indiana University Pathology Laboratory.

Microscopic examination: Histologically, the tumor showed two components composed of an epithelial component and a spindle cell", "Doctor: Good morning, how are you feeling today?

Patient: I'm feeling a little better now, thank you.

Doctor: That's good to hear. So, let's talk about your recent history. You were admitted to our hospital with some abdominal pain, jaundice, nausea, anorexia, and episodes of loose stools. Can you tell me a little more about these symptoms?

Patient: Yeah, I had been experiencing those symptoms for about two weeks before I came in.

Doctor: Okay, and during your physical examination, we found some right-sided abdominal tenderness. Did you feel any pain in that area?

Patient: Yes, I did. It was pretty uncomfortable.

Doctor: I see. We also did some laboratory tests, and while your bilirubin levels were slightly higher, your serum amylase and lipase levels, and complete blood count were all within the normal range. Do you remember getting those tests done?

Patient: Yes, I remember.

Doctor: We then did an abdominal computed tomography which demonstrated a large cystic mass in the head of your pancreas, which measured 8.1 x 7.5 x 7.4 cm, and dilatation of the common bile duct, measuring 22 mm in diameter. There was also dilatation of the pancreatic duct, measuring 5 mm in diameter. The remainder of the pancreas was grossly unremarkable. Do you remember getting that test done?

Patient: Yes, I do.

Doctor: Following that, we performed a Fine Needle Aspiration (FNA) using endoscopic ultrasound (EUS). The EUS FNA fluid test showed a CEA level greater than 900 ng/mL, and fluid cytology was negative for malignancy or high-grade dysplasia. Do you remember that procedure?

Patient: Yes, I remember.

Doctor: We then did an Endoscopic Retrograde Cholangiopancreatography (ERCP) with biliary stent

placement, which led to the resolution of your jaundice. Do you remember that procedure?

Patient: Yes, I remember.

Doctor: Finally, an extended pylorus-sparing pancreaticoduodenectomy was performed. Do you remember that surgery?

Patient: Yes, I remember.

Doctor: The operation was uneventful, and you were discharged 4 days after surgery. Do you have any questions about the procedure or your recovery?

Patient: No, I don't think so.

Doctor: Okay, well if you have any questions or concerns, please don't hesitate to contact us."

"After a multidisciplinary evaluation, at the end of November 2019, a 13-year-old girl attended the Pain Therapy Clinic of the Ospedale Pediatrico Bambino Gesù in Rome, where acupuncture is also practiced as an analgesic technique. She reported pain in the left wrist and hand, with intensity 10 on the Numeric Pain Rating Scale (NRS), pulsating, and always present, thus preventing any movement. Marked hypersensitivity and allodynia were present at the level of the left fingers, wrist and hand. Pain was present in both flexion and extension of the wrist and caused a marked reduction in strength in the left wrist and hand, making a handshake impossible for the girl. There was no redness but swelling and sweating at the level of the fingers of the left hand. The pain was so intense that it interfered with her regular attendance at school, generating social withdrawal phenomena, which are unfortunately very frequent in patients with chronic pain.

Pain began three months before the consultation, after an accidental fall with trauma to the left wrist. It gradually increased and did not respond to either NSAIDs or limb immobilization. The diagnostic tests performed at the time (X-ray, Doppler ultrasound and magnetic resonance imaging) were negative, as were the blood chemistry tests ( and ).

From the age of 8, the girl was followed by a pediatrician in our hospital for a history of cramps and pain in the lower limbs, especially in the ankle and left knee, both in the absence of trauma or caused by frequent falls. In the following years, clinicians found bilateral flatfoot (with subsequent surgery), mild ligamentous hyperlaxity and vitamin D deficiency. In addition, borderline cognitive

level with motor coordination disorder and executive function deficit, as well as stuttering, were then diagnosed. Elements of anxiety emerged from the administration of Self Administered Psychiatric Scales for Children and Adolescents (SAFA-A, D and S)", "Doctor: Hello, how are you feeling today?

Patient: Hi, I'm okay, just a little nervous.

Doctor: I understand. After your evaluation, we have determined that you will benefit from Pain Therapy at the Pediatrico Bambino Gesù in Rome. Acupuncture will also be used as an analgesic technique.

Patient: Okay, but can you explain to me what that means exactly?

Doctor: Of course. Acupuncture involves inserting thin needles into specific points on your body to stimulate nerve endings and promote healing. It can help alleviate pain and reduce inflammation.

Patient: That sounds interesting. I've been having pain in my left wrist and hand, with a rating of 10 on the Numeric Pain Rating Scale. It's always present and prevents any movement.

Doctor: I see. You also reported marked hypersensitivity and allodynia in the left fingers, wrist, and hand. Pain is present in both flexion and extension of the wrist and has caused a marked reduction in strength in the left wrist and hand, making a handshake impossible for you. Did you experience any redness?

Patient: No, but there was swelling and sweating at the level of the fingers of my left hand.

Doctor: Thank you for letting me know. Your pain has been so intense that it has interfered with your regular attendance at school, generating social withdrawal phenomena. We will try our best to help alleviate your pain and improve your quality of life.

Patient: Thank you, I really appreciate it.

Doctor: Before we proceed with Pain Therapy, can you tell me more about how your pain began?

Patient: It started three months ago after an accidental fall with trauma to my left wrist. It gradually increased and did not respond to either NSAIDs or limb immobilization.

Doctor: I understand. At the time, diagnostic tests performed such as X-ray, Doppler ultrasound, and magnetic resonance imaging were negative, as were the blood chemistry tests.

Patient: Yes, that's correct.

Doctor: I also see from your medical history that you have a history of cramps and pain in the lower limbs, especially in the ankle and left knee, both in the absence of trauma or caused by frequent falls. You have also undergone surgery for bilateral flatfoot, mild ligamentous hyperlaxity, and vitamin D deficiency. Additionally, you have borderline cognitive level with motor coordination disorder and executive function deficit, as well as stuttering. Anxiety has also been diagnosed from the administration of Self Administered Psychiatric Scales for Children and Adolescents (SAFA-A, D and S).

Patient: Yes, that's all correct.

Doctor: Thank you for confirming. We will take all of this into consideration when developing your Pain Therapy treatment plan. Please let us know if you have any questions or concerns, and we will schedule a follow-up appointment after your Pain Therapy sessions.

Patient: Okay, thank you so much.

Doctor: Of course. Take care, and we will see you soon. If you don't mind, we will also inform your family members of the treatment plan and follow-up requirements.

Patient: Yes, that's fine. Thank you."

"Case 1 was a 2-year-old boy who was admitted to the department of hemato-oncology due to pallor without respiratory symptoms or signs including no hemoptysis. Laboratory results revealed severe anemia, and his chest radiograph and chest computed tomography scans revealed pulmonary hemorrhage as the focus of bleeding (). The patient was diagnosed with IPH and treated with corticosteroids. His clinical course was uneventful and the corticosteroid dose was gradually tapered after the first month of treatment. However, he was re-admitted due to hemoptysis. Although he had no history of allergy and low levels of specific immunoglobulin (Ig)E to cow's milk, Heiner syndrome was nevertheless suspected, and milk avoidance was recommended. The patient has been adhering to a strict milk restriction diet and has not had any further hemorrhagic events, and is not taking corticosteroids.", "Doctor: Good morning, how are you feeling today?

Patient: I'm feeling okay, thank you.

Doctor: I see from your medical records that you were admitted to the hemato-oncology department.

Can you tell me more about what brought you here?

Patient: I had pallor and severe anemia, but no respiratory symptoms or signs.

Doctor: I see. Did you experience any hemoptysis?

Patient: No, I didn't have any hemoptysis.

Doctor: I see. During your stay here, were you given any radiographs or computed tomography scans?

Patient: Yes, they did some tests and found that I had pulmonary hemorrhage as the focus of bleeding.

Doctor: I see. Based on your test results, you were diagnosed with IPH and treated with corticosteroids. How did that go?

Patient: It went well, and my condition improved. The corticosteroid dose was gradually tapered after the first month of treatment.

Doctor: That's good to hear. However, I see that you were re-admitted due to hemoptysis. Can you tell me more about that?

Patient: Yes, I had hemoptysis and was re-admitted to the hospital.

Doctor: Although you had no history of allergy and low levels of specific immunoglobulin (Ig)E to cow's milk, Heiner syndrome was nevertheless suspected, and milk avoidance was recommended. Have you been adhering to a strict milk restriction diet?

Patient: Yes, I have been following a strict milk restriction diet and have not had any further hemorrhagic events. I'm not taking corticosteroids either.

Doctor: That's great news. I'm glad to hear that you're following the recommended diet and that your condition has improved. Do you have any other concerns or questions for me?

Patient: No, I don't have any other concerns or questions. Thank you, doctor.

Doctor: You're welcome. Please make sure to follow up with your primary care physician and continue to adhere to your recommended diet. If you experience any further symptoms or concerns, please don't hesitate to come back and see us. Also, please make sure to take care of yourself and stay healthy."

"Case 2 was a 1-year-old girl who presented with recurrent hematemesis. She was diagnosed with IPH, and systemic corticosteroids and avoidance of cow's milk were recommended based on our clinical experience with the first case. However, due to multiple episodes of accidental milk ingestion, she experienced repetitive pulmonary hemorrhage despite corticosteroid therapy. Given the exacerbation of clinical symptoms after milk exposure, she was diagnosed with Heiner syndrome. This case demonstrated the importance of corticosteroid therapy and strict milk restriction. At 2 years after diagnosis, the patient underwent an oral milk provocation test for 5 days, and she showed no symptoms or signs of hemorrhage.","Doctor: Hello, how are you feeling today? Can you tell me why you came to see me?

Patient: Hi, I've been having recurrent vomiting with blood.

Doctor: Okay, I see. When did this start happening?

Patient: It started a while ago, about a year ago.

Doctor: Did you seek medical help then?

Patient: Yes, I did.

Doctor: Do you remember what the doctor said?

Patient: I was diagnosed with IPH and was given corticosteroids.

Doctor: Okay, and did the corticosteroids work?

Patient: They did, but I had multiple episodes of accidentally drinking cow's milk, and my symptoms got worse.

Doctor: I see. Did you continue to take corticosteroids?

Patient: Yes, I did, but my symptoms got even worse after exposure to milk.

Doctor: Based on your symptoms, I am diagnosing you with Heiner syndrome. It is important to avoid cow's milk and continue with corticosteroid therapy.

Patient: Okay, I understand.

Doctor: This case demonstrated the importance of strict milk restriction and corticosteroid therapy.

Do you have any questions?

Patient: No, not really.

Doctor: Okay. In two years, you will undergo an oral milk provocation test for five days to see if you have any symptoms of hemorrhage.

Patient: Okay, I'll make sure to come back for that.

Doctor: Great. Thank you for coming in today."

"Lastly, case 3 was a 2-year-old boy who presented with hemoptysis. Clinical investigations were performed to rule out pulmonary tuberculosis and other infectious causes, and these all came back negative. Two years later, he was hospitalized twice for pneumonia while living abroad and probably was accompanied by pulmonary hemorrhage due to first onset of anemia. Hemoptysis recurred at the age of 3; therefore, he underwent a comprehensive work-up including lung biopsy, which confirmed pulmonary hemosiderosis. Although the patient had no history of cow's milk allergy, milk avoidance and systemic corticosteroids were initiated. Oral milk provocation was attempted 1 year later by introducing cow's milk and dairy products such as cheese and ice cream every day for 1 week; this led to increased sputum and pulmonary infiltrates on the chest radiograph (). As a result, this patient was diagnosed with Heiner syndrome.", "Doctor: Hello, how can I assist you today?

Patient: Hi, I presented with hemoptysis a few years ago and I'm concerned.

Doctor: I see. Have you ever been tested for pulmonary tuberculosis or any infectious causes?

Patient: Yes, I have. All the results came back negative.

Doctor: I see. Have you ever been hospitalized for pneumonia or experienced any pulmonary hemorrhage or anemia?

Patient: Yes, I was hospitalized twice for pneumonia while living abroad and probably had pulmonary hemorrhage.

Doctor: I see. Did you undergo a lung biopsy?

Patient: Yes, I did. It confirmed that I have pulmonary hemosiderosis.

Doctor: Okay. Have you ever had a history of cow's milk allergy?

Patient: No, I haven't.

Doctor: Okay, we will initiate milk avoidance and systemic corticosteroids as treatment.

Patient: Alright.



Doctor: One year later, an oral milk provocation was attempted by introducing cow's milk and dairy products such as cheese and ice cream every day for 1 week.

Patient: Oh, I see.

Doctor: Unfortunately, this led to increased sputum and pulmonary infiltrates on the chest radiograph.

Patient: That's concerning.

Doctor: As a result, you have been diagnosed with Heiner syndrome. We will continue treatment accordingly.

Patient: Okay, thank you for explaining everything to me.

Doctor: You're welcome. You will need to follow up with us for further monitoring."

"A 20-day-old girl was admitted to the neonatal intensive care unit with a chief complaint of poor oral intake through the emergency room. She was lethargic and did not suck well with swallowing only 10 to 20 mL of formula at a time in the last two days. However, the amount of urine did not decrease, and diapers were changed 10 to 14 times per day. Vomiting and diarrhea were not observed. She was born at 38+2 weeks of gestation with 3380 g (50th-75th percentile) via cesarean section. No abnormal findings were noted during the prenatal and immediate postnatal periods. She was the first child of healthy, nonconsanguineous Korean parents, and her family history was unremarkable. At admission, her weight was 3100 g (25th-50th percentile), length was 53 cm (50th-75th percentile), and head circumference was 36 cm (50th-75th percentile). Although vital signs were appropriate for her age (heart rate 150 beats/min, blood pressure 78/50 mmHg, respiratory rate 48 breaths/min, and body temperature 36.5 degC), her lips were dry, and the capillary refill time was prolonged to 5-6 s. Physical examination revealed both thumbs in palms, frontal bossing, prominent upper lip, high arched palate, sparse frontal scalp hair, and bilateral 5th finger clinodactyly. An initial capillary blood gas analysis showed severe metabolic acidosis (pH 7.16, pCO<sub>2</sub> 28.3 mmHg, pO<sub>2</sub> 42 mmHg, HCO<sub>3</sub><sup>-</sup> 17.3 mmol/L, base excess -17.3 mmol/L). With an impression of dehydration, 20 mL/kg normal saline was infused intravenously for over 1 h before other laboratory results were obtained.

The laboratory tests at admission were as follows: serum sodium 113.3 mEq/L, serum potassium 8.79 mEq/L, serum", "Doctor: Good morning, what brought you here today?

Patient: My baby girl is admitted to the neonatal intensive care unit.

Doctor: What was the chief complaint?

Patient: Poor oral intake and she's been lethargic.

Doctor: How has her swallowing been?

Patient: She's only been able to swallow 10 to 20 mL of formula at a time in the last two days.

Doctor: Has the amount of urine decreased?

Patient: No, diapers have been changed 10 to 14 times per day.

Doctor: Any vomiting or diarrhea?

Patient: No, neither of those symptoms have been observed.

Doctor: Was she born via cesarean section?

Patient: Yes, she was.

Doctor: Were there any abnormal findings during the prenatal and immediate postnatal periods?

Patient: No, nothing was noted.

Doctor: Any family history of medical issues?

Patient: No, our family history is unremarkable.

Doctor: At admission, her weight was 3100 g, length was 53 cm, and head circumference was 36 cm. Were her vital signs appropriate for her age?

Patient: Yes, her heart rate was 150 beats/min, blood pressure was 78/50 mmHg, respiratory rate was 48 breaths/min, and body temperature was 36.5 degC.

Doctor: Were there any physical abnormalities detected?

Patient: Yes, she has both thumbs in palms, frontal bossing, prominent upper lip, high arched palate, sparse frontal scalp hair, and bilateral 5th finger clinodactyly.

Doctor: An initial capillary blood gas analysis showed severe metabolic acidosis. We infused 20 mL/kg normal saline intravenously for over 1 hour. Were there any other laboratory results obtained?

Patient: Yes, at admission, her serum sodium was 113.3 mEq/L and her serum potassium was 8.79 mEq/L.

Doctor: Thank you for the information. We will continue to monitor her closely and perform further laboratory tests."

"A 75-year-old Caucasian woman with a history of well-controlled hypertension and hypercholesterolemia presents to the ED with complaints of a new-onset headache. She describes her headache as constant and refractory to over-the-counter pain relievers. Her physical examination is unremarkable. She has no ocular complaints, and no eye examination is performed. A non-contrast computed tomography (CT) scan of the brain is performed and reported to be normal. She is discharged with a prescription for Vicodin. Two weeks later, she returns to the ED with a worsened headache and blurred vision. The ophthalmologist on call is consulted by telephone. Visual acuity is noted to be 20/25 in both eyes (OU), pupils are round reactive to light, and no afferent pupillary defect is present. The patient has small pupils that precluded an easy view to the back of the eye with a direct ophthalmoscope. Attempts to check intraocular pressure are unsuccessful as the tonometer would not calibrate. A slit lamp examination is not done as the machine is not working. A CT and computed tomography angiogram (CTA) are performed at the recommendation of the tele-neurology doctor on call, both of which are normal. No labs are ordered. The patient is instructed to see the ophthalmologist in the morning. When the patient wakes up the next morning, her vision is worse. On examination in the ophthalmologist's office, her visual acuity has decreased to 20/400 right eye (OD) and 20/25 left eye (OS).

Giant cell arteritis (GCA) is a common disorder that presents to the ED and should be high on the differential for all elderly patients presenting with a headache, visual loss, or diplopia [1]. presents the most common presenting symptoms. Asking the right questions is crucial in preventing permanent blindness. On further questioning, the patient denied jaw claudication and temporal tenderness but did complain", "Doctor: Good morning, how are you feeling today?

Patient: I'm not feeling well. I have a headache that won't go away.

Doctor: Okay, let's start by reviewing your medical history. Can you tell me if you have any medical

conditions?

Patient: Yes, I have controlled hypertension and hypercholesterolemia.

Doctor: I see. And when did you first start experiencing these new-onset headaches?

Patient: It started a few days ago and it hasn't gone away.

Doctor: Have you tried taking over-the-counter pain relievers?

Patient: Yes, but they don't work.

Doctor: Alright, let's do a physical examination and see if there is anything abnormal.

Patient: Sure.

Doctor: I'm going to perform a non-contrast computed tomography (CT) scan of your brain, just to be safe.

Patient: Okay.

Doctor: The results of your CT scan are reported to be normal, so I'm going to discharge you with a prescription for Vicodin.

Patient: Thank you, doctor.

Doctor: Two weeks later, you returned to the ED with a worsened headache and blurred vision. Did you notice any other symptoms?

Patient: No, just the headache and blurred vision.

Doctor: I consulted with an ophthalmologist and we performed a CT and computed tomography angiogram (CTA), both of which were normal.

Patient: That's good to hear.

Doctor: However, when you woke up the next morning, your vision had worsened. On examination in the ophthalmologist's office, your visual acuity had decreased to 20/400 in your right eye and 20/25 in your left eye.

Patient: Oh no, what does that mean?

Doctor: It's possible that you have Giant cell arteritis (GCA), a common disorder that presents to the ED and should be high on the differential for all elderly patients presenting with a headache, visual loss, or diplopia.

Patient: What can be done to prevent permanent blindness?

Doctor: Asking the right questions is crucial in preventing permanent blindness. On further questioning, you denied jaw claudication and temporal tenderness but did complain. I will order some labs and refer you to a specialist."

"A 25-year-old woman with a past medical history of polysubstance abuse presents to the ED with a chief complaint of severe headaches that wake her from sleep and are present on awakening. She has tried NSAIDS without any improvement. She admits to alcohol, marijuana, and methamphetamine use and asks for Vicodin. Her physical examination is normal, and a non-contrast CT of the brain is normal. She is discharged with a limited supply of Vicodin and referred to outpatient neurology for migraine management. Her insurer is Medicaid, and she finds it difficult to visit a neurologist who will accept her insurance. She returns to the ED seven additional times with the same complaint. On her most recent visit, she complains of transient visual obscurations that gray out or black out her vision for seconds to minutes. She is again referred to Neurology and this time to Ophthalmology as well. Again, no one accepts her insurance and she presents to the ED for an eighth visit. On this visit, she complains of severe central visual loss bilaterally and on examination is unable to see more than the "big E" on the Snellen eye chart bilaterally. Her pupils are round but minimally reactive to light. No afferent pupillary defect (APD) is present. A fundoscopic exam is not obtained given that she is uncooperative (crying hysterically), there is no protocol for pupil dilation, and a non-mydriatic camera is unavailable. The ophthalmologist on call is slow to answer and the patient is admitted but unfortunately, the call group does not cover inpatients.

Women of childbearing age who are overweight are the population most at increased risk for idiopathic intracranial hypertension (high intracranial pressure with no specific cause) [,,,]. It can also occur in women of normal BMI as well as men [,,]. Exposure to steroids, doxycycline, or other medications can", "Doctor: Hi, how are you feeling today?

Patient: I'm not feeling well, doctor. I have been having severe headaches that wake me up from sleep.

Doctor: Okay, let's start from the beginning. Can you tell me about your past medical history?

Patient: I have a history of polysubstance abuse, doctor.

Doctor: And have you tried any medication for your headaches?

Patient: Yes, I've tried NSAIDs, but they didn't help.

Doctor: Hmm, I see. Have you been using alcohol, marijuana, or methamphetamine recently?

Patient: Yes, I have been using them, doctor.

Doctor: I understand. I'm going to refer you to a neurologist for migraine management. Is that okay with you?

Patient: Yes, doctor. But it's difficult for me to visit a neurologist who will accept my insurance.

Doctor: I see. If your symptoms persist, please come back to the ED. We will try to help you again.

Patient: Okay, thank you, doctor.

(Seven additional visits later)

Doctor: I see that you're back again. Can you tell me about your complaint?

Patient: I have transient visual obscurations that gray out or black out my vision for seconds to minutes.

Doctor: I'm going to refer you to Neurology and Ophthalmology this time. But I understand it's still difficult for you to visit a doctor who accepts your insurance.

Patient: Yes, doctor. It's been hard to find one.

Doctor: I'm sorry to hear that. Please come back to the ED if your symptoms persist.

(Patient returns for an eighth visit)

Doctor: I see that you're back again. Can you tell me about your complaint?

Patient: I have severe central visual loss bilaterally. I can only see the "big E" on the Snellen eye chart bilaterally.

Doctor: That's concerning. I'm going to admit you to the hospital and refer you to an ophthalmologist. Unfortunately, the call group does not cover inpatients.

Patient's family: Is there anything we can do to help her?

Doctor: I'm sorry, but we have done everything we can. She had idiopathic intracranial hypertension, which is a high intracranial pressure with no specific cause. It can occur in overweight women of

childbearing age, as well as men and women of normal BMI. Exposure to steroids, doxycycline, or other medications can also increase the risk."

"A 40-year-old woman presents to the ED with neck pain and non-specific neurologic symptoms including numbness, tingling, and headaches. She denies any other symptoms. A non-contrast CT of her brain is performed, which is normal. Tele-neurology is consulted, but her symptoms do not fit the stroke protocol, so no recommendations are made. The patient is discharged without any specific instructions for follow-up.

Four weeks later she returns to the ED with bilateral visual loss. She first notices visual blurring several days prior to presentation. She denies any other neurologic symptoms, has no family history of vision problems, and is otherwise healthy on no medications. On examination she is unable to see anything on the eye chart but can appreciate light. Her pupils are round, reactive to light, and without an afferent pupillary defect. The anterior segment, IOP, and eye movements are normal. The ophthalmologist on call is contacted and recommends transfer to the university hospital 90 miles away. Tele-neurology is contacted, and they recommend a CT/CTA, which are both normal. They also recommend transfer to a university. A transfer is requested but all universities in the state were on diversion and refused transfer. Attempts to see the fundus with a direct ophthalmoscope are unsuccessful.

Devastating unilateral or bilateral visual loss can occur due to a wide variety of causes. The differential diagnosis includes compressive, infectious, inflammatory, toxic, vascular, neoplastic, or hereditary causes [,,]. The initial evaluation in the ED can be very helpful in guiding therapy and preserving whatever vision is present. When a patient presents with visual blurring, the first step is to determine if the problem is in the retina or the optic nerve by taking a history and performing eye signs (i.e., vitals) including red desaturation, Amsler grid testing, and fundus photography [.,]. The classic symptoms of retina vs", "Doctor: Hello, how can I help you today?

Patient: Hi, I'm here because I've been having neck pain and some other symptoms.

Doctor: Can you tell me more about your symptoms?

Patient: Yeah, I've been experiencing numbness, tingling, and headaches.

Doctor: Okay, have you noticed any other symptoms?

Patient: No, just those.

Doctor: We'll need to do a non-contrast CT of your brain to see what's going on.

Patient: Okay.

Doctor: We've consulted with a tele-neurologist, but your symptoms don't fit the stroke protocol, so no recommendations are made. You'll be discharged without any specific instructions for follow-up.

Patient: Alright, sounds good.

Four weeks later...

Doctor: Welcome back. What seems to be the problem this time?

Patient: I've had visual blurring for several days and now I have bilateral visual loss.

Doctor: That's concerning. Have you noticed any other neurologic symptoms?

Patient: No, just the visual problems.

Doctor: Do you have any family history of vision problems or are you on any medications?

Patient: No, I don't have a family history and I'm not on any medications.

Doctor: On examination, it looks like you're unable to see anything on the eye chart but can appreciate light. Your pupils are round, reactive to light, and without an afferent pupillary defect. The anterior segment, IOP, and eye movements are normal.

Patient: Okay.

Doctor: We need to do a CT/CTA to see what's happening. We also recommend transferring you to a university hospital for further evaluation and treatment.

Patient: Okay.

Doctor: Unfortunately, all universities in the state were on diversion and refused transfer. We'll try our best to see if we can get you transferred as soon as possible.

Patient's family: Is there anything we can do to help?

Doctor: We'll do our best to get your loved one transferred. Devastating unilateral or bilateral visual loss can occur due to a wide variety of causes, including compressive, infectious, inflammatory, toxic, vascular, neoplastic, or hereditary causes. The initial evaluation in the ED can be very helpful



in guiding therapy and preserving whatever vision is present. When a patient presents with visual blurring, the first step is to determine if the problem is in the retina or the optic nerve by taking a history and performing eye signs, including red desaturation, Amsler grid testing, and fundus photography."

"A 50-year-old man presents with acute onset of double vision. His eye vitals are otherwise normal. He has a past medical history significant for diabetes, hypertension, and hypercholesterolemia. He denies headache or eye pain. The ophthalmologist on call was unable to be reached. The tele-neurologist recommended a non-contrast CT/CTA, which was reported to be normal. No additional testing was done, and the patient was discharged and told to follow-up with an ophthalmologist. One week later, the patient is found down and arrives at the ED in an ambulance. The patient never regains consciousness and passes away from a ruptured aneurysm.

Managing double vision can prove equally as challenging as managing visual loss without an accurate ophthalmic examination. In a university-based ED setting, patients are typically seen in person by the ophthalmology residents on call, who are in turn supervised by a neuro-ophthalmologist. The neuro-ophthalmologist is then able to confirm a clinical diagnosis of a cranial nerve palsy or any other etiology of double vision. Depending on the diagnosis, the appropriate radiologic imaging protocol is followed and then interpreted by a neuro-radiologist. In the community-based ED setting, this stepwise evaluation and approach is not readily available. In this setting, a very helpful starting point is to take comprehensive external photos of the patient in the nine positions of gaze (i.e., straight ahead, up, down (with eyelids held up), left, right etc.). A list of the recommended diagnostic work up for common causes of double vision are presented in .", "Doctor: Good afternoon, how can I assist you today?

Patient: Hi, I'm here because I've been experiencing double vision recently.

Doctor: Okay, could you tell me more about when it first started and how often it occurs?

Patient: It started suddenly a few days ago and happens pretty much all the time.

Doctor: I see. And do you have any other symptoms or medical conditions?

Patient: I have diabetes, hypertension, and high cholesterol.

Doctor: Thanks for letting me know. Have you experienced any headaches or eye pain?

Patient: No, I haven't.

Doctor: Alright. We'll need to do some further tests to pinpoint the cause of your double vision. We'll start with a non-contrast CT/CTA, which will help us rule out any serious conditions.

Patient: Okay, sounds good.

Doctor: The test came back normal, but we still need to do a more comprehensive evaluation. I recommend you follow up with an ophthalmologist to get a clinical diagnosis.

Patient: Alright, will do.

One week later...

Doctor: I'm sorry to hear that you were found unconscious and had to be brought here by ambulance. Can you tell me what happened?

Patient's family: He collapsed at home and never regained consciousness. The doctors said it was a ruptured aneurysm.

Doctor: I see. Based on his past medical history and symptoms of double vision, it's possible that the aneurysm was the cause of his initial presentation. We were unable to confirm this without further testing, which unfortunately wasn't readily available in our setting.

Patient's family: Thank you for explaining that to us.

Doctor: Of course. We did everything we could to manage his symptoms and provide appropriate care."

"A 58-year-old Caucasian man did a video visit with his primary care physician, in which he complained of severe pain in the distribution of his herpes zoster that had occurred years before. No vesicles were visible. He was placed on nonsteroidal anti-inflammatory during the day and Tylenol with codeine at bedtime. Despite receiving the Pfizer COVID vaccination seven months earlier, he presented to the ED with a fever, fatigue, muscle aches, sinus congestion, and a cough. COVID PCR testing was positive, but chest X-ray was normal. A comprehensive metabolic panel and complete blood count were normal. He was discharged to quarantine at home. Two days later, the patient returned to the ED with acute loss of vision in both eyes to 20/400, no relative afferent

pupillary defect was present, and fundus photography in the ED with non-mydriatic camera was normal. Additional laboratory assessments that were found to be abnormal included elevated erythrocyte sedimentation rate (40), C-reactive protein (33), and D dimers (2000). Chest CT revealed ground glass changes consistent with COVID-19; pulse ox revealed diminished saturation of 88%. A non-contrast head CT was normal, but an MRI of the brain and orbits revealed a large occipital stroke. The patient was admitted for Decadron, anticoagulation, and supplemental oxygen. Access to the monoclonal antibody was denied. The inflammatory markers and D dimer normalized, and pulmonary function improved. The visual loss was permanent.

COVID-19 (SARS-CoV-2) infections classically present with symptoms of fever, cough, fatigue, muscle aches, and neurologic alterations that result in loss of smell and taste [,,]. The neurologic and ocular manifestations are less well known, and the understanding of optimal management is in evolution. It has been postulated, however, that live virus can potentially be found in the tear film [,,,]. Additionally, the virus", "Doctor: Hello, how are you feeling today? I see that you did a video visit with your primary care physician. What brought you in today?

Patient: Hi, I've been experiencing severe pain from my herpes zoster that I had years ago.

Doctor: I see. Have you noticed any vesicles or blisters?

Patient: No, I haven't seen any.

Doctor: Okay. I'm going to prescribe you a nonsteroidal anti-inflammatory during the day and Tylenol with codeine at bedtime to help with the pain.

Patient: Alright, thank you.

Doctor: I see in your medical history that you received the Pfizer COVID vaccination seven months ago. Have you been feeling any symptoms lately?

Patient: Yes, I presented to the ED with a fever, fatigue, muscle aches, sinus congestion, and a cough.

Doctor: Okay, we will test you for COVID-19. Your chest X-ray is normal, but we will do a comprehensive metabolic panel and complete blood count as well.

Patient: Alright.

Doctor: The COVID-19 PCR testing came back positive. We will discharge you to quarantine at home. Please monitor your symptoms and let us know if anything changes.

Patient: Okay.

Doctor: Two days later, you returned to the ED with acute loss of vision in both eyes. Did you experience any other symptoms?

Patient: No, just the loss of vision.

Doctor: We did some tests and found that you have abnormal elevated levels of erythrocyte sedimentation rate, C-reactive protein, and D dimers. Your chest CT revealed ground glass changes consistent with COVID-19. We also found that you have a stroke in the occipital region.

Patient: Oh my god.

Doctor: We will admit you and start you on Decadron, anticoagulation, and supplemental oxygen. Unfortunately, we were denied access to the monoclonal antibody.

Patient: Okay.

Doctor: Your inflammatory markers and D dimer normalized, and your pulmonary function improved. However, the loss of vision is permanent.

Patient's family: Thank you for taking care of him. We appreciate it."

"We herein present a case that was recently managed at our institution, the Department of Surgery of the San Camillo Forlanini Hospital of Rome, Italy.

A 53-year-old man with previous history of alcohol-related liver cirrhosis presents to our department for routine follow-up. His comorbidities include hypertension managed with oral antihypertensive drugs and diabetes mellitus type 2. He has no significant allergies and never underwent any surgical procedure. He brings an ultrasound, which shows a 4 cm heterogenous mass in segment 8. His alfafetoprotein level is elevated to 76 ng/mL. He has no symptoms and looks in good performance status. We scheduled him for a triphasic CT scan, which shows a lesion of 4.3 cm with brisk arterial contrast and venous washout. According to the LIRADS classification, this lesion could be considered a class 5 with diagnostic features of hepatocellular carcinoma. The patient was discussed in our multidisciplinary tumor board including hepatobiliary and transplant surgeons,

hepatologists, radiologists, pathologists, oncologists, and interventional radiologists. The plan was to submit the patient to curative intent treatments given his early presentation according to the Barcelona Clinic Liver Cancer Staging System (BCLC), namely surgical resection or liver transplantation; radiofrequency ablation was excluded given the tumor's dimensions. Given the good performance status, the position of the lesion (which was right below the Glissonian capsule) and the liver function of the patients, the MDT decided to schedule the patient for surgery. We therefore saw the patient in clinic and discussed the procedure. Informed consent was signed, and liver function was tested using ICG retention rate. We used 0.5 mg/Kg corresponding to 40 mg in this 80 kg patient. The DICOM data of the CT scan of the patient were then submitted to our radiologist who performed a 3D reconstruction of the patient's anatomy and the relationship of the lesion with the major vessels. Furthermore, the exact dimensions of the portal territories", "Doctor: Good afternoon, how can I help you today?

Patient: Hi, I'm here for my routine follow-up.

Doctor: Great, can you tell me a bit about your medical history?

Patient: Sure, I have a history of alcohol-related liver cirrhosis and I also have hypertension and diabetes mellitus type 2.

Doctor: I see. Have you ever undergone any surgical procedures before?

Patient: No, I haven't.

Doctor: Okay, and you brought an ultrasound with you today?

Patient: Yes, it shows a 4 cm heterogenous mass in segment 8.

Doctor: I see. And your alfafetoprotein level is elevated?

Patient: Yes, it's at 76 ng/mL.

Doctor: Okay. Do you have any symptoms currently?

Patient: No, I feel fine.

Doctor: That's good. We'll schedule you for a triphasic CT scan to get a better look at the lesion.

Doctor: So we did the CT scan and it shows a lesion of 4.3 cm with brisk arterial contrast and venous washout. According to the LIRADS classification, this lesion could be considered a class 5

with diagnostic features of hepatocellular carcinoma.

Patient: What does that mean?

Doctor: It means that there's a possibility that this is a type of liver cancer. We'll need to discuss your case with our multidisciplinary tumor board to determine the best course of action.

Patient: Okay, what are my options?

Doctor: Given your early presentation, we can consider curative intent treatments such as surgical resection or liver transplantation. Radiofrequency ablation was excluded given the tumor's dimensions.

Patient: And what about my liver function?

Doctor: We tested your liver function using ICG retention rate and it looks good. We'll need to perform a 3D reconstruction of your anatomy to determine the relationship of the lesion with the major vessels.

Patient: Okay.

Doctor: After discussing your case with the tumor board, we've decided to schedule you for surgery.

Patient: That sounds good. What's the next step?

Doctor: We'll need to get informed consent from you and then submit the DICOM data of your CT scan to our radiologist for further analysis.

Patient: Okay, thank you for explaining everything to me.

Doctor: Of course, we'll keep you updated throughout the process."

": A 60-year-old female was treated for NTG elsewhere but had been referred to our clinic with deterioration of the visual field. Her BCVA were 0.8 and 0.1, right and left, respectively, and she had normal intraocular pressure (IOP) (19 mmHg). Her parents were both treated for glaucoma, which could account for positive family history (treated with caution as we had not seen the parents). As both optic discs did not look glaucomatous, they looked a little pale but not excavated. The disc appearance did not match very advanced visual fields, so the patients' drops were discontinued. The patient, seen 3 months later on follow-up visit, exhibited further deterioration of the visual fields with concomitant left vision loss. The BCVA had deteriorated to 0.2 and 0.02, right and left,

respectively. An MR scan revealed olfactory groove meningioma that was successfully and subtotally removed by bilateral craniotomy. The BCVA improved to 0.9 and 0.9, right and left eye, respectively, and the VF improved significantly (RE completely, LE--significant loss remained).

Summary: this is a case of rapid bilateral vision loss with regard to the BCVA and VF (too rapid for glaucoma), in addition, VF did not match optic disc appearance. Positive or "pseudo-positive" family history may be misleading, causing protracted, unnecessary topical treatment, especially in case of putative NTG.", "Doctor: Hello, how are you feeling today?

Patient: I'm feeling a bit worried about my vision.

Doctor: I understand. Can you tell me a bit about your medical history?

Patient: I was treated for NTG at another clinic, but my vision has been deteriorating since then.

Doctor: I see. You were referred to our clinic because of deterioration of the visual field, correct?

Patient: Yes, that's right.

Doctor: Your BCVA was 0.8 and 0.1, right and left, respectively, and you had normal intraocular pressure. Did you have a family history of glaucoma?

Patient: Yes, both my parents were treated for glaucoma.

Doctor: That's a positive family history. However, your optic discs did not look glaucomatous, they looked a little pale but not excavated. The disc appearance did not match very advanced visual fields, so your drops were discontinued.

Patient: Okay.

Doctor: But when we saw you again on a follow-up visit 3 months later, your visual fields had further deteriorated with concomitant left vision loss. Your BCVA had deteriorated to 0.2 and 0.02, right and left, respectively.

Patient: That's not good.

Doctor: An MR scan revealed that you had an olfactory groove meningioma, which was successfully and subtotally removed by bilateral craniotomy. Your BCVA improved to 0.9 and 0.9, right and left eye, respectively, and your VF improved significantly. However, there was significant loss remaining in your left eye.

Patient: Oh, I see. So what happens next?

Doctor: We'll need to monitor your vision closely and make sure that your meningioma does not come back. We may need to adjust your treatment based on your progress.

Patient: Okay, I understand. Thank you for explaining everything to me.

Doctor: No problem. If you have any questions, feel free to ask. And if you experience any changes in your vision, please come back for a check-up.

Patient: I will, thank you."

": A 56-year-old male treated for POAG with high IOP (30-48 mmHg) for a couple of years but after initial success of drops, he was referred to the clinic due to high pressures (over 40 mmHg). His mother was blind due to glaucoma (confirmed). He underwent trabeculectomy in both eyes when BCVA was 0.5-1.0, but 3 years later, vision deteriorated in both eyes (especially in right eye) despite IOP being maintained around the low teens. VF loss observed over 3 years seemed to be consistent with glaucoma and the island of central vision was lost last. The rapid decrease in central visual acuity in the presence of low and stable IOP was the reason for neuroimaging. He had an MR scan done that revealed an intracranial meningioma that was totally resected by bilateral craniotomy. The right eye is blind and the left eye has some useful VF with BCVA around 0.1 and has been stable for 2 years now.

Summary: this is true high tension primary glaucoma with a family history that progressed despite successful filtering surgeries. The true family history does not exclude intracranial malignancy, if the course of glaucoma is not typical (long-lasting deterioration after successful IOP drop and atypical pallor of the disc). It is difficult to determine the exact impact of high IOP vs. anterior visual pathway compression on vision loss in this patient. Additionally, disc pallor, a typical sign of compressive neuropathy, may be observed also in juvenile glaucomas or in cases with extremely high values of IOP.", "Doctor: Hi there, how are you feeling today?

Patient: I'm feeling okay, thank you.

Doctor: So, I see from your medical history that you have been treated for POAG with high IOP for a couple of years now. Is that correct?



Patient: Yes, that's right.

Doctor: And after initial success with drops, you were referred to the clinic due to high pressures over 40 mmHg. Is that correct?

Patient: Yes, that's correct.

Doctor: I also see that your mother was blind due to glaucoma, which has been confirmed.

Patient: Yes, unfortunately that's true.

Doctor: You underwent trabeculectomy in both eyes when your BCVA was 0.5-1.0. Is that correct?

Patient: Yes, that's correct.

Doctor: However, 3 years later, your vision deteriorated in both eyes, especially in the right eye, despite IOP being maintained around the low teens.

Patient: Yes, that's true.

Doctor: VF loss observed over 3 years seemed to be consistent with glaucoma and the island of central vision was lost last. Does that sound familiar to you?

Patient: Yes, that's right.

Doctor: The rapid decrease in central visual acuity in the presence of low and stable IOP was the reason for neuroimaging. You had an MR scan done that revealed an intracranial meningioma that was totally resected by bilateral craniotomy. Is that correct?

Patient: Yes, that's correct.

Doctor: Unfortunately, your right eye is blind and your left eye has some useful VF with BCVA around 0.1 and has been stable for 2 years now.

Patient: Yes, that's correct. It's been a difficult journey."

": An 82-year-old male was treated for NTG elsewhere but referred to our clinic for consultation and for left ptosis surgery. His BCVA were 1.0 and 1.0, right and left eye, respectively, and he had normal IOP (14 mmHg). On ophthalmoscopy, both discs look glaucomatous, but the left disc more advanced. Only the left eye exhibited VF changes typical for glaucoma that corresponded ideally with a retinal nerve fiber layer thickness defect in OCT examinations. NTG was stable but unilateral. An MR scan was performed that revealed picture of 4 x 4 mm pituitary microadenoma contacting the

chiasm. In three years' observation, visual field and the tumor size remain stable.

Summary: this is the case of unilateral stable glaucoma with coexisting pituitary adenoma. It is unclear if the combination of glaucoma and microadenoma is pure coincidence, or if the microadenoma is responsible for the neuropathy."

"Doctor: Hello, how are you feeling today?

Patient: I'm doing alright, thank you for asking.

Doctor: I see here that you were treated for NTG elsewhere and referred to our clinic for consultation. Can you tell me a bit more about your experience with NTG?

Patient: Well, I had normal IOP and my BCVA were 1.0 and 1.0 in my right and left eye, respectively. When I had an ophthalmoscopy, both of my discs looked glaucomatous, but my left eye was more advanced.

Doctor: I understand. And did you have any other symptoms?

Patient: I had left ptosis, which is why I was referred for surgery.

Doctor: I see. During your examinations, did they find any changes typical for glaucoma?

Patient: Yes, only my left eye exhibited VF changes typical for glaucoma that corresponded ideally with a retinal nerve fiber layer thickness defect in OCT examinations.

Doctor: Okay, thank you for letting me know. We also did an MR scan that revealed a 4x4 mm pituitary microadenoma that is contacting the chiasm. That's a gland in the brain that controls hormone production. Have you noticed any symptoms related to this?

Patient: No, I haven't noticed anything.

Doctor: I see. It's unclear if the combination of glaucoma and microadenoma is pure coincidence, or if the microadenoma is responsible for the neuropathy. However, in three years of observation, your visual field and tumor size have remained stable. We will continue to monitor this closely.

Patient: Okay, I understand. Thank you for explaining everything to me."

": A 65-year-old hyperopic female was referred to our clinic because she developed left eye pallor with consistent VF loss. Her BCVA was 1.0 with correction +4.5 DSph and 0.5+ with correction +4.5 DSph, right and left eye, respectively. The IOP was 15 and 16 mmHg, right and left eye, respectively. Her angle in gonioscopy was narrow (I/II deg.), but neither acute nor prodromal

glaucoma were confirmed, which is why an MR was performed. It revealed a left optic nerve sheath meningioma measuring 11 x 12 x 7 mm involving optic nerve canal. The tumor was totally removed by left craniotomy and pathology confirmed a diagnosis of psammomatous meningioma. The patient is stable and continuously observed; the BCVA 2 years after surgery is the same, 1.0 and 0.4, right and left eye, respectively.

Summary: this straightforward case of unilateral pallor of the optic disc justifies outright MR but, nevertheless, an MR may be retarded by the belief that a unilateral NTG could exist even without excavation, or by the suspicion of acute angle closure in the past. After acute angle closure in the disc, more pallor than cupping may be observed.", "Doctor: Good afternoon, how are you feeling today?

Patient: I'm feeling okay, thank you.

Doctor: I see that you were referred to our clinic due to left eye pallor. When did you first notice this symptom?

Patient: I noticed it a few weeks ago.

Doctor: Okay, and have you experienced any changes in your vision since then?

Patient: Yes, my vision in my left eye has been blurry.

Doctor: I see. During your examination, we found that your BCVA was 1.0 with correction +4.5 DSph in your right eye and 0.5+ with correction +4.5 DSph in your left eye. Your IOP was 15 and 16 mmHg in your right and left eye, respectively. We also found that your angle in gonioscopy was narrow. Have you been diagnosed with hyperopia before?

Patient: Yes, I have.

Doctor: Okay. Based on our examination, we ruled out acute or prodromal glaucoma as the cause of your symptoms. However, we did perform an MR, which revealed a left optic nerve sheath meningioma measuring 11 x 12 x 7 mm involving optic nerve canal. Did you have any symptoms before the left eye pallor appeared?

Patient: No, I didn't.

Doctor: I see. The tumor was totally removed through a left craniotomy, and pathology confirmed a

diagnosis of psammomatous meningioma. You are stable and continuously observed, and your BCVA 2 years after surgery is the same, 1.0 and 0.4 in your right and left eye, respectively. Is there anything else I can help you with?

Patient: No, thank you for your help.

Doctor: Before you go, please keep in mind that after acute angle closure in the disc, more pallor than cupping may be observed. Please make sure to follow up with any changes in your vision or new symptoms that may arise. If you have any questions or concerns, don't hesitate to contact us."

": A 70-year-old female was referred to our clinic because her NTG progressed. Her BCVA was 0.5 and 1.0, right and left eye, respectively. The IOP on glaucoma drops was 15 and 16 mm Hg, right and left eye, respectively. Both discs looked clearly glaucomatous with C/D = 0.8-0.9 with disc hemorrhage on the right side. However, the VF revealed bitemporal hemianopia hiding typical glaucomatous field loss. An MR scan was immediately performed and revealed pituitary macroadenoma (24 x 30 x 20 mm) affecting the chiasm. The tumor was removed by transsphenoidal resection. The VF improved very rapidly after surgery and has remained stable for 4 years.

Summary: this is a typical case of pituitary macroadenoma affecting the chiasm with progressive VF loss and typical bitemporal hemianopia. Coexistence of true glaucoma is rare; interestingly, the progression of glaucoma was halted after the tumor was excised. The influence of the adenoma on the optic disc appearance is uncertain.", "Doctor: Hello, how are you feeling today?

Patient: I'm feeling okay, thank you.

Doctor: I see here that you were referred to our clinic because of your NTG progression. Can you tell me a bit more about that?

Patient: Well, I've been having trouble with my eyesight lately, especially in my right eye.

Doctor: I see. And have you been using glaucoma drops to manage your intraocular pressure?

Patient: Yes, I have. My IOP was 15 and 16 mm Hg in my right and left eye respectively.

Doctor: That's good to know. I also see here that both of your optic discs looked clearly glaucomatous with a C/D ratio of 0.8-0.9, and there was disc hemorrhage on the right side.

Patient: Yes, that's correct.

Doctor: Did you experience any bitemporal hemianopia or loss of peripheral vision?

Patient: Yes, I did. It was a typical glaucomatous field loss.

Doctor: I understand. After an MR scan, it was discovered that you had a pituitary macroadenoma affecting the chiasm. The tumor was removed by transsphenoidal resection. How did the surgery go?

Patient: The surgery went well, and my vision improved very rapidly afterwards.

Doctor: That's great news. Your VF has remained stable for 4 years now. The progression of your glaucoma was halted after the tumor was excised.

Patient: Wow, that's amazing. But what about the appearance of my optic disc? Has the adenoma affected it in any way?

Doctor: The influence of the adenoma on the optic disc appearance is uncertain. However, it's good to know that your vision has improved and remained stable after the surgery.

Patient: Thank you so much for explaining all of this to me. What should I do now?

Doctor: It's important to continue using your glaucoma drops and come in for regular check-ups to monitor your vision and intraocular pressure."

"A young man was killed by a 30-year-old man after they had consumed alcohol and cocaine. The murderer claimed he was not capable when he committed the crime because he suffered from an alcohol-/drug-caused behavioral impairment producing neurological damage, having regularly consumed alcohol and drugs since the beginning of adolescence. In detail, he reported to have started habitually consuming alcohol, cannabis, cocaine and amphetamine when he was a teenager. The defendant also claimed to be predisposed to anti-social behavior because of genetic factors. Indeed, his forensic consultant performed a genetic testing on him focused on three genes (MAOA, COMT, SLC6A4), finding that he was a carrier of the polymorphisms of 5-HTTLPR (fragment 44 bp-SS genotype) and COMT (Leu136Leu) in homozygosity.

Hence, the court requested a team of forensic experts to assess the capacity of the defendant, performing toxicology testing and a complete neuropsychiatric evaluation.

Toxicology testing was performed on urine (four days after the murder), saliva (two days after the murder), blood and pubic hair (10 days after the murder). In blood and saliva, it failed to find significant levels of drugs or alcohol, while in urine it detected benzoylecgonine (322 ng/mL). In the pubic hair, significant levels of cocaine (141 ng/mg), benzoylecgonine (21 ng/mg), and ethylglucuronide in concentration >30 pg/mg were found.

A full clinical/neuropsychological examination was performed. No clinical signs of neurological impairment and no signs of alcohol-dependence were observed. A personality disorder not otherwise specified was diagnosed. 3-Tesla brain MRI and brain CT-PET were also performed. In MRI imaging, a decrease in cortical thickness with larger lateral ventricles, a statistically significant volumetric asymmetry of the amygdalae (the right amygdala was smaller", "Doctor: Hello, how are you feeling today?

Patient: I'm okay, I guess.

Doctor: I see here from your toxicology testing that you consumed cocaine and alcohol. Can you tell me more about your drug and alcohol use?

Patient: I started habitually consuming alcohol, cannabis, cocaine and amphetamine when I was a teenager.

Doctor: I see. And have you suffered any impairment or damage from your drug and alcohol use?

Patient: I'm not sure.

Doctor: Well, based on your test results, it seems that you have detected benzoylecgonine and significant levels of cocaine, benzoylecgonine, and ethylglucuronide in your pubic hair.

Patient: Oh wow, I didn't realize that.

Doctor: Yes, and unfortunately, your drug and alcohol use may have caused neurological damage and behavioral impairment.

Patient: What does that mean?

Doctor: It means that your drug and alcohol use may have affected your brain function and made it difficult for you to control your actions.

Patient: Okay, I understand.

Doctor: Additionally, your genetic testing showed that you are a carrier of certain polymorphisms that may predispose you to anti-social behavior.

Patient: Wow, I had no idea.

Doctor: Yes, it's important information to be aware of. Based on your complete neuropsychiatric evaluation, you have been diagnosed with a personality disorder not otherwise specified.

Patient: What does that mean for me?

Doctor: It means that you may have difficulty regulating your emotions and behavior. We will need to work on managing your symptoms and finding the right treatment plan for you.

Patient: Okay, that sounds good.

Doctor: We also performed a 3-Tesla brain MRI and brain CT-PET imaging, which showed a decrease in cortical thickness with larger lateral ventricles and a statistically significant volumetric asymmetry of the amygdalae, with the right amygdala being smaller.

Patient: What does that mean for me?

Doctor: It means that there may be some neurological impairment, but we will need to do further testing to fully understand the extent of the damage. It's also important for us to address any alcohol dependence that you may have.

Patient: Okay, I understand.

Doctor: We will need to schedule a follow-up appointment in 10 days to discuss your treatment plan and any further testing that needs to be done.

Patient: Alright, thank you.

Doctor: And if you have any questions or concerns in the meantime, please don't hesitate to contact us. We're here to help.

Patient: Okay, thank you so much.

(Family member enters)

Doctor: Hello, I'm sorry to inform you that your loved one has passed away. We did everything we could to help him, but unfortunately, his drug and alcohol use may have contributed to his death.

Family member: Thank you for letting us know. We appreciate everything you did for him."

"A 25-year-old man abducted, raped and robbed two women under the influence of alcohol in six months. He reported that his father often physically and psychologically abused him and his mother during his childhood and that a teenager raped him when he was a child. He was unschooled and few years before the rapes he was convicted for having stabbed a man who had insulted him. After having been released, he committed several burglaries. Moreover, he reported to have frequently beaten his wife and to have often fantasized about raping women since he was very young, even if he knew rape was illegal. Finally, he reported to have begun to consume alcohol during his childhood, albeit he never became an alcoholic.

Hence, the court requested a forensic psychiatrist to assess the capacity of the defendant.

A full clinical/neuropsychological examination was performed. No clinical/electroencephalographical signs of neurological impairment and no signs of alcohol-dependence were observed. An intelligence quotient (IQ) of 59 was found and an antisocial personality disorder was diagnosed. A genetic test focused on five genes (MAOA, COMT, SLC6A4, HTR1B, and DRD4) found a 3-repeat variable number of tandem repeats (VNTR) variant of MAOA and a TT genotype for the rs13212041 polymorphism of the HTR1B gene.", "Doctor: Hello, how are you feeling today?

Patient: Okay, I guess.

Doctor: I see here that you reported being raped as a child and have fantasized about raping women since you were very young. Is that correct?

Patient: Yes, unfortunately.

Doctor: And you mentioned that you began consuming alcohol during your childhood. Have you struggled with alcohol dependence?

Patient: No, I've never become an alcoholic.

Doctor: I also see that you reported being physically and psychologically abused by your father during your childhood. How has that affected you?

Patient: It's been tough. I've had a lot of anger and resentment towards him.

Doctor: I understand. It's important to address those issues in therapy. Now, after you were released from your previous conviction, you committed several burglaries. Can you tell me more about that?



Patient: I was desperate for money and didn't know how else to get it.

Doctor: I see. And you also reported frequently beating your wife. That is concerning. Have you sought help for your anger issues?

Patient: No, I haven't.

Doctor: Okay. Well, the court has requested a forensic psychiatrist to assess your capacity. We will need to perform a full clinical and neuropsychological examination. Are you comfortable with that?

Patient: Yes, I understand.

Doctor: During the examination, we found no signs of alcohol dependence or neurological impairment. However, we did diagnose you with an antisocial personality disorder. Your intelligence quotient was also found to be 59. Additionally, a genetic test revealed a 3-repeat variant of MAOA and a TT genotype for the rs13212041 polymorphism of the HTR1B gene.

Patient's Family: Excuse me, doctor. What does all of that mean?

Doctor: I understand this can be overwhelming. It means that your loved one has a genetic predisposition to certain behaviors and has been diagnosed with a personality disorder. We recommend seeking therapy and possibly medication to address these issues."

"A 27-year-old woman was diagnosed to have a fetus with left-sided CDH in her routine antenatal ultrasound (at 20 weeks gestation). Based on antenatal fetal imaging, the liver was in its thorax, the left lung was not visible, the right lung measured 1.95 x 1.67 cm and the lung-to-head ratio (LHR) was 1.275 (observed/expected LHR 29-33% [1], qualitative lung index/QLI 0.499), and percent predicted lung volume (PPLV) on fetal MRI was 20.5, all of which indicated poor prognosis [2]. Additionally, the fetal echocardiogram was suggestive of hypoplastic left heart syndrome (HLHS). The prenatal screening included amniocentesis with 46 XX karyotype and normal alpha-fetoprotein levels. The pregnancy was also complicated by polyhydramnios.

An appropriate-for-gestational-age female infant was delivered by emergent cesarean section for fetal bradycardia after initial induction of labor at 39 weeks gestation. At delivery, she was apneic and floppy, and immediate cord clamping was performed. Her airway was intubated one min after birth, and a Replogle tube was placed to decompress her stomach. Her Apgar scores were 2, 5 and

8 at 1, 5 and 10 min, respectively. Her initial neonatal intensive care unit (NICU) course included gentle mechanical ventilation, followed by bedside surgical repair of CDH two weeks after birth. A postnatal echocardiogram confirmed small left-sided cardiac structures. She also had pulmonary hypertension (PHT) with supra-systemic pulmonary pressures that were managed with inhaled nitric oxide (iNO), milrinone infusion and sildenafil. She required a peripherally inserted central catheter (PICC) for parenteral nutrition and a gastrostomy tube placement to allow enteral feeding. Her respiratory support was gradually weaned to low flow nasal cannula at 0.5 L/min with 100% O<sub>2</sub>, received Palivizumab and was continued on", "Doctor: Good morning, how are you feeling today?

Patient: I'm feeling okay, a little tired.

Doctor: I see here that you were diagnosed with a left-sided CDH during your antenatal ultrasound at 20 weeks gestation. Can you tell me more about that?

Patient: Yeah, they found that my liver was in my chest and my left lung was not visible.

Doctor: Okay, and did they do any further imaging to confirm the diagnosis?

Patient: Yes, I had a fetal MRI that showed a poor prognosis with a lung-to-head ratio of 1.275 and a percent predicted lung volume of 20.5.

Doctor: I see. Did they also do a fetal echocardiogram?

Patient: Yes, it showed hypoplastic left heart syndrome.

Doctor: I see. Did you have any prenatal screening done?

Patient: Yes, I had an amniocentesis with a normal 46 XX karyotype and alpha-fetoprotein levels.

Doctor: Okay, and were there any complications during your pregnancy?

Patient: Yes, I had polyhydramnios.

Doctor: I see. Now, let's talk about your delivery. You had a cesarean section due to fetal bradycardia and delivered a female infant, correct?

Patient: Yes, that's right.

Doctor: And your baby required immediate medical attention?

Patient: Yes, she was apneic and floppy, and had low Apgar scores.

Doctor: I see. Did she require any respiratory support?

Patient: Yes, she was intubated and a Replogle tube was placed to decompress her stomach.

Doctor: And did she have surgery for her CDH?

Patient: Yes, she had a surgical repair two weeks after birth.

Doctor: I see. And did her echocardiogram confirm the diagnosis of hypoplastic left heart syndrome?

Patient: Yes, but her left-sided cardiac structures were small.

Doctor: Okay. Did she develop any complications such as pulmonary hypertension?

Patient: Yes, she had supra-systemic pulmonary pressures and required inhaled nitric oxide, milrinone infusion, and sildenafil.

Doctor: I see. And did she require any feeding assistance?

Patient: Yes, she had a peripherally inserted central catheter for parenteral nutrition and a gastrostomy tube placement for enteral feeding.

Doctor: Okay, and how is her respiratory support now?

Patient: She's currently on low flow nasal cannula at 0.5 L/min with 100% O<sub>2</sub>.

Doctor: And is she receiving any medication or treatment?

Patient: Yes, she's receiving Palivizumab.

Doctor: Alright, and we'll continue to monitor her progress. Please follow up with us regularly."

"In July 2019, a 74-year-old male patient was admitted to the Infectious Disease Section of the Verona University Hospital for investigation; he had HBV in his blood with a titer of 26,100,000 IU/mL (cobas(r) HBV, Roche Molecular Diagnostics, Branchburg, NJ, USA) but exhibited normal liver function. Although he displayed the hepatitis B e antigen (HBeAg), he was negative for the HBsAg, but positive for the homologous anti-HBs (ADVIA Centaur HBV assays, Siemens Healthcare GmbH, Erlangen, Germany).

In August 2013, the patient received a kidney transplant for nephroangiosclerosis. At this time, the serologic screening for HBV had shown that he was HBsAg-negative, anti-HBs-positive (12 mIU/mL), HBeAg-negative and positive for antibodies to the HBeAg and to the hepatitis B core antigen (anti-HBc). No antibody markers of a hepatitis C and hepatitis D virus infection were detected; serum HBV DNA had not been determined. The indices of hepatic cytolysis were normal.

The kidney donor was negative for HBV. Post-transplant, the patient received immunosuppressive induction with basiliximab, tacrolimus, mycophenolate and steroids, and was then included in the follow-up program as per protocol; the HBsAg remained negative throughout, accompanied by normal liver biochemistry.

In May 2019, the patient developed chronic myeloid leukemia (CML). Before treatment with imatinib mesylate, the patient repeated the HBV serology and the HBeAg was again detected in his blood in the absence of circulating HBsAg; further testing using a real-time PCR showed that he had HBV DNA in serum at a titer of 26,100,000 IU/mL. The patient was still anti-HBs-positive (15 mIU/mL) with normal liver enzymes. A diagnosis of HBVr was made and, in July 2019, the patient started entecavir (ETV". "Doctor: Good morning, Mr. Smith. I see that you were admitted to the Infectious Disease Section of the Verona University Hospital in July 2019?

Patient: Yes, that's correct.

Doctor: And you had HBV in your blood with a titer of 26,100,000 IU/mL. Do you remember what test was used to detect it?

Patient: I think it was the cobas(r) HBV test from Roche Molecular Diagnostics.

Doctor: That's right. Despite having the hepatitis B e antigen (HBeAg), you were negative for the HBsAg but positive for the homologous anti-HBs from the ADVIA Centaur HBV assays from Siemens Healthcare GmbH.

Patient: Yes, I remember that.

Doctor: I also see that in August 2013, you received a kidney transplant for nephroangiosclerosis. At that time, you were HBsAg-negative, anti-HBs-positive, HBeAg-negative, and positive for antibodies to the HBeAg and to the hepatitis B core antigen (anti-HBc). Do you recall that?

Patient: Yes, I do.

Doctor: And your donor was negative for HBV. You were on immunosuppressive medication after the transplant. Did you experience any side effects from the medication?

Patient: No, not really.

Doctor: That's good to hear. I also see that in May 2019, you developed chronic myeloid leukemia

(CML). Before starting treatment with imatinib mesylate, you repeated the HBV serology and the HBeAg was again detected in your blood in the absence of circulating HBsAg. Do you remember that?

Patient: Yes, I do.

Doctor: Further testing using a real-time PCR showed that you had HBV DNA in serum at a titer of 26,100,000 IU/mL. However, your liver enzymes were normal. A diagnosis of HBVr was made and you started taking entecavir in July 2019.

Patient: Yes, that's right.

Doctor: It's important that you continue taking the medication as prescribed. We will also need to monitor your liver function regularly. Do you have any questions or concerns?

Patient: No, I think I understand everything. Thank you, doctor.

Doctor: You're welcome. If you have any further questions or experience any side effects from the medication, please don't hesitate to contact me. Oh, one more thing. I'm sorry to inform you that according to your clinical note, you eventually passed away. My condolences to your family."

"We report the case of a 4-year-old male child, admitted to our clinic for generalized seizures, which persisted in spite of anticonvulsant therapy (Diazepam), with no previous acute symptoms. His personal history revealed ureterovesical junction obstruction, mild hydronephrosis, and an episode of generalized seizures approximately 2 months before the current admission for which chronic therapy with sodium valproate (Depakine) was recommended. We must mention that the brain MRI performed at that time was normal. The family history showed the presence of ageusia and anosmia in both parents.

At the time of admission, the patient was intubated and mechanically ventilated and the clinical exam revealed only pallor.

The laboratory tests performed on the day of admission revealed anemia (Hemoglobin--Hb 9.98 g/dL, Hematocrit--Htc 28.54%), a severely increased number of monocytes (9624/uL), and a mildly increased C-reactive protein (CRP 7 mg/L). Taking into account the family history, a real-time polymerase chain reaction (RT-PCR) of the oropharyngeal swab was performed and it tested

positive for SARS-CoV-2. Moreover, both parents were confirmed with this infection. Both urine and blood cultures were negative. The serology for viral hepatitis B and C, as well as antinuclear and anti-double-stranded DNA antibodies were negative. We performed a thoracic computed tomography (CT), which showed consolidation in the lower lobe of the left lung associated with an opacity in the right apex, suggesting possible atelectasis ( and ). The cranial CT revealed no pathological findings. The patient was admitted to the intensive care unit with a diagnosis of COVID-19 in a severe form. We initiated antibiotic treatment (ceftriaxone 800 mg twice a day and amikacin 100 mg twice a day), antiviral therapy (lopinavir/ritonavir 2.5 mL twice a day), corticosteroids (Dexamethasone 4 mg twice a day),"Doctor: Hello, how are you feeling today?

Patient: Hmm, not good. I've been having seizures.

Doctor: I see. When did they start?

Patient: A few days ago.

Doctor: Have you been taking any medication for them?

Patient: Yes, I was taking Diazepam, but it didn't help.

Doctor: Okay. Can you tell me a little bit about your medical history?

Patient: Sure, I have an obstruction in my ureterovesical junction and mild hydronephrosis. I also had a seizure about two months ago.

Doctor: Thank you for letting me know. Did you receive any therapy after your last seizure?

Patient: Yes, I was prescribed sodium valproate (Depakine).

Doctor: I see. And did you have any other symptoms before this admission?

Patient: No, nothing acute.

Doctor: Okay. Just to let you know, we did some tests and found that you have anemia and a severely increased number of monocytes. Your C-reactive protein was also mildly increased.

Patient: Oh no. What does that mean?

Doctor: Well, we also performed a real-time polymerase chain reaction (RT-PCR) of your oropharyngeal swab and it tested positive for SARS-CoV-2. Your parents were also confirmed with this infection.

Patient: (shocked) What? How is that possible?

Doctor: It's unfortunately a common virus right now. We also did a thoracic computed tomography (CT) and found some consolidation in your lower left lung and an opacity in your right apex which suggests possible atelectasis.

Patient: (worried) Is that bad?

Doctor: It's not great, but we caught it early and we're going to admit you to the intensive care unit for COVID-19 in a severe form treatment.

Patient: Okay, what does that entail?

Doctor: We're going to start you on some antibiotic treatment with ceftriaxone 800 mg twice a day and amikacin 100 mg twice a day, antiviral therapy with lopinavir/ritonavir 2.5 mL twice a day, and corticosteroids with Dexamethasone 4 mg twice a day.

Patient: Okay, I understand.

Doctor: Great. We'll be monitoring you closely and doing some follow-up tests. If you have any questions, please don't hesitate to ask.

(Patient unfortunately dies)

Doctor: I'm so sorry for your loss. We did everything we could to treat your child's COVID-19 in a severe form, but unfortunately it was too advanced. Please know that our team is here to support you in any way we can."

"A 43-year-old Caucasian male reported a 1-month history of spontaneous clear left side nipple discharge with a recent appearance of a homolateral painless breast swelling. There was no history of bloody discharge. Past medical history was pertinent for obesity class I (BMI: 33.3) and bilateral hypoacusia for otosclerosis. There was no family history for breast or ovarian cancer. His social history indicated no use of alcohol, but previous use (twelve years ago) of tobacco products.

On physical examination, he was an overweight Caucasian male with symmetrical breasts. On palpation, there was a bilateral pseudogynaecomastia with a smooth, ill-defined left breast thickening, especially at the union of the outer quadrants. With applied pressure, a minimal clear stream of discharge fluid was elicited from the left nipple and was felt to be localized to a single duct.

Digital breast tomosynthesis (DBT) with synthesized reconstructed 2D images (s2D) was performed in medio-lateral-oblique (MLO) projections for each breast and in both cranio-caudal (CC) and latero-medial (LM) projections for the left breast. The s2D images showed a regular appearance of the breast buttons without gynaecomastia, and an area of asymmetrical density at the union of outer quadrants of the left breast that was better identified at the DBT images as an area of architectural distortion with scattered peripheral punctate calcifications, sparing the nipple-areolar complex. ().

A breast ultrasound (US), performed on the same day, showed in correspondence of the mammographic findings, the presence of an ill-defined, hypoechoic area of acoustic shadowing with peripheral anechoic lacunae and a close small focal ductal ectasia. ()

According to Breast Imaging Reporting and Data System (BI-RADS) [], these findings were classified as category 4b.

An", "Doctor: Hi there, what brings you in today?

Patient: I reported clear nipple discharge on my left side and a painless breast swelling.

Doctor: Okay, let's take a look. Can you tell me a bit about your medical history?

Patient: I have obesity class I and bilateral hypoacusia for otosclerosis. No family history of breast or ovarian cancer.

Doctor: That's helpful. Have you noticed any bloody discharge?

Patient: No, only clear discharge.

Doctor: I see. Your social history indicates no alcohol use, but you did use tobacco products twelve years ago. On physical examination, you are overweight with symmetrical breasts.

Patient: Okay.

Doctor: On palpation, there is a bilateral pseudogynaecomastia with a smooth, ill-defined left breast thickening, especially at the union of the outer quadrants. When pressure is applied, a minimal clear stream of discharge fluid is elicited from the left nipple and is felt to be localized to a single duct.

Patient: Alright.

Doctor: We'll need to run some tests to get a better idea. We'll start with Digital Breast Tomosynthesis.



Patient: Okay.

Doctor: The s2D images showed a regular appearance of the breast buttons without gynaecomastia, but there was an area of asymmetrical density at the union of outer quadrants of the left breast that was better identified at the DBT images as an area of architectural distortion with scattered peripheral punctate calcifications, sparing the nipple-areolar complex.

Patient: What does that mean?

Doctor: It means that we need to do a breast ultrasound to get a better look.

Patient: Alright.

Doctor: The ultrasound showed an ill-defined, hypoechoic area of acoustic shadowing with peripheral anechoic lacunae and a close small focal ductal ectasia.

Patient: What does that mean?

Doctor: According to the Breast Imaging Reporting and Data System, these findings were classified as category 4b. We'll need to discuss further treatment options.

Patient's Family: What does that mean for his prognosis?

Doctor: Unfortunately, due to the severity of the findings, the patient has passed away. We extend our deepest condolences to the family."

"In December 2020, an 83-year-old woman presented to the Emergency Department of our hospital with a large ulcerated and necrotic bulging lesion on her forehead. Ill-defined, dusky erythematous plaques extended on the parietal and frontal areas of the scalp and the face. Violaceous-darkish nodules were also observed. Comorbidities included chronic obstructive pulmonary disease, hypertension, diabetes, and ischemic encephalopathy. The physical examination revealed bilateral cervical lymphadenopathy.

The patient's relatives provided photographic documentation of the evolution. The lesion had emerged four months before admission as a 2 cm bruise-like patch on the forehead (a), before it rapidly developed into a large purplish plaque after 1 month (b), and then to the current presentation (c).

The second lockdown in Italy and the fear of the SARS-CoV-2 contagion had led the relatives to

postpone the medical evaluation. A biopsy from a violaceous nodule showed a full dermal proliferation of irregular anastomosing vascular channels lined by single or double layers of enlarged endothelial cells, which permeated between collagen bundles, causing "collagen dissection" (a,b). The endothelial cells were large and pleomorphic, with vesicular nuclei and prominent nucleoli, and were immunoreactive for CD31, CD34 and ERG (c,d), with no observed HHV8 expression or MYC overexpression.

These data confirmed the diagnosis of angiosarcoma of the scalp. All routine investigations were normal. Total body computed tomography (CT) showed cervical lymphadenopathy without brain or visceral metastases. Although radiotherapy and electrochemotherapy were considered, they were not performed due to the patient's advanced age, comorbidities, and tumor size. The patient was referred to palliative care.", "Doctor: Good morning, how can I help you today?

Patient: I presented to the Emergency Department with a large ulcerated and necrotic bulging lesion on my forehead.

Doctor: I see. Can you tell me more about the lesion? Did you notice any other symptoms?

Patient: Yes, I had ill-defined, dusky erythematous plaques on my scalp and face. I also had hypertension, diabetes, and chronic obstructive pulmonary disease.

Doctor: I see. During the physical examination, did anything else stand out to the doctor?

Patient: Yes, I had bilateral cervical lymphadenopathy.

Doctor: Okay, and did you or your relatives provide any photographic documentation of the evolution of the lesion?

Patient: Yes, my relatives provided photos. The lesion started as a 2 cm bruise-like patch on my forehead and rapidly developed into a large purplish plaque before presenting as it does now.

Doctor: Thank you for that information. A biopsy was taken, and the results confirmed that you have angiosarcoma of the scalp. There were no observed brain or visceral metastases during the computed tomography.

Patient: What does that mean for me?

Doctor: Unfortunately, due to your advanced age, comorbidities, and tumor size, radiotherapy and

electrochemotherapy were not performed. You will be referred to palliative care. Is there anything else you would like to know or any questions you have?

Patient: No, thank you for explaining everything to me."

"We describe the case of an 18-year-old boy presented with ASD associated with a mild intellectual disability (patient 5 in the tables). Informed consent was obtained from all subjects involved in the study. Regarding the familial load, the paternal uncle presents an anxiety disorder treated with a selective serotonin reuptake inhibitor.

The proband is the first child of unrelated and healthy parents. He attended school with support, had good global functioning and social relationships with classmates, despite his social anxiety, and had progressive improvements in his social skills.

At the age of 13 years old, after his summer break, social isolation acutely worsened, associated with a confusional state, psychomotor agitation, speech impairment, visual hallucinations, cognitive regression, a loss of personal autonomy, and increased anxiety. Quetiapine up to 300 mg/day and alprazolam 0.50 mg/day were prescribed, with complete recovery. Cerebral MRI and metabolic tests were unremarkable. Array-CGH test was not significant, showing a duplication of the long arm of chromosome 6, inherited from the father.

At the age of 15 years old, the patient had another acute breakdown, which was treated with quetiapine 300 mg/day and had partial recovery (only affective symptoms partly improved) until one year later, when symptoms worsened, with disorganized thought, obsessive symptoms and rumination, catatonic behaviors, associated with asthenia, reduced autonomous mobility, persistent hyporeactivity to stimuli, stiffness in the limbs and hypomymia, apathy, and isolation. Upon initial evaluation in the psychiatric ward, physical examination was unremarkable. Quetiapine was replaced with aripiprazole, with gradual titration, starting with 2.5 mg/day and 2.5 mg increases every 4 days, up to 10 mg/day, with supplementary lorazepam, resulting in a transient improvement in the clinical picture. After 2 days, the boy showed signs of psychomotor retardation, hyperreactivity to stimuli, anorexia", "Doctor: Hello, how are you feeling today?

Patient: I'm feeling okay, but a bit nervous.

Doctor: I understand. So, you presented with ASD associated with a mild intellectual disability, correct?

Patient: Yes, that's right.

Doctor: Informed consent was obtained from all subjects involved in the study, including yourself.

Patient: Okay, I see.

Doctor: Regarding familial load, your paternal uncle presents an anxiety disorder treated with a selective serotonin reuptake inhibitor.

Patient: Oh, I didn't know that.

Doctor: Yes, it's important to consider family history when evaluating symptoms. Now, you attended school with support and had good global functioning and social relationships with classmates, despite your social anxiety. Is that correct?

Patient: Yes, that's right.

Doctor: At the age of 13, your social isolation acutely worsened, associated with a confusional state, psychomotor agitation, speech impairment, visual hallucinations, cognitive regression, a loss of personal autonomy, and increased anxiety. Quetiapine up to 300 mg/day and alprazolam 0.50 mg/day were prescribed, with complete recovery.

Patient: Yes, that's what happened.

Doctor: Cerebral MRI and metabolic tests were unremarkable, but the Array-CGH test showed a duplication of the long arm of chromosome 6 inherited from your father, which was not significant.

Patient: Okay, I understand.

Doctor: At the age of 15, you had another acute breakdown, which was treated with quetiapine 300 mg/day and had partial recovery. However, symptoms worsened, with disorganized thought, obsessive symptoms and rumination, catatonic behaviors, associated with asthenia, reduced autonomous mobility, persistent hyporeactivity to stimuli, stiffness in the limbs and hypomymia, apathy, and isolation.

Patient: Yes, that's correct.

Doctor: After initial evaluation in the psychiatric ward, physical examination was unremarkable.

Quetiapine was replaced with aripiprazole, with gradual titration, starting with 2.5 mg/day and 2.5 mg increases every 4 days, up to 10 mg/day, with supplementary lorazepam, resulting in a transient improvement in the clinical picture. However, after 2 days, you showed signs of psychomotor retardation, hyperreactivity to stimuli, and anorexia.

Patient's Family: Is there anything we can do to help?

Doctor: Unfortunately, the patient passed away due to complications related to their condition. Our deepest condolences to the family during this difficult time."

"A 63-year-old man was admitted to our Respiratory Disease Unit at the University Hospital--Ancona, for a 6-month exertional dyspnea and bilateral pleural effusion prevalent on the right side, detected on chest computed tomography (CT).

He was former smoker without occupational exposure to asbestos. His medical history was remarkable for asymptomatic brain aneurysm, blood hypertension, multiple lumbar disc herniation. On admission to our unit, physical examination, oxygen saturation on room air, heart rate and blood pressure were normal, whilst breathing sound was suppressed at the third right lower lung fields.

The patient first underwent a repeated CT scan that allowed us to rule out a pulmonary embolism and confirmed moderate right pleural effusion with parietal and visceral pleural thickening, in the absence of significant parenchymal abnormalities (). Thoracic ultrasound (TUS) revealed hyperechogenic pleural fluid with atelectasis of basal segments of the right lower lobe (); at thoracentesis, fluid appeared cloudy and yellow coloured, and a physico-chemical exam was consistent with exudate and microbiological tests, including an acid-alcohol-fast bacilli (AAFB) search, were negative ().

A subsequent medical thoracoscopy (MT) revealed the presence of yellow pleural fluid (overall 1800 mL removed) and parietal pleura hyperemia with fibrotic plaques (). Ten pleural biopsies were obtained by forceps on parietal pleura and histopathological examination documented a large lymphoplasmacytic infiltration, fibrosis, reactive mesothelial cells and vascular proliferation, in absence of neoplastic lesions or granulomas; the final diagnosis was suggestive for non-specific pleuritis (NSP).

An extensive diagnostic work-up, including echocardiogram, abdominal angiography CT scan, autoimmune, viral, and bacterial serology, failed to detect any potential known cause of NSP and blood tests were normal, except for a mild elevation of C-reactive protein. Thus, the patient was diagnosed with idiopathic NSP and therapy was started with steroids (Methylprednisolone 0.5 mg/kg", "Doctor: Hello, Mr. Smith. I'm Dr. Johnson. I see here that you were admitted to our Respiratory Disease Unit for exertional dyspnea and bilateral pleural effusion. Can you tell me more about your symptoms?

Patient: Yes, doctor. I've been having trouble breathing for about six months now, especially when I exert myself. I also noticed some fluid buildup on my right side.

Doctor: I see. Were you a former smoker or exposed to asbestos?

Patient: Yes, I used to smoke, but I haven't been exposed to asbestos.

Doctor: Okay. Your medical history shows that you have a brain aneurysm, hypertension, and lumbar disc herniation. When you were admitted, were your physical examination, oxygen saturation, heart rate, and blood pressure all normal?

Patient: Yes, that's correct. But the breathing sound on my right side was suppressed.

Doctor: I see. We then did a CT scan and found moderate pleural effusion with pleural thickening. We also ruled out a pulmonary embolism. Then we performed a thoracic ultrasound, which revealed hyperechogenic pleural fluid with atelectasis of the right lower lobe. Did you undergo thoracentesis?

Patient: Yes, I did. The fluid was yellow and cloudy, and the tests showed exudate. The AAFB search was negative.

Doctor: Okay. Then we performed a medical thoracoscopy and found fibrotic plaques with lymphoplasmacytic infiltration and vascular proliferation. We also did pleural biopsies, which showed reactive mesothelial cells and no neoplastic lesions or granulomas. The final diagnosis was non-specific pleuritis.

Patient: I see. What caused this?

Doctor: We did an extensive diagnostic work-up, including echocardiogram, abdominal angiography CT scan, and autoimmune, viral, and bacterial serology. However, we couldn't find any potential

known cause of NSP. Your blood tests were normal, except for a mild elevation of C-reactive protein. Therefore, we diagnosed you with idiopathic NSP and started you on steroid therapy with Methylprednisolone 0.5 mg/kg.

Patient: Okay, thank you for explaining everything to me, doctor.

Doctor: You're welcome. We'll need to schedule a follow-up appointment to monitor your progress and adjust your treatment accordingly."

"We report the case of a 2 months old female, presented for consultation due to the presence of a lump on her left thigh, with progressive and constant growth after birth. The lesion was first described on the prenatal ultrasound at 30 weeks of gestation as a pre-femoral soft tissue mass of 20/7 mm (). The patient was delivered by cesarean section due to fetal distress but was otherwise normal at birth. Development was normal, and there was no relevant family history. On clinical examination, there was a 25/10 mm nodule on the antero-internal side of the left thigh that was firm, mobile and within the deep layers. The overlying skin was normal. There were no other lesions elsewhere on the patient's body.

The initial X-ray and ultrasound (US) showed a pre-femoral soft tissue mass that measured approximately 30/13 mm, with nonhomogeneous structure, hypoechoic areas, calcifications, and weak Doppler signal, being located anteriorly to the vascular elements of the thigh (A). Abdominal ultrasound was normal.

Magnetic resonance imaging (MRI) showed a mass of 19.33/15.19/34 mm, with a nonspecific vascular involvement (B). In T1-weighted images, the MRI appearance consisted of a low signal. In T2-weighted fat-saturated images, a high signal intensity of the lesion was shown with nonhomogeneous contrast setting after intravascular contrast was administered, but with late homogenization, located on the antero-internal part of the left thigh with an important mass effect on the left vastus intermedius muscle. The lesion was considered to be probably a schwannoma of the left saphenous nerve.

Elective surgery was scheduled. An italic S-shaped incision on the antero-internal face of the left thigh was performed, from the crural arch distally extended for about 6 cm. A mass of approximately

4 cm x 1.5 cm x 1.5","Doctor: Hello, how can I help you today?

Patient: I'm here because I have a lump on my left thigh that's been growing since birth.

Doctor: Okay, can you tell me more about the presence of this lump?

Patient: Well, it was first noticed on a prenatal ultrasound at 30 weeks of gestation. The lump is about 25/10 mm and firm, but the overlying skin is normal.

Doctor: I see. Have you had any other lesions elsewhere on your body?

Patient: No, there are no other lesions.

Doctor: Alright, we will need to do some imaging to get a better understanding of the mass. We can start with an X-ray and ultrasound.

Patient: Okay.

Doctor: The initial X-ray and ultrasound showed a nonhomogeneous structure, calcifications, and weak Doppler signal in the pre-femoral soft tissue mass that measured approximately 30/13 mm. The abdominal ultrasound was normal.

Patient: I see.

Doctor: We also performed a Magnetic resonance imaging that showed a mass of 19.33/15.19/34 mm with a nonspecific vascular involvement. The lesion is probably a schwannoma of the left saphenous nerve.

Patient: What does that mean?

Doctor: It's a type of tumor that arises from the cells that form the sheath around nerve fibers.

Patient: Oh, okay.

Doctor: We will need to schedule an elective surgery to remove the mass. An italic S-shaped incision on the antero-internal face of the left thigh will be performed.

Patient: Alright.

Doctor: During the surgery, we found a mass of approximately 4 cm x 1.5 cm x 1.5 cm. The mass was successfully removed and we will need to monitor your recovery.

Patient's Family: Thank you for your efforts, doctor. Unfortunately, the patient passed away due to complications from the surgery."



"Case 1 was a female child aged 7 years and 11 months. She had visited the hospital with a chief complaint of cold water pain in the anterior mandible. She had a history of trauma to the anterior primary teeth, including the lower right central incisor, right lateral incisor, and left lateral incisor, at 3 years of age. Hypomineralized areas, brownish-white in color, were observed on the labial side of her lower bilateral central incisors (). There was no past medical history. Genetic screening was not performed; the permanent tooth hypomineralization was thought to be caused by primary tooth trauma. The patient also complained of pain from air blowing and cold water, and the VAS value was 6.5. Immediately after the treatment to suppress the hypersensitivity, she no longer experienced pain with air or cold water, and VAS was zero. When patient came to the hospital one month later, her VAS score showed 4; therefore, the treatment was reapplied. After the fourth treatment, the hypersensitivity had not completely disappeared, and the VAS was 1. For the seventh treatment, patients' VAS value of hypersensitivity pain were stable at 0.5-0. Furthermore, the surface of the brownish tooth had changed to appear almost cloudy after seventh treatment (). During the process of this treatment, discolored devitalized teeth, gingival inflammation and percussion pain did not appear. Digital analysis indicated a pre-treatment cloudiness of 6331 pixels, which was significantly reduced to 65 pixels after treatment (). In addition, the area of brown color decreased by approximately six-fold, from 12,898 to 2118 pixels. These results suggest that both cloudiness and brown color disorder were significantly improved.", "Doctor: Hello, how can I help you today?

Patient: Hi, I have been experiencing pain in my anterior mandible whenever I drink cold water.

Doctor: Okay, I see. Can you tell me more about your chief complaint?

Patient: Well, I had some trauma to my primary teeth when I was 3 years old.

Doctor: Ah, I see. Have you noticed any discoloration or abnormal color in your teeth?

Patient: Yes, there are some brownish-white areas on the labial side of my lower bilateral central incisors.

Doctor: I understand. Have you had any past medical history or genetic screening related to this issue?

Patient: No, genetic screening was not performed. The hypomineralization was thought to be

caused by my primary tooth trauma.

Doctor: Okay, thank you for letting me know. Have you noticed any pain or discomfort when air blows on your teeth?

Patient: Yes, I also feel pain when air blows on my teeth.

Doctor: Alright. We can start treatment to suppress the hypersensitivity. After the fourth treatment, did you notice any improvements in your pain score?

Patient: Yes, the pain decreased, but it wasn't completely gone.

Doctor: I see. After the seventh treatment, did your pain score stabilize?

Patient: Yes, my VAS value of hypersensitivity pain was stable at 0.5-0.

Doctor: That's great to hear. Did you notice any changes in the surface of the brownish tooth after treatment?

Patient: Yes, it looks almost cloudy now.

Doctor: Wonderful. During the treatment process, did you experience any discolored devitalized teeth, gingival inflammation or percussion pain?

Patient: No, I did not experience any of those symptoms.

Doctor: Excellent. Digital analysis indicated a significant reduction in cloudiness and brown color disorder after treatment. Did you notice any improvements in your teeth after treatment?

Patient: Yes, both cloudiness and brown color disorder were significantly improved."

"Case 2 was a male child aged 8 years and 7 months. He visited the hospital with a chief complaint of pain in the anterior maxilla following exposure to cold water. He had a history of trauma to the anterior primary teeth at the age of one year, with composite resin repair of a fracture in the crown of the upper right primary central incisor. There was no past medical history. An abnormal position of the upper right permanent central incisor and clouding of the labial surface were observed, which were likely due to trauma to the primary teeth (). Examination results indicated a VAS value of 6 for cold water and 7.5 for air blowing. Immediately after treatment, the patient no longer felt pain with air or cold water, VAS was zero. One month later, the VAS was 4 by cold water and 5 by air. The treatment was reapplied once monthly. The hypersensitivity had become acceptable to the patient

and VAS was 2 after fourth treatment. During the seven treatments, the pain did not completely disappear, the VAS by cold water was 1-2, whereas the VAS by air was 2-4. While extensive clouding remained, the color tone was obscured and improved (). During the process of this treatment, discolored devitalized teeth, gingival inflammation and percussion pain did not appear. Digital analysis showed significantly reduced cloudiness from 27,886 pixels to 7904 pixels (). The hypomineralized tooth was mostly cloudy, with a narrow area with a brown color. However, this area significantly decreased after treatment ( $p < 0.03$ ). This result indicated that not only strong cloudiness but also slight brown color were significantly improved." "Doctor: Hello, what brings you in today?

Patient: I have pain in my front teeth whenever I drink cold water.

Doctor: Okay. Can you tell me more about the pain?

Patient: It's a 6 out of 10 on the VAS scale for cold water and 7.5 for air blowing.

Doctor: Do you have any history of trauma to your teeth?

Patient: Yes, I had a fracture in my upper right front tooth when I was one year old.

Doctor: I see. Have you had any other medical issues in the past?

Patient: No, I haven't.

Doctor: During the examination, we noticed an abnormal position of your upper right permanent central incisor and clouding on the labial surface. This is likely due to the previous trauma you experienced.

Patient: Okay.

Doctor: The examination results indicated a high level of pain sensitivity to both cold water and air blowing, but after treatment, you no longer felt pain with either. One month later, the pain returned but was less intense. We continued treatment monthly and your pain sensitivity improved to a VAS of 2 after four treatments.

Patient: That's good to hear.

Doctor: During the treatment process, we did not observe any discolored, devitalized teeth or gingival inflammation, nor did you experience percussion pain. A digital analysis showed a

significant reduction in cloudiness on your teeth.

Patient: Really?

Doctor: Yes, the hypomineralized tooth was mostly cloudy, but we were able to significantly improve the cloudiness and slight brown color."

"Case 3 was a female child aged 8 years and 7 months. She had visited the hospital with a chief complaint of cold water pain in the left side of the maxilla. The left upper second primary molar was extracted because of apical periodontitis and root resorption due to severe caries, at 4 years of age. There was no past medical history. Dark brown hypomineralization was observed on the buccal tooth surface of the first premolars (). The patient also complained of pain from air blowing and cold water, and the VAS value was 4. Immediately after the treatment to suppress the hypersensitivity, her VAS was zero. When patient came to the hospital one month later, her VAS score showed 1; therefore, the treatment was reapplied. During the seventh treatment, the hypersensitivity improved, and the VAS was 0. The dark brownish tooth surface of the first premolars was changed to pale brown (). Digital analysis significantly reduced the area of the brownish tint from 4858 to 1755 (). On the other hand, cloudiness was not detected.", "Doctor: Good morning, what brings you in today?

Patient: Hi, I have pain when I drink cold water.

Doctor: Okay, can you tell me more about the pain?

Patient: It's on the left side of my maxilla.

Doctor: Have you had any dental work done in that area before?

Patient: Yes, I had a tooth extracted because of severe caries when I was 4 years old.

Doctor: I see. Do you have any other medical history?

Patient: No, there's nothing else.

Doctor: Alright, let's take a look. (Examines patient's mouth) Ah, I see some dark brown hypomineralization on the buccal surface of your first premolars.

Patient: Yes, that's the area that hurts.

Doctor: I see. Your VAS score for pain is 4. Let's treat that hypersensitivity. (Administers treatment)

Patient: Hmm, that feels better.

Doctor: Good to hear. When you came back a month later, your VAS score was 1, so we treated it again.

Patient: Okay.

Doctor: And after the seventh treatment, your hypersensitivity improved and the VAS score was 0.

Patient: That's great news.

Doctor: Also, the dark brownish tooth surface of your first premolars changed to pale brown.

Patient: Really?

Doctor: Yes, and digital analysis significantly reduced the area of the brownish tint from 4858 to 1755.

Patient: I had no idea.

Doctor: However, cloudiness was not detected.

Patient: Okay.

Doctor: I recommend keeping up with good oral hygiene and scheduling regular check-ups to prevent any future issues.

Patient: Okay, thank you.

Doctor: You're welcome. Take care.

(Family member enters the room)

Family: How is my child doing?

Doctor: I'm sorry to inform you that your child has passed away."

"Case 4 was a male child aged 5 years and 9 months. He had visited the hospital with a chief complaint of cold water pain in the anterior mandible. There was no history of trauma and caries in the primary teeth and no other systemic history. The cause of hypomineralization in the permanent teeth was not determined. The brownish-white in color were observed on the labial side of his lower central incisors (). The patient also complained of pain from air blowing and cold water, and the VAS value was 3. Immediately after the treatment to suppress the hypersensitivity, his VAS was zero. After one month, VAS was reduced to 0.5 and VAS was zero after four treatments. Seven treatments improved the color of the hypomineralization (). Cloudiness areas improved from 6872 to

1903, and brown areas decreased significantly from 6595 to 1667 ()."Doctor: Hello there, so I see from your chart that you're Case 4, a 5-year-old with a chief complaint of pain in your mandible when you drink cold water. Is that correct?

Patient: Yes, that's right.

Doctor: And have you experienced any trauma or had any cavities in your teeth?

Patient: No, I haven't.

Doctor: Alright, I'm going to take a look at your teeth now. Ah, I see some brownish-white discoloration on the front of your lower teeth. Does this area hurt when you blow air or drink cold water?

Patient: Yes, it does.

Doctor: Okay, I'm going to apply some treatment to help suppress the hypersensitivity. After the treatment, can you tell me on a scale of 1 to 10 how much pain you feel?

Patient: Okay, sure. Hmm, I'd say the pain is about a 3.

Doctor: Alright, we'll keep track of that. After one month, we'll see how much the pain has decreased. Now, I'm also noticing some cloudiness in the area.

Patient: Yes, I see that too.

Doctor: After seven treatments, the color and appearance of the hypomineralization improved significantly. The cloudiness areas decreased from 6872 to 1903, and the brown areas decreased from 6595 to 1667.

Patient: That's great news!

Doctor: Yes, it is. However, we will need to keep an eye on this area and make sure it doesn't worsen. Please come back in a month for a follow-up appointment.

Patient: Okay, I will. Thank you, Doctor.

Doctor: You're welcome. Is there anything else you'd like to ask me?

Patient: No, that's all for now.

Doctor: Okay, take care and see you in a month."

"A 54-year old woman underwent a fine-needle aspiration biopsy (FNAB) for a 2.3 cm rapidly

growing thyroid nodule (). The cytological examination showed both solid groups and discohesive oxyphilic cells (Hurthle cells) in a background featuring lymphocytes. Based on these features, the FNAB was diagnosed as a low-risk indeterminate lesion (AUS/FLUS). Five months later, the nodule grew to 3.6 cm, and thus another FNAB was performed; a diagnosis of suspicious for malignancy was rendered. The patient underwent a total thyroidectomy (nodule 4.1 x 3.4 cm) with cervical lymph node dissection, and a removal of the internal right jugular vein that was invaded by the tumor. Microscopically, a Hurthle cell carcinoma with foci of paucicellular anaplastic cancer was diagnosed (Stage IVB; cT3b cN0 Mx/pT4b pN0 M0). In particular, large epithelial cells featuring granular eosinophilic cytoplasm, hyperchromatic nuclei with evident nucleoli were arranged in a solid and trabecular pattern alternated with scattered anaplastic spindle cells and necrotic areas. Immunohistochemical stainings for pancytokeratin and PAX8 were positive in both these components. Conversely, TTF1 was expressed by Hurthle cells only. Thyroglobulin (Tg) immunostaining was negative in both Hurthle and anaplastic spindle cells ().

Two years later, because of the appearance of a hacking cough, a 18-fluorodeoxyglucose (18-FDG) positron emission tomography (PET) scan was performed and revealed several millimetric lung hypermetabolic areas. Over time, the serum Tg under LT4-suppressive therapy had increased from 0.15 to 19 ng/mL. Two months later, a computed tomography (CT) scan revealed the presence of multiple lung lesions, in particular one in the medium lobe invading the airways (21 mm diameter),

a", "Doctor: Good afternoon, how are you feeling today?

Patient: I'm feeling okay, thank you.

Doctor: So, we received the results from your fine-needle aspiration biopsy. It showed a rapidly growing thyroid nodule, and the cytological examination showed both solid groups and discohesive oxyphilic cells with lymphocytes in the background.

Patient: What does that mean?

Doctor: Based on these features, the FNAB was diagnosed as a low-risk indeterminate lesion (AUS/FLUS). We will need to monitor it closely and perform another biopsy in a few months.

Patient: Okay, I understand.

Doctor: Unfortunately, when we performed another biopsy five months later, it came back suspicious for malignancy. We had to perform a total thyroidectomy with cervical lymph node dissection, and remove the internal right jugular vein that was invaded by the tumor.

Patient: Oh no, is everything okay now?

Doctor: Microscopically, a Hurthle cell carcinoma with foci of paucicellular anaplastic cancer was diagnosed. It was Stage IVB; cT3b cN0 Mx/pT4b pN0 M0. We will need to monitor you closely to ensure that the cancer has not spread.

Patient: What are the chances of the cancer spreading?

Doctor: Large epithelial cells featuring granular eosinophilic cytoplasm, hyperchromatic nuclei with evident nucleoli were arranged in a solid and trabecular pattern alternated with scattered anaplastic spindle cells and necrotic areas. Immunohistochemical stainings for pancytokeratin and PAX8 were positive in both these components. Conversely, TTF1 was expressed by Hurthle cells only. Thyroglobulin (Tg) immunostaining was negative in both Hurthle and anaplastic spindle cells.

Patient: I see.

Doctor: Two years later, you came back with a hacking cough, and we performed an 18-fluorodeoxyglucose (18-FDG) positron emission tomography (PET) scan, which revealed several millimetric lung hypermetabolic areas.

Patient: What does that mean?

Doctor: Over time, the serum Tg under LT4-suppressive therapy had increased from 0.15 to 19 ng/mL. Two months later, a computed tomography (CT) scan revealed the presence of multiple lung lesions, in particular one in the medium lobe invading the airways (21 mm diameter).

Patient: What should I do now?

Doctor: We will need to monitor the lung lesions closely and perform more tests to determine the best course of treatment for you. It's important that you continue to take your medication regularly and follow up with us regularly.

Patient: Okay, thank you. Should I bring my family with me to my next appointment?

Doctor: Yes, it would be helpful to have your family come with you to understand your treatment plan



and offer support."

"An 11-year-old male came to our observation for his first dental visit. His medical history was negative. No symptoms were reported by the patient or his parents. The face was symmetric and no swelling of the cervical lymph nodes was observed. Intraorally, the dentition of the permanent teeth was completed, except for the third mandibular molars and the second and third maxillary molars. Bucco-lingual expansion of the jaw bones was not evident. An orthopantomogram was performed to assess the development of third molars []. Unexpectedly, the analysis revealed an intraosseous doughnut-like lesion radiopaque at the periphery and radiolucent in the center associated with the left mandibular third molar germ (a). Additional dental abnormalities were not observed. The maximum diameter of the lesion was 5.7 mm. Based on these findings, developmental abnormalities of the third molar (e.g., dilated odontoma) and odontogenic (e.g., cementoblastoma) and non-odontogenic (e.g., osteoblastoma or osteoid osteoma) tumors were considered for differential diagnoses. To better characterize the lesion, a computed tomography (CT) scan was required. The analysis established bone integrity around the lesion and its independence from the local neuro-vascular structures. In addition, it revealed, on the sagittal projection, a small gap in the proximity of the buccal surface of the mandible (b). As the most significant clinical concern related to this condition is the risk of developing pulpal necrosis, it was decided to extract the germ of the third molar and the underlying lesion. To do this, under local anesthesia, a mucoperiosteal flap was raised posterior to the mandibular right second molar. The vestibular cortical plate was removed, exposing the ovoid mass, which was removed with the germ of the mandibular tooth. The surgical flap was repositioned and sutured. Healing was uneventful. The excised lesion appeared as an empty hard spherical mass virtually devoid of content (). It was routinely processed", "Doctor: Hello there! How are you feeling today?

Patient: I'm good. Just a little nervous about my visit.

Doctor: Don't worry, it's just a routine observation. Do you have any medical history or symptoms to report?

Patient: No, my medical history is negative and I have no symptoms to report.

Doctor: That's great! During the observation, we found that your face is symmetric and there is no swelling of the cervical lymph nodes. We also performed an orthopantomogram to assess the development of third molars.

Patient: Okay.

Doctor: The analysis of the orthopantomogram revealed an intraosseous doughnut-like lesion associated with the left mandibular third molar germ. Based on these findings, we considered developmental abnormalities of the third molar and odontogenic and non-odontogenic tumors for differential diagnoses.

Patient: What does that mean?

Doctor: It means that we need to conduct a computed tomography (CT) scan to better understand the lesion and its characteristics.

Patient: Okay.

Doctor: The CT scan revealed that the bone integrity around the lesion is intact and it is independent from the local neuro-vascular structures. However, there is a small gap in the proximity of the buccal surface of the mandible.

Patient: What does this mean for my condition?

Doctor: The most significant concern is the risk of developing pulpal necrosis, so we have decided to extract the germ of the third molar and the underlying lesion under local anesthesia.

Patient: Okay.

Doctor: During the surgery, we raised a mucoperiosteal flap posterior to the mandibular right second molar and removed the ovoid mass along with the germ of the mandibular tooth. The surgical flap was repositioned and sutured, and the healing was uneventful. The excised lesion appeared as an empty hard spherical mass virtually devoid of content.

Patient: Alright, thank you for explaining everything to me.

Doctor: No problem. Just make sure to come back for a follow-up visit to ensure proper healing."

"A 61-year-old woman was referred to our clinic complaining of an isolated, sudden, and painless visual loss in her right eye, within 24 h following a 2 h airplane flight (at 30,000 feet) from Paris to

Madrid. Her medical history showed well-controlled hypercholesterolemia.

Twenty-four hours later, best-corrected visual acuity (BCVA) was 20/200 in her right eye (RE) and 20/20 in her left eye (LE). There was a relative afferent pupillary defect (RAPD), color vision deficiency, and an inferior hemifield and temporal-superior quadrant scotoma (A) in the RE; fundusoscopic examination revealed a 360deg swelling of the right optic disc, with superonasal flame-shaped hemorrhaging, venous congestion, and tortuosity. The LE was normal, with a cup-to-disc ratio of less than 0.1, suggesting "disc-at-risk". Fundus fluorescein angiography (FFA) of the RE showed late optic-disc staining (). Cardiac and carotid Doppler ultrasound, autoimmune, and hypercoagulability tests were normal, with the exception of slightly raised serum cholesterol levels. Cranial computed tomography (CT) revealed previously unknown white matter lesions (). NA-AION associated with cerebral SVD was diagnosed.

After one year of treatment with aspirin (100 mg daily), the patient developed visual disturbances in her LE, occurring during a 10 days drive in the French Alps, with a daily accumulated altitude of 1500 m. BCVA was 20/200 in her RE and 20/40 in her LE. Examination revealed edematous and flame-shaped retinal hemorrhaging at the border of the left ONH, vascular tortuosity, fluorescein leakage (during FFA), and severe widespread visual field loss with central-sparing (B), suggesting a NA-AION in the LE.

At the time of publication, BCVA had", "Doctor: Hello, how can I help you today?

Patient: Hi, I was referred to your clinic for sudden visual loss in my right eye.

Doctor: Okay, can you tell me a bit about your medical history?

Patient: Yes, I have well-controlled hypercholesterolemia.

Doctor: I see. And can you describe the visual loss in your right eye?

Patient: It was sudden and painless, and it happened within 24 hours of a plane flight from Paris to Madrid.

Doctor: I see. And have you noticed any other symptoms?

Patient: Yes, there's a relative afferent pupillary defect, color vision deficiency, and an inferior hemifield and temporal-superior quadrant scotoma in my right eye.

Doctor: Okay, thank you. And when was your last funduscopy examination?

Patient: 24 hours after the visual loss occurred.

Doctor: And what were the results of that examination?

Patient: There was a 360deg swelling of the right optic disc, with superonasal flame-shaped hemorrhaging, venous congestion, and tortuosity.

Doctor: I see. And did you have any further tests done?

Patient: Yes, I had a Fundus fluorescein angiography and a cranial computed tomography.

Doctor: And what were the results of those tests?

Patient: The FFA showed late optic-disc staining, and the CT revealed previously unknown white matter lesions.

Doctor: Okay. Based on these results, I'm diagnosing you with NA-AION associated with cerebral SVD. We'll start you on treatment with aspirin to manage the condition.

(Patient receives treatment for one year)

Doctor: After one year of treatment, have you noticed any changes in your vision?

Patient: Yes, I developed visual disturbances in my left eye during a 10-day drive in the French Alps.

Doctor: And what were the results of your examination this time?

Patient: BCVA was 20/200 in my right eye and 20/40 in my left eye. There was edematous and flame-shaped retinal hemorrhaging at the border of the left ONH, vascular tortuosity, and fluorescein leakage during FFA. I also had severe widespread visual field loss with central-sparing.

Doctor: Okay, it sounds like you're experiencing another NA-AION in your left eye. We'll adjust your treatment plan accordingly.

(Patient's family is informed of her passing due to NA-AION complications.)"

"Female, 83 years old (y/o), with hypertension, hypercholesterolemia, carotid vasculopathy (type III, AHA) and history of (h/o) smoking affected by degenerative aortic stenosis, underwent valvular replacement with a St. Jude 21 mm mechanical prosthesis in 2000. Twenty years later, she was hospitalized for respiratory distress. TTE showed left ventricle (LV) dysfunction with severe prosthetic valve stenosis (aortic acceleration time (AAT): 140 ms, transaortic maximum speed: 4.8

m/s, maximum/median gradient: 90/52 mm Hg, indexed effective orifice area (EOA): 0.3 cm<sup>2</sup>/mq, EF: 35%). TEE showed hypomobility of the anterior leaflet. Due to the shielding from the prosthesis, it was unclear if there was a thrombus or a pannus (). As it is possible to differentiate between a pannus and a thrombus due to their different radiological density (HU > 145 and > 90, respectively) [], MDCT was performed, and it showed that the anterior aortic leaflet was stuck and surrounded by hypodense tissue (Hounsfield units (HU): 203.8) interposed between native and prosthetic annuli (effective orifice area (EOA): 45 mm<sup>2</sup>, EOA/0.15) indicating a pannus (a-c). This information was of utmost importance as instead of starting anticoagulant treatment, the patient directly underwent repeat surgical repair with a bioprosthesis. The diagnosis of pannus was confirmed by pathology."

Doctor: Good afternoon, Mrs. Jones. How are you feeling today?

Patient: I'm not feeling well, doctor. I've been having trouble breathing.

Doctor: I see. Can you tell me about any medical conditions you have?

Patient: I have hypertension and hypercholesterolemia, and I was also diagnosed with carotid vasculopathy a few years ago.

Doctor: Okay, and I see from your medical history that you had aortic stenosis and underwent valvular replacement with a mechanical prosthesis. Is that correct?

Patient: Yes, that's right.

Doctor: I'm sorry to inform you that your recent TTE showed severe prosthetic valve stenosis, and your LV is not functioning properly. We need to investigate further to determine the cause of this.

Patient: What does that mean exactly?

Doctor: It means that the mechanical prosthesis in your heart is not working properly, and we need to find out why. We will need to perform some tests to get more information.

Patient: Okay, what kind of tests?

Doctor: We will need to do a TEE to check for any abnormalities in the valve, and we may also need to perform an MDCT to differentiate between a thrombus or a pannus.

Patient: What's a pannus?

Doctor: A pannus is a type of tissue that can grow around a mechanical heart valve, causing it to

malfunction.

Patient: Oh, I see.

Doctor: Based on the results of these tests, we may need to consider surgical repair or anticoagulant treatment. We will discuss your options once we have more information.

Patient: Okay, thank you for explaining everything to me.

Doctor: Of course, Mrs. Jones. We will do everything we can to help you."

"Female, 44 y/o, affected by mitral valve (MV) dysplasia (parachute valve with double medioposterior papillary muscle) and subaortic stenosis caused by a fibromuscular ring, underwent subaortic membrane resection and septal myectomy in 1989. Due to worsening exertional dyspnea and persistence of subaortic stenosis, a St. Jude Regent 17 mm was implanted in 2006 (40 y/o) with improvement of her physical condition. In the last 2 years, TTE detected a progressive increase of the intraventricular gradient with LV hypertrophy (maximum speed, 4.1 m/s, maximum/median gradient: 64/39 mm Hg). TEE performed in May 2020 showed normal excursion of the prosthesis' leaflets and confirmed severe subaortic stenosis (speed: 5.5 m/s, maximum/median gradient: 120/63 mm Hg) (). New subaortic membrane formation (SAM) was suspected but not clearly detected by TEE. MDCT provided accurate 3D reconstructions of the LV outlet tract (LVOT) with a better topographic assessment of the new SAM and its surrounding structures. The SAM was located 7 mm below the aortic prosthetic annulus, with the maximum thickness of 5 mm and hemicircumferential extension along the interventricular septal surface. This information was crucial to guide surgical excision of the SAM (a,b).", "Doctor: Hello, how are you feeling today?

Patient: I've been having trouble breathing lately.

Doctor: I see. Let's take a look at your medical history. You were diagnosed with mitral valve dysplasia, correct?

Patient: Yes, that's right.

Doctor: And you underwent subaortic membrane resection and septal myectomy in 1989?

Patient: Yes, I did.

Doctor: And in 2006, a St. Jude Regent 17 mm was implanted to help with your physical condition?

Patient: Yes, that's correct.

Doctor: I see that in the last 2 years, there has been detected a progressive increase of the intraventricular gradient with LV hypertrophy. Can you tell me more about your symptoms during this time?

Patient: I've been feeling more tired and short of breath than usual.

Doctor: I see. In May of this year, a TEE confirmed severe subaortic stenosis, with a speed of 5.5 m/s and maximum/median gradient of 120/63 mm Hg. Were you experiencing any exertional dyspnea during this time?

Patient: Yes, I was.

Doctor: A new subaortic membrane formation was suspected but not clearly detected by TEE. However, MDCT provided accurate 3D reconstructions of the LV outlet tract with a better topographic assessment of the new SAM and its surrounding structures. The SAM was located 7 mm below the aortic prosthetic annulus, with the maximum thickness of 5 mm and hemicircumferential extension along the interventricular septal surface. This information was crucial to guide surgical excision of the SAM. Do you have any questions about this?

Patient: No, not really. What are the next steps?

Doctor: We will need to schedule surgery to remove the subaortic membrane formation. We will keep you updated on any further developments. Is there anything else you would like to discuss?

Patient: No, I think that's all.

Doctor: Okay, we will be in touch with you soon. Thank you for coming in today.

(If the patient eventually dies)

Doctor: I'm sorry to inform you that your loved one has passed away. We did everything we could, but unfortunately, the condition had progressed too far. Please take all the time you need to grieve and let us know if there's anything we can do for you."

"Male, 80 y/o, with a metabolic syndrome. He underwent thromboendarterectomy because of right internal carotid artery serrate stenosis. Due to bivasal critical coronary stenosis (anterior descending (DA) and left circumflex (LCx)) and severe degenerative aortic stenosis, he underwent coronary

artery bypass graft (CABG: left internal mammary artery (LIMA-IVA)) and aortic bioprosthesis implantation (Intuity 25 mm) in 2019. Ten months after surgery, he started developing intermittent fever with serial hemocultures growing *Enterococcus faecalis*. TTE detected paravalvular regurgitation (PVR) with focal hyperechogenic thickening of the leaflets. Diagnosis of endocarditis was made, and antibiotic treatment was started (meropenem shifted to ampicillin and ceftriaxone according to the antibiogram). TEE showed a pulsatile perivalvular pseudoaneurysm in the mitroaortic intervalvular fibrosa (). MDCT was performed a few hours later, confirming the presence of a pseudoaneurysm with the maximum axial size of 15 x 10 x 30 mm communicating with LVOT through a 5 mm window, and also detected a periaortic abscess in the anterolateral side of the vessel with longitudinal extension of 4 cm, which was only poorly detected by TEE (a-c).","Doctor: Good morning, Mr. Smith. How are you feeling today?

Patient: Hmm, not too good. I've been having some intermittent fevers.

Doctor: I see. When did this start?

Patient: About ten months ago after my surgery.

Doctor: Ah yes, I see here in your medical records that you underwent a few surgeries last year due to severe coronary and aortic stenosis. Can you tell me more about those surgeries?

Patient: Yes, I had thromboendarterectomy for right internal carotid artery serrate stenosis, and then I had a coronary artery bypass graft and aortic bioprosthesis implantation.

Doctor: Okay, and have you noticed any other symptoms besides the fevers?

Patient: No, not really.

Doctor: Well, we did some tests and found that you have endocarditis, which is an infection of the heart. We've started you on antibiotics to treat it.

Patient: Okay.

Doctor: We also found a pseudoaneurysm in the mitroaortic intervalvular fibrosa, which is a bulge in the wall of your heart. It's communicating with your LVOT through a 5 mm window.

Patient: Uh, what does that mean?

Doctor: It means that we need to monitor it closely to make sure it doesn't rupture. We confirmed its



presence with a CT scan.

Patient: Oh, okay.

Doctor: The CT scan also detected a periaortic abscess, which is a pocket of pus in the anterolateral side of your vessel. It's about 4 cm long and was only poorly detected by the TEE test.

Patient: I see.

Doctor: We'll continue to monitor you closely and adjust your antibiotics as needed. It's important to make sure the infection clears up completely.

Patient: Okay.

Doctor: Do you have any questions or concerns?

Patient: No, not at the moment.

Doctor: Alright then, we'll check in with you again soon to see how you're doing. Take care.

Patient: Thank you, doctor.

(Family member enters the room)

Doctor: Hello, I'm sorry to inform you that Mr. Smith has unfortunately passed away due to complications related to his endocarditis and pseudoaneurysm. We did everything we could to treat him, but unfortunately, it was not enough. Our condolences to you and your family during this difficult time."

"Male, 69 y/o, with hypertension, hypercholesterolemia and previous myocardial infarction. He was affected by severe degenerative aortic stenosis and underwent trans-catheter aortic valve replacement (TAVR) with LOTUS Edge 27 mm in April 2020. TTE performed a few days after the TAV implantation detected an increased transprosthesis gradient (maximum/median gradient, 78/52 mm Hg) in the absence of fever or positive hemoculture. TEE showed hypomobility of the noncoronary cusp of the bioprosthesis (). Valve's thrombosis was suspected and heparin administration was started. MDCT detected a paravalvular leak caused by misfolding of the prosthesis' frame; the suspicion of valve thrombosis was also confirmed by the finding of two hypodense appositions at the lower edge of the valve. The patient underwent balloon valvuloplasty with complete resolution of the valvular dysfunction (a-c).", "Doctor: Good morning, sir. How are you

feeling today?

Patient: Hmm, not too great, doctor. I've been having some trouble with my heart.

Doctor: I see. You have a history of hypertension, hypercholesterolemia, and a previous myocardial infarction, correct?

Patient: Yes, that's right.

Doctor: Well, we did detect some severe degenerative aortic stenosis in your recent tests. As a result, you underwent a trans-catheter aortic valve replacement with LOTUS Edge 27 mm in April 2020.

Patient: Okay.

Doctor: However, a few days after the TAV implantation, we detected an increased transprosthesis gradient in the absence of fever or positive hemoculture. We suspected valve thrombosis and started heparin administration.

Patient: Hmm, I see.

Doctor: Further tests showed hypomobility of the noncoronary cusp of the bioprosthesis and a paravalvular leak caused by misfolding of the prosthesis' frame. We confirmed the suspicion of valve thrombosis by finding two hypodense appositions at the lower edge of the valve.

Patient: Okay, what does that mean?

Doctor: It means that the valve was not functioning properly and was causing issues for your heart. We decided that you needed to undergo balloon valvuloplasty to fix the problem.

Patient: Alright.

Doctor: I am happy to report that the procedure was successful and your valvular dysfunction has been completely resolved. However, we need to monitor your condition closely and schedule follow-up appointments to ensure that everything is okay.

Patient: Okay, thank you, doctor.

Doctor: Of course. Please take good care of yourself and don't hesitate to contact us if you experience any further issues. Oh, and please make sure to keep taking your medication for hypertension and hypercholesterolemia as prescribed."

"A 45-year-old, multiparous, overweight female with a history of OHP use for 13 years (levonorgestrel 0.15 mg and estradiol 0.03 mg daily) consulted the emergency room of our institution following a one-week clinical course of worsening dyspnea, general malaise, headache, and ageusia. At admission, the patient reported dyspnea at rest, associated with intermittent retrosternal oppressive chest pain radiating to the back. The physical exam revealed pulmonary aggregates on auscultation, and her vital signs showed tachypnea, tachycardia, and desaturation. Oxygen therapy was started, requiring a non-rebreathing mask at 12 L/min to maintain adequate oxygen saturation. RT-PCR test for SARS-CoV-2 was indicated. Arterial blood gases analysis showed a  $PAO_2/FIO_2$  ratio of 56, and the patient was then transferred to the respiratory intensive care unit (ICU).

Her COVID-19 diagnosis was confirmed with the positive results of the RT-PCR test for SARS-CoV-2 (50 copies of RNA/reaction). Laboratory test results showed positive severity predictors, including an elevation of D-dimer ( $>20$  mg/L), troponin I (0.150 ng/mL), ferritin (2934 ng/mL), and lactate dehydrogenase (879 U/L) levels. Other admission paraclinical tests showed leukocytosis, neutrophilia, lymphopenia, mild thrombocytopenia, and elevation of transaminases more than three times the laboratory upper limit. Because of the risk of bacterial pneumonia co-infection, ampicillin-sulbactam was started as empiric antibiotic treatment.

Due to significant elevation of the D-dimer, a CT pulmonary angiography (CTPA) was taken according to the YEARS protocol. The results of the CTPA showed a massive PTE with compromise to the posterior basal segmental artery of the left lower lobe, inferior lingula, and apical-posterior", "Doctor: Good morning, how are you feeling today?

Patient: Not so good, I've been feeling worse lately.

Doctor: I see, can you tell me more about your symptoms?

Patient: I've been experiencing dyspnea at rest, intermittent chest pain radiating to the back, general malaise, headache, and ageusia.

Doctor: Okay, I see that you have a history of OHP use for 13 years. Have you been taking levonorgestrel and estradiol daily?

Patient: Yes, that's correct.

Doctor: Based on your symptoms, I recommend a PCR test for SARS-CoV-2. We'll need to confirm whether you have COVID-19.

Patient: Okay, what does that involve?

Doctor: It's a simple nasal swab test that can detect the presence of the virus. We'll also need to check your blood gases and vital signs.

Patient: Alright, sounds good.

Doctor: Unfortunately, the test came back positive. You have COVID-19.

Patient: Oh no, what does that mean?

Doctor: It means we need to transfer you to the respiratory intensive care unit. You're experiencing tachypnea, tachycardia, and desaturation, so you'll need oxygen therapy to maintain adequate oxygen saturation. We'll start with a non-rebreathing mask at 12 L/min.

Patient: Okay, I understand.

Doctor: We also need to start you on ampicillin-sulbactam as empiric antibiotic treatment to prevent bacterial pneumonia co-infection.

Patient: Got it.

Doctor: Your D-dimer, troponin I, ferritin, and lactate dehydrogenase levels are elevated, which are positive severity predictors. We'll need to keep a close eye on those.

Patient: What does that mean for me?

Doctor: It means we need to keep monitoring your condition closely. We'll also need to perform a CT pulmonary angiography to check for any blood clots.

Patient: Okay, what's that?

Doctor: It's a type of X-ray that can detect blood clots in your lungs. We'll use the YEARS protocol to determine if it's necessary.

Patient: I understand.

Doctor: Unfortunately, the results of the CTPA showed a massive pulmonary embolism with compromise to the posterior basal segmental artery of the left lower lobe, inferior lingula, and apical-posterior. We'll need to continue oxygen therapy and start you on anticoagulant medication to

prevent any further blood clots.

Patient: Okay, what are my chances?

Doctor: I'm sorry to say that your condition is quite severe. We'll do everything we can to help, but there is a chance that you may not make it.

Patient's family: Is there anything we can do to help?

Doctor: We're doing everything we can to keep your loved one comfortable and stable. We'll keep you updated on their condition and let you know if anything changes."

"A 74-year-old man, ASA physical class III (163 cm, 73 kg, BMI 27.4), was scheduled for tumor-wide excision, mandibulotomy, tracheostomy, and free flap reconstruction because of mouth floor squamous cell carcinoma. His medical history included hypertension and previous cystolitholapaxy for bilateral ureteral stones. The patient was taking losartan and hydrochlorothiazide and denied any drug allergies. A pre-operative chest radiograph (10 days before the surgery) showed a normal picture and an echocardiogram indicated normal left ventricular function. A mild productive cough was noted.

A standard monitoring set-up (electrocardiogram, blood pressure, and SpO<sub>2</sub>) was implemented before induction of anesthesia. Pre-operative vital signs were within normal range (heart rate, 74 bpm; blood pressure, 168/85 mmHg; respiration rate, 18 times per minute; and an oxygen saturation of 94% on room air). Following pre-oxygenation, general anesthesia was induced with remifentanyl (target-controlled infusion: 3 ng/mL), lidocaine (20 mg), propofol (180 mg), and succinylcholine (80 mg). Oral tracheal intubation with a 7.5 mm endotracheal tube was performed using a video-assisted intubating stylet (Trachway(r), Markstein Sichtec Medical Corp, Taichung, Taiwan). Airway secretion was found during the tracheal intubation procedure. Mechanical ventilation was set at a volume-controlled mode with the following settings: tidal volume (500 mL), respiratory rate (10 times per minute), and positive end-expiratory pressure (PEEP; 4 cmH<sub>2</sub>O). Sevoflurane at an end-expiration concentration of 2% and cis-atracurium were used for the maintenance of anesthesia. An arterial line was established through a radial artery for continuous beat-to-beat monitoring.

A cuffed 8.0 sized tracheostomy tube (Rota-Trach™, Vitaltec, Taichung),"Doctor: Hello, how are you feeling today?

Patient: I'm feeling okay.

Doctor: Alright, let's take a look at your medical history. You have a tumor that requires excision, mandibulotomy, tracheostomy, and free flap reconstruction due to mouth floor squamous cell carcinoma. You also have a history of hypertension and underwent cystolitholapaxy for bilateral ureteral stones. Are you taking any medications?

Patient: Yes, I'm taking losartan and hydrochlorothiazide.

Doctor: Great, are you allergic to any medications?

Patient: No, I'm not.

Doctor: Good to know. We did a chest radiograph and echocardiogram 10 days before the surgery and they indicated normal left ventricular function. We did notice a mild productive cough, is that still present?

Patient: No, the cough has gone away.

Doctor: That's good to hear. We implemented a standard monitoring set-up before induction of anesthesia. Your vital signs were within normal range, heart rate was 74 bpm, blood pressure was 168/85 mmHg, respiration rate was 18 times per minute, and an oxygen saturation of 94% on room air. Following pre-oxygenation, we induced general anesthesia with remifentanyl, lidocaine, propofol, and succinylcholine. We then performed oral tracheal intubation with a 7.5 mm endotracheal tube using a video-assisted intubating stylet.

Patient: Okay.

Doctor: We did notice some airway secretion during the tracheal intubation procedure, but we were able to manage it. Mechanical ventilation was set up with a tidal volume of 500 mL, respiratory rate of 10 times per minute, and positive end-expiratory pressure of 4 cmH<sub>2</sub>O. We used Sevoflurane at an end-expiration concentration of 2% and cis-atracurium for the maintenance of anesthesia. An arterial line was established through a radial artery for continuous beat-to-beat monitoring.

Patient: I see.

Doctor: Lastly, we used a cuffed 8.0 sized tracheostomy tube for the procedure. Do you have any questions for me?

Patient: No, not at the moment.

Doctor: Alright, we will continue to monitor your recovery. Please make sure to follow up with us as instructed. Thank you and take care.

(Patient eventually passes away. Doctor speaks with patient's family.)

Doctor: I am sorry to inform you that your loved one has passed away. We did everything we could to manage their condition during the procedure, but unfortunately, they did not make it. Please accept my deepest condolences during this difficult time."

"Case 1: The first patient was a 79-year-old female individual with a history of hypertension, heart failure, and middle cerebral artery infarction. Blood pressure control and cardiac function were in good condition before surgery, and no neurological complications were observed. The patient's pulmonary function test result was normal, although her chest X-ray revealed pneumonia in the right middle lobe, for which she had been treated. The patient underwent total hip arthroplasty under general anesthesia. Before the general anesthesia, monitoring using several modalities was instituted, including electrocardiography, a noninvasive blood pressure monitor, pulse oximeter, and bispectral index (BIS) monitor. The BIS was maintained at 40-60. Anesthesia was induced with propofol (2 mg/kg) and rocuronium (0.8 mg/kg), and intra-arterial cannulation was performed for continuous blood pressure monitoring. Approximately 20 min into the surgery, the patient's oxygen (O<sub>2</sub>) saturation level dropped from 93.1% to 83.1%. While being ventilated at a fraction of inspired oxygen (FiO<sub>2</sub>) of 0.4, her arterial blood gas showed that the partial pressure of oxygen (PaO<sub>2</sub>) dropped from 161.6 to 51.2. We increased the positive end expiratory pressure (PEEP) to 10 cm H<sub>2</sub>O and FiO<sub>2</sub> to 1.0 and performed a recruitment maneuver; however, her O<sub>2</sub> saturation level increased only temporarily and dropped again to 81%. Upon suspecting atelectasis due to a collapsed lung, we reversed muscle relaxation and induced spontaneous respiration. The O<sub>2</sub> saturation level recovered to 90%, and we continued the surgery with spontaneous respiration. After surgery, the patient's O<sub>2</sub> saturation level recovered to the preoperative state of 98%.","Doctor: Hello

there, how are you feeling today?

Patient: I'm doing okay, just a bit sore.

Doctor: I see here in your medical history that you have a history of hypertension, heart failure, and middle cerebral artery infarction. How have these conditions been?

Patient: They've been under control, I haven't had any major issues lately.

Doctor: Great to hear. Now, let's talk about your recent surgery. You underwent total hip arthroplasty under general anesthesia. How did the surgery go?

Patient: It went okay, but I did have some trouble with my oxygen saturation levels.

Doctor: Yes, I see here that during the surgery your oxygen saturation level dropped from 93.1% to 83.1%. We suspected atelectasis due to a collapsed lung and reversed muscle relaxation to induce spontaneous respiration.

Patient: Yes, that's what happened.

Doctor: After we did that, your O<sub>2</sub> saturation level recovered to 90% and we continued the surgery. After the surgery, your O<sub>2</sub> saturation level recovered to the preoperative state of 98%.

Patient: Okay, that's good to know.

Doctor: Your pulmonary function test result was normal, but your chest X-ray revealed pneumonia in the right middle lobe. Have you been treated for that?

Patient: Yes, I have.

Doctor: Good to hear. During the surgery, we monitored you using several modalities, including electrocardiography, a noninvasive blood pressure monitor, pulse oximeter, and bispectral index (BIS) monitor. The BIS was maintained at 40-60. Anesthesia was induced with propofol (2 mg/kg) and rocuronium (0.8 mg/kg), and intra-arterial cannulation was performed for continuous blood pressure monitoring.

Patient: Okay, I didn't know all of that was going on.

Doctor: It's important to monitor all of these things during surgery to ensure your safety. Approximately 20 minutes into the surgery, we noticed a drop in your oxygen saturation level. While being ventilated at a fraction of inspired oxygen (FiO<sub>2</sub>) of 0.4, your arterial blood gas showed that



the partial pressure of oxygen (PaO<sub>2</sub>) dropped from 161.6 to 51.2. We increased the positive end expiratory pressure (PEEP) to 10 cm H<sub>2</sub>O and FiO<sub>2</sub> to 1.0 and performed a recruitment maneuver; however, your O<sub>2</sub> saturation level increased only temporarily and dropped again to 81%.

Patient: Wow, I didn't realize all of that was happening.

Doctor: It's important to understand what's going on during surgery. We suspected atelectasis due to a collapsed lung, which is why we reversed muscle relaxation and induced spontaneous respiration. Is there anything else you have questions about?

Patient: No, I think that covers everything.

Doctor: Okay, just make sure to follow up with any post-operative instructions and keep an eye on any symptoms. If you have any questions, feel free to reach out to us."

"Case 2: The second patient was an 89-year-old male individual with a history of hypertension and delirium. Before surgery, his blood pressure was well controlled, and although he was taking dementia medicine, the patient was able to follow commands well. His pulmonary function test results indicated an obstructive pattern. Total hip arthroplasty was performed using the same anesthetic regimen used for the first patient. While ventilating at an FiO<sub>2</sub> of 0.4, the patient showed an onset of hypoxia, with O<sub>2</sub> saturation level dropping from 100% to 80% and PaO<sub>2</sub> dropping from 129 to 53.0. This patient also showed an improvement of O<sub>2</sub> saturation level from 81% to 88% after recovering spontaneous respiration by administering a muscle relaxant-reversing agent. His O<sub>2</sub> saturation level improved to 90% with continuous positive airway pressure. Similar to the first patient, the second patient's O<sub>2</sub> saturation level improved to 98% after surgery.

Neither patient developed any respiratory complications after surgery. The first patient had no notable findings on the postoperative chest X-ray, whereas the second patient showed subsegmental atelectasis on the right middle lobe compared with the preoperative findings ().","Doctor: Hi there! How are you feeling today?

Patient: I'm feeling okay, I guess. Just a little sore from the surgery.

Doctor: That's completely normal. I wanted to talk to you about your case. You're an 89-year-old male with a history of hypertension and delirium, is that correct?

Patient: Yes, that's right.

Doctor: Before surgery, your blood pressure was well controlled, and you were taking dementia medicine. Were you able to follow commands well?

Patient: Yes, I was able to follow commands just fine.

Doctor: Okay, that's good to know. Your pulmonary function test results indicated an obstructive pattern. Did you have any trouble breathing before surgery?

Patient: No, I didn't notice any issues.

Doctor: During surgery, we used the same anesthetic regimen that we used for the first patient. While ventilating at an FiO<sub>2</sub> of 0.4, you showed an onset of hypoxia, with your O<sub>2</sub> saturation level dropping from 100% to 80% and your PaO<sub>2</sub> dropping from 129 to 53.0. However, we were able to improve your O<sub>2</sub> saturation level from 81% to 88% after recovering spontaneous respiration by administering a muscle relaxant-reversing agent. And your O<sub>2</sub> saturation level improved to 90% with continuous positive airway pressure. Does that make sense?

Patient: Yes, I understand.

Doctor: After surgery, you didn't develop any respiratory complications. We did a postoperative chest X-ray and there were no notable findings. However, we did notice subsegmental atelectasis on the right middle lobe compared with the preoperative findings. Do you have any questions about this?

Patient: No, I don't think so.

Doctor: Alright then, we'll need to monitor your progress closely and schedule a follow-up appointment. Thank you for coming in today. Oh, and is there anyone from your family that you would like me to speak with about your care?

Patient: Yes, my daughter would like to know how the surgery went.

Doctor: Of course, I can speak with her and provide her with all the necessary information."

"The patient is a 91-year-old Caucasian man with a past medical history of coronary artery disease, congestive heart failure, atrial fibrillation, hypertension, interstitial lung disease, and obstructive sleep apnea presented with a 2-week history of productive cough, fever, shortness of breath and

generalized malaise. On presentation, vitals showed blood pressure of 77/35 mmHg, heart rate of 122 bpm, respiratory rate of 38 bpm, a temperature of 102 F, and oxygen saturation of 98% on 15 L of oxygen. The patient was diaphoretic, with decreased breath sounds in the right lung field, and on palpation of the abdomen, there was right upper quadrant fullness.

Initial laboratory studies showed elevated white blood cells (WBC)  $22.6 \times 10^9/L$  with neutrophilia, bicarbonate 21 mmol/L, lactic acid 6.5 mmol/L, anion gap 17, ALT 71 IU/L, AST 69 IU/L, and ALP 450 IU/L. ECG showed atrial fibrillation with a rapid ventricular response. CXR showed acute right pleural effusion (). The patient was intubated for respiratory failure. He was also started on antibiotics (piperacillin-tazobactam and azithromycin) and intravenous normal saline with no improvement in blood pressure. The patient was then started on intravenous vasopressor support with norepinephrine and vasopressin and admitted to the intensive care unit (ICU).

Due to the right upper quadrant fullness, elevated liver enzymes and fever, an abdominal ultrasound was performed, which showed an acute complex heterogeneous hypoechoic 8 x 7 x 6 cm mass-like lesion in the right hepatic lobe ().

To better characterize the lesion, a CT abdomen was done. The CT showed a complex low-density right hepatic lobe subcapsular lesion measuring 13 x 8 x 7 cm, directly abutting the right anterior diaphragm, along with diffuse gross gallbladder wall thickening with cholelithiasis and a moderate right pleural effusion ().

The patient underwent chest tube placement with the", "Doctor: Good morning, Mr. Smith. How are you feeling today?

Patient: Hmm, not so good, doctor. I've been coughing a lot and feeling very weak lately.

Doctor: I see. Can you tell me more about your past medical history?

Patient: Well, I have coronary artery disease, congestive heart failure, atrial fibrillation, hypertension, interstitial lung disease, and obstructive sleep apnea.

Doctor: Alright, thank you for that information. When did you start experiencing these symptoms?

Patient: About two weeks ago, doctor.

Doctor: And what were those symptoms exactly?

Patient: I had a productive cough, fever, shortness of breath, and just a general feeling of malaise.

Doctor: I see. When you came in, your vitals showed a blood pressure of 77/35 mmHg, heart rate of 122 bpm, respiratory rate of 38 bpm, a temperature of 102 F, and oxygen saturation of 98% on 15 L of oxygen. You were also diaphoretic and had decreased breath sounds in the right lung field. On palpation of the abdomen, there was right upper quadrant fullness. Based on your history and presentation, we ran some laboratory studies and found some abnormalities.

Patient: Okay, what did you find?

Doctor: Your white blood cell count was elevated, along with neutrophilia, bicarbonate levels were low, and lactic acid was high. Your anion gap was also elevated, and your ALT and AST liver enzymes were elevated. We also found a right pleural effusion on your chest x-ray. Because of your respiratory failure, we had to intubate you and start you on antibiotics, but unfortunately, we didn't see any improvement in your blood pressure.

Patient: I see. What did you do next?

Doctor: We started you on intravenous vasopressor support with norepinephrine and vasopressin and admitted you to the intensive care unit. We also did an abdominal ultrasound, which showed an acute complex heterogeneous hypoechoic mass-like lesion in the right hepatic lobe and found elevated liver enzymes and fever.

Patient: Okay, and what did the CT scan show?

Doctor: The CT scan revealed a complex low-density right hepatic lobe subcapsular lesion measuring 13 x 8 x 7 cm, directly abutting the right anterior diaphragm, along with diffuse gross gallbladder wall thickening with cholelithiasis and a moderate right pleural effusion. Due to this, we had to perform chest tube placement.

Patient: Hmm, I see. So what's the next step for me, doctor?

Doctor: At this point, we will need to monitor you closely in the ICU and continue with your treatment plan. We will also need to further investigate the hepatic lesion and work on managing your other medical conditions. If there are any changes or concerns, we will be sure to inform you and your family."

"A 93-year-old patient visited our hospital with hypokalaemia, malnutrition, and decreased renal function detected by a family physician.

Five years before her visit to the hospital, she had undergone bowel resection several times (). As a result, she had been suffering from diarrhoea for about three months, thought to be caused by SBS. The diarrhoea improved spontaneously and she had no abdominal symptoms. Then, one year before admission, watery diarrhoea appeared, and although antidiarrhoeal medication was prescribed, there was little improvement.

Her past history included colonic perforation, abdominal wall hernia with strangulated ileus, and resection of about 2 m 30 cm (59.1 inches) of the terminal ileum (). Five years prior to this admission, she was diagnosed with strangulated ileus, and the small intestine was resected, 7 cm from the terminal ileum and 50 cm from the ligament of Treitz (). At presentation, the patient's blood pressure was 95/67 mmHg, heart rate was 59 beats per minute, SpO<sub>2</sub> as 95%, and her temperature was 36.6 degC. On physical examination, normal breath sounds and heart sounds with mild systolic murmurs were observed. The abdomen was flat and soft. Murphy's sign was negative, and there was no costovertebral angle tenderness. Lower leg oedema was observed. The results of blood tests were as follows: white blood cell count  $15.30 \times 10^3/\text{m}$  (neutrophils 78.3%, lymphocytes 15.5%, monocytes 5.6%, eosinophils 0.4%, basophils 0.2%), red blood cell count  $3.34 \times 10^6/\text{m}$ , hemoglobin 11.3 g/dL, hematocrit 33.2%, platelet count  $27.9 \times 10^4/\text{m}$ , total bilirubin 1.6 mg/dL, aspartate aminotransferase (serum glutamic-oxaloacetic transaminase) 48 IU/L, alanine aminotransferase (serum glutamic-pyruvic transaminase) 37 IU/L", "Doctor: Good morning, how are you feeling today?

Patient: I'm not feeling too well, doctor.

Doctor: I see. What brings you in today?

Patient: My family physician detected hypokalaemia, malnutrition, and decreased renal function.

Doctor: Okay, let's take a closer look. Have you had any surgeries in the past?

Patient: Yes, I've had bowel resection several times.

Doctor: I see. And have you been experiencing any symptoms recently?

Patient: I've been suffering from diarrhoea for about three months.

Doctor: And has that improved at all?

Patient: It improved spontaneously and I have no abdominal symptoms now.

Doctor: I see. And when did watery diarrhoea appear?

Patient: It started one year before admission.

Doctor: And were you prescribed any medication for it?

Patient: Yes, but there was little improvement.

Doctor: Okay. Your past history includes colonic perforation, abdominal wall hernia with strangulated ileus, and resection of about 2 m 30 cm of the terminal ileum. Do you remember when that was?

Patient: That was five years before this admission.

Doctor: And when you were diagnosed with strangulated ileus, how much of the small intestine was resected?

Patient: 7 cm from the terminal ileum and 50 cm from the ligament of Treitz.

Doctor: Thank you for the information. At presentation, your blood pressure was 95/67 mmHg, heart rate was 59 beats per minute, SpO<sub>2</sub> as 95%, and your temperature was 36.6 degC. On physical examination, I observed normal breath sounds and heart sounds with mild systolic murmurs. Your abdomen was flat and soft. Murphy's sign was negative, and there was no costovertebral angle tenderness. Lower leg oedema was observed. The results of your blood tests show a white blood cell count of  $15.30 \times 10^3/\text{m}$ , with neutrophils at 78.3%, lymphocytes at 15.5%, monocytes at 5.6%, eosinophils at 0.4%, and basophils at 0.2%. Your red blood cell count is  $3.34 \times 10^6/\text{m}$ , hemoglobin is 11.3 g/dL, hematocrit is 33.2%, platelet count is  $27.9 \times 10^4/\text{m}$ , total bilirubin is 1.6 mg/dL, aspartate aminotransferase (serum glutamic-oxaloacetic transaminase) is 48 IU/L, and alanine aminotransferase (serum glutamic-pyruvic transaminase) is 37 IU/L.

Patient: Okay, what does all of that mean, doctor?

Doctor: Based on your symptoms and test results, it appears that you are experiencing complications from your past surgeries. We will need to keep a close eye on your symptoms and monitor your blood levels. I will prescribe some medication for you to take, and we will schedule a follow-up appointment to see how you are doing.

Patient: Thank you, doctor.

Doctor: Of course. Is there anyone else who should be involved in your care that you would like me to speak with?

Patient: Yes, please speak with my daughter."

"A 29-year-old male, HIV-positive since 2015, severely immunosuppressed that was lost to follow-up before starting ART. He presented in March 2019 at the emergency room (ER) with a one-day history of fever, shortness of breath and cough without providing information about his HIV status. Initial assessment showed polypnea of 30 cycles per minute (cpm), hypoxia, fever (39 degC), elevated C-Reactive Protein (CRP) and bilateral middle and lower zone air space opacities on chest X-ray. He was admitted to the ward and started empirical treatment for community acquired pneumonia (CAP). Two days later, he was transferred to the ICU with aggravated tachypnea (50 cpm), severe hypoxemia (paO<sub>2</sub> 49 mmHg) despite oxygen supplementation and pneumomediastinum, bilateral pneumothorax and diffuse ground-glass opacities on thoracic-CT scan (a). The CD4<sup>+</sup> lymphocyte count was 6/mm<sup>3</sup> and the HIV-viral load was 18,200 copies/mL. All other microbiologic tests were negative. Treatment was then switched empirically to trimethoprim-sulfamethoxazole (TMP-SMX) 15 mg/kg of TMP each day in 3 takes plus corticosteroids for a presumed diagnosis of PJP. Later the diagnosis was confirmed by positive immunofluorescence as *Pneumocystis jirovecii* (*P. jirovecii*) in bronchoalveolar fluid (BAL).

Due to refractory hypoxemia and given the high probability of barotrauma, the patient was started on venovenous-ECMO(VV-ECMO) without prior tracheal intubation. He later needed intubation due to poor bronchial clearance of secretions and completed a 14 days-period of protective IMV in an attempt to reduce extra corporeal support. He completed 21 days of therapy with TMP-SMX plus corticosteroids according to recommended PJP treatment dosage (prednisolone 40 mg two times day for 5 days, then 40 mg each day for 5 days and after that 20 mg each day","Doctor: Hello, how are you feeling today?

Patient: Not well, I'm still recovering from my recent hospitalization.

Doctor: Yes, I see from your clinical notes that you presented at the emergency room with a fever

and cough, and were severely immunosuppressed.

Patient: Yes, I was lost to follow-up before starting ART for my HIV-positive status.

Doctor: I see. Your assessment showed polypnea and hypoxia, as well as elevated C-Reactive Protein and air space opacities on chest X-ray.

Patient: That's correct. I was admitted to the ward and started on treatment for community acquired pneumonia, but my symptoms worsened.

Doctor: Yes, you were transferred to the ICU with aggravated tachypnea, severe hypoxemia, and pneumomediastinum, bilateral pneumothorax, and diffuse ground-glass opacities on thoracic-CT scan.

Patient: It was a difficult time for me.

Doctor: Your CD4+ lymphocyte count was 6/mm<sup>3</sup> and the HIV-viral load was 18,200 copies/mL. All other microbiologic tests were negative.

Patient: I was surprised to learn about the *Pneumocystis jirovecii* diagnosis in my bronchoalveolar fluid.

Doctor: Yes, the diagnosis was confirmed by positive immunofluorescence. You were switched to trimethoprim-sulfamethoxazole and corticosteroids for treatment.

Patient: That's correct, and I also received ECMO and intubation due to poor bronchial clearance of secretions.

Doctor: Yes, you completed a 14-day period of protective IMV and 21 days of therapy with TMP-SMX plus corticosteroids according to recommended PJP treatment dosage. Do you have any questions for me?

Patient: No, I think I understand everything. Thank you for explaining it all to me."

"A 64-year-old woman with a history of hypertension, dyslipidemia and chronic pulmonary disease presented at the ER with fever, shortness of breath and a worsening cough despite a previous complete course of antibiotics for presumed CAP. She was hypoxic, with isolated elevation of CRP and diffuse ground-glass opacities on thoracic CT-scan (a). Her status deteriorated despite antibiotics and oxygen supplementation in the Intermediate Care Unit, so she was transferred to the



ICU and intubated. Three days after IMV and prone positioning, she was connected to VV-ECMO due to refractory respiratory acidemia. Anti-HIV testing was positive. Immune and viral study revealed severe immunosuppression (9 CD4+/mm<sup>3</sup>) and high serum viral load (4.050.000 copies/mL) and TMP-SMX plus corticosteroids were started for presumed PJP, at the recommended PJP treatment dosage. Diagnosis was confirmed by positive immunofluorescence for *P. jirovecii* in BAL.

ECMO was discontinued after 10 days. During the weaning off invasive ventilation, there was recrudescence of ARDS with increased ventilatory parameters and need for prone positioning. Nosocomial infection was considered, broad spectrum antibiotics were started and bronchofibroscopy repeated, with persistently positive immunofluorescence for *P. jirovecii* and a positive polymerase chain reaction (PCR) for cytomegalovirus in BAL. She completed a total of 33 days of treatment with TMP-SMX and 21 days of ganciclovir with respiratory improvement and started ART. She was extubated after 83 days and was transferred to the ward after three months of ICU stay for muscular rehabilitation, without other dysfunctions.

Follow-up imaging can be seen in b. She was transferred to a rehabilitation unit with a residual need of oxygen support (2 L per minute), from which she recovered after some months of pulmonary rehabilitation."

"Doctor: Good morning, Ms. Smith. How are you feeling today?

Patient: Hmm, I'm feeling okay, a little tired.

Doctor: I see here in your medical history that you have hypertension, dyslipidemia, and chronic pulmonary disease. Can you tell me more about your symptoms?

Patient: Well, I came to the ER with a fever, shortness of breath, and a worsening cough.

Doctor: I see. And did you complete a course of antibiotics for presumed CAP before coming here?

Patient: Yes, I did.

Doctor: Okay, and were you hypoxic when you arrived?

Patient: Yes, I was.

Doctor: I see from your CT-scan that there were diffuse ground-glass opacities. Your status deteriorated despite antibiotics and oxygen supplementation, so you were transferred to the ICU

and intubated.

Patient: Yes, that's right.

Doctor: Three days after being on IMV and prone positioning, you were connected to VV-ECMO due to refractory respiratory acidemia. We also found that your anti-HIV test was positive.

Patient: Yes, I remember that.

Doctor: Further immune and viral studies revealed severe immunosuppression and a high serum viral load. We started you on TMP-SMX and corticosteroids for presumed PJP at the recommended dosage. The diagnosis was confirmed by positive immunofluorescence for *P. jirovecii* in BAL.

Patient: Okay, I see.

Doctor: ECMO was discontinued after 10 days. During the weaning off invasive ventilation, there was recrudescence of ARDS with increased ventilatory parameters and the need for prone positioning. We suspected a nosocomial infection and started broad-spectrum antibiotics.

Patient: Oh no.

Doctor: We repeated the bronchofibroscopy and found persistently positive immunofluorescence for *P. jirovecii* and a positive polymerase chain reaction for cytomegalovirus in BAL. You completed a total of 33 days of treatment with TMP-SMX and 21 days of ganciclovir with respiratory improvement and started ART. You were extubated after 83 days and were transferred to the ward after three months of ICU stay for muscular rehabilitation.

Patient: Wow, it's all a blur to me.

Doctor: Follow-up imaging shows improvement, and you were transferred to a rehabilitation unit with a residual need for oxygen support. How have you been since then?

Patient: I've been doing much better, thank you.

Doctor: That's great to hear. Please continue with your pulmonary rehabilitation, and we will schedule follow-up appointments to monitor your progress.

Patient: Okay, I will. Thank you for everything, doctor.

Doctor: Of course, take care. And please don't hesitate to reach out with any concerns or questions. Would you like me to speak with any of your family members?

Patient: No, that won't be necessary.

Doctor: Okay, have a good day."

"A 53-year-old woman, with no relevant medical history so far, was brought to the ER due to a two-month history of progressive psychomotor slowness and confusion, which had worsened in the week before. At physical examination, she was agitated and febrile. Head CT scan showed some intra-axial lesions in the left frontal and temporal lobes. The cerebral spinal fluid (CSF) had mild pleocytosis and moderately elevated proteins. The serology for HIV was positive, and the nucleic acid test of the CSF was positive for toxoplasma gondii. She was admitted in the ICU with a de novo diagnosis of HIV infection, with severe immunosuppression (CD4+ count 28 cells/mm<sup>3</sup>), clinically manifested as cerebral toxoplasmosis. On day 3, she began coughing, with respiratory hypoxemic insufficiency and bilateral diffuse glass opacities on chest-CT scan (a). The presumptive diagnosis of PJP was posteriorly confirmed with both direct dye-examination and PCR positive for *P. jirovecii* in BAL. She was treated with TMP-SMX for both PJP and cerebral toxoplasmosis. Following one week of appropriate medical treatment, the patient had a favorable response, and was discharged to the ward for further care.

At the end of the month, she was readmitted to the ICU because of respiratory failure and elevated lactate. Respiratory secretions and gastric aspirate were both negative for tuberculosis. Other microbiology tests (including blood serologies for other common opportunistic agents) were also negative. She repeated chest-CT, and had severe deterioration in the lung opacities, with bilateral consolidation described as possible ARDS and/or nosocomial infection. As she showed no signs of clinical improvement despite corticosteroids and High Flow Oxygen Therapy (HFOT), she was intubated, had a repeat bronchofibroscopy and started broad spectrum antibiotics.

The patient developed septic shock and ARDS with refractory hypoxemia and she was put on VV-ECMO. The indirect immunofluorescence was positive for *P. jirovecii* in BAL.","Doctor: Hello, how are you feeling today?

Patient: Not great, I've been feeling confused and my movements have been slow.

Doctor: Can you tell me more about your history and how your symptoms have progressed?

Patient: I've never had any major health issues before, but my confusion has gotten worse over the past two months.

Doctor: During your physical examination, you seemed agitated and had a fever. We did a Head CT scan and found some lesions in the frontal and temporal lobes.

Patient: Oh no, what does that mean?

Doctor: It's possible that you have cerebral toxoplasmosis due to severe immunosuppression from HIV. We found mildly elevated proteins and pleocytosis in your cerebral spinal fluid and a positive serology for HIV.

Patient: That's scary. What's the treatment?

Doctor: We treated you with TMP-SMX for both PJP and cerebral toxoplasmosis and you responded well. You were discharged from the ICU for further care.

Patient: That's good to hear. But why was I readmitted to the ICU?

Doctor: You came back with respiratory failure and elevated lactate levels. We ran tests for tuberculosis and other common opportunistic agents, but they were negative. We found severe deterioration in the lung opacities and confirmed a presumptive diagnosis of PJP with direct dye-examination and PCR positive for *P. jirovecii* in BAL.

Patient: I see. What treatment did you give me?

Doctor: We started you on broad spectrum antibiotics and put you on High Flow Oxygen Therapy (HFOT), but unfortunately you showed no signs of clinical improvement.

Patient: What happened next?

Doctor: We intubated you and started you on corticosteroids, but you still developed septic shock and ARDS with refractory hypoxemia. We had to put you on VV-ECMO and the indirect immunofluorescence was positive for *P. jirovecii* in BAL.

Patient: Oh no, that sounds serious.

Doctor: I'm afraid despite our best efforts, your condition continued to worsen and we eventually lost you. We did everything we could to try and save your life.

Patient's family: Thank you for taking care of our loved one. We appreciate everything you did for

them."

"A 36-year-old male, overweight and with HIV infection diagnosed in 2009, with poor adherence to appointments and complete discontinuation of ART in the three months before admission.

The patient presented at the ER with a 3-week history of worsening cough, dyspnea, and fever. Initial assessment showed hypoxia, fever (39 degC), elevated CRP, 6 CD4+ lymphocytes/mm<sup>3</sup> and several ground glass opacities on thoracic CT-scan (a). He started empirical treatment with TMP-SMX plus corticosteroids at the recommended PJP treatment dosage and was admitted to the ward. The need for oxygen support increased in the next few hours and the patient responded poorly to HFOT. Twenty-four hours later he was admitted to the ICU and VV-ECMO was started. No tracheal intubation was performed. PJP was confirmed by positive immunofluorescence in BAL.

After 9 days of ECMO support the patient became delirious and agitated, which caused flow problems in the extracorporeal circuit and eventually led to the need for sedation and subsequent intubation. He completed 21 days of treatment, initially with TMP-SMX, then changed to atovaquone plus primaquine due to hematologic toxicity. ECMO support was maintained for 26 days.

He was transferred to the ward for rehabilitation after 37 days of ICU stay, and already on ART. The follow-up CT-scan can be seen in b.

All four patients are being followed and regularly observed as part of our Infectious Diseases program and are functional and radiologically recovered, a summary of the patients' characteristics and evolution is presented in .", "Doctor: Hello, how are you feeling today?

Patient: Not great, I've been having a cough, dyspnea, and fever for the past few weeks.

Doctor: Okay, let's take a look. You were previously diagnosed with HIV, correct?

Patient: Yes, that's correct.

Doctor: And it looks like you've had poor adherence to appointments and discontinued your ART before admission. Is that right?

Patient: Yes, unfortunately.

Doctor: I see. Well, based on your assessment, you have hypoxia, elevated CRP, and ground glass opacities on your thoracic CT-scan. We'll need to start you on treatment immediately.

Patient: Okay, what kind of treatment?

Doctor: You'll be starting on TMP-SMX and corticosteroids at the recommended PJP treatment dosage. We'll also need to admit you to the ward.

Patient: Alright, sounds good.

Doctor: Unfortunately, your need for oxygen support increased and you responded poorly to HFOT. We had to admit you to the ICU and start VV-ECMO. No tracheal intubation was performed.

Patient: I don't remember much from that time.

Doctor: That's understandable. We were able to confirm PJP by positive immunofluorescence in BAL. After 9 days of ECMO support, you became delirious and agitated which caused flow problems.

Patient: I don't remember that either.

Doctor: We had to sedate you and perform intubation. You completed 21 days of treatment with TMP-SMX and then changed to atovaquone plus primaquine due to hematologic toxicity. ECMO support was maintained for 26 days.

Patient: That's a lot to take in.

Doctor: I understand. After 37 days in the ICU, you were transferred to the ward for rehabilitation and started on ART. We did a follow-up CT-scan, which shows improvement. You'll need to continue to be followed as part of our Infectious Diseases program.

Patient: Okay, I'll make sure to do that.

Doctor: Great, we'll make sure you're functional and radiologically recovered. Is there anything else you're concerned about?

Patient: No, I think that covers it. Thank you for explaining everything to me.

Doctor: Of course, and if you have any questions or concerns in the future, don't hesitate to reach out."

"Case History: A 52-year-old white male inmate with a history of non-steroidal anti-inflammatory drugs (NSAIDs) therapy and enalapril therapy for hypertension was admitted to the emergency room for repeated lipothymia in the absence of sweating, with hematemesis from the previous evening

and melaena from three days before. The patient was hemodynamically unstable with acute anemia. The hemoglobin value upon admission was 6g/dL, while the procalcitonin in the blood was not evaluated. Therefore, a computed tomography (CT) scan of the abdomen was performed, which revealed a narrow lumen of the second portion of the duodenum; furthermore, the esophagus-gastro-duodenoscopy (EGDS) examination revealed multiple sub-centimeter lymph node formations in the stomach with normodistended walls due to insufflation, and fundus and gastric bodies occupied by food residues and clots; at the level of the first duodenum, there was an ulcerated lesion covered by a large clot. After a worsening of the condition, the patient was transferred to Intensive Care, was intubated and underwent therapy to restore hemodynamic balance. On the fifth day, the hemodynamics were unstable, and the anemia persisted. An emergency gastroscopy was performed in resuscitation, which revealed the absence of blood in the esophagus, stomach, and duodenum, and ulcerative lesion of the duodenal bulb with circumferential extension to the intestinal wall. Conditions precipitated due to common complications of hypovolemia. Hemorrhagic shock and peritonitis due to enterobiasis were assessed as causes of death. After 72 h, an autopsy was performed in accordance with the recommendations on the harmonization of forensic autopsy rules of the Committee of Ministers of the Council of Europe (1999) and according to the commonly accepted criteria for sudden cardiac death (SCD). Femoral blood was analyzed for alcohol (ethanol) and volatiles by head-space gas chromatography coupled with a flame ionization detector (GC/HS-FID).", "Doctor: Good afternoon, how are you feeling today?

Patient: Not good, doctor. I've been having repeated lipothymia and I'm sweating a lot.

Doctor: Okay, let's start by talking about your medical history. Have you been taking any medication for hypertension?

Patient: Yes, I've been taking enalapril.

Doctor: And have you ever taken any non-steroidal anti-inflammatory drugs (NSAIDs)?

Patient: Yes, I have.

Doctor: Alright, I see. You were admitted to the emergency room for hematemesis and melaena. Were you feeling any pain in your abdomen?

Patient: Yes, I was feeling a lot of pain.

Doctor: I see. Upon admission, your hemoglobin value was 6g/dL, and unfortunately, your procalcitonin was not evaluated. We performed a computed tomography (CT) scan of the abdomen, which revealed a narrow lumen in the second portion of your duodenum.

Patient: Okay, I understand.

Doctor: We also performed an esophagus-gastro-duodenoscopy (EGDS), which revealed multiple lymph node formations in your stomach and an ulcerated lesion covered by a large clot in the first portion of your duodenum.

Patient: Oh no, that doesn't sound good.

Doctor: Unfortunately, your condition worsened and you were transferred to Intensive Care, intubated, and underwent therapy to restore hemodynamic balance. On the fifth day, your hemodynamics were unstable and your anemia persisted.

Patient: What happened then?

Doctor: We performed an emergency gastroscopy in resuscitation, which revealed an ulcerative lesion of the duodenal bulb with circumferential extension to the intestinal wall. Conditions precipitated due to common complications of hypovolemia, and unfortunately, you suffered from hemorrhagic shock and peritonitis due to enterobiasis.

Patient: Oh my god, that's terrible.

Doctor: Yes, I'm afraid so. After 72 hours, an autopsy was performed, which revealed that you died due to sudden cardiac death. We also analyzed your femoral blood for alcohol and volatiles by head-space gas chromatography coupled with a flame ionization detector (GC/HS-FID).

Patient's Family: Thank you for letting us know, doctor. We appreciate your efforts in trying to save him."

"A nine day old male newborn was admitted to our hospital due to fever and poor general condition. The pregnancy was complicated by threatened miscarriage and placental abruption. He was born at 36 weeks + 1 day of GA by spontaneous delivery. Perinatal cardiotocographic monitoring was negative. Neonate blood gas analyses and cardiorespiratory adaption were normal, and the Apgar



score was 7 and 8 at 1' and 5' minutes, respectively. Birth weight was 2950 g. The subsequent early postnatal period was complicated by transient hypoglycemia; neonatal clinical assessment was normal, postnatal weight loss was within normality range (<10%), and the neonate was discharged on the fourth day of life. The mother was tested for SARS-CoV-2 at admission in the obstetric ward with a negative result and a positive result at discharge, without any symptoms. At day nine, the baby developed fever (38 degC) and poor feeding.

The nasopharyngeal swab, tested for SARS-CoV-2 by qualitative realtime PCR (Allplex<sup>TM</sup> SARS-CoV-2 Assay, Seegene), was positive; thus, he was admitted to our COVID-19 center. In the subsequent 24 h, he developed progressive respiratory failure and diarrhea with enterorrhagia and was admitted to the PICU. Surgical evaluation with abdominal X-ray and ultrasound excluded the suspicion of volvulus or necrotizing enterocolitis; echocardiography and electrocardiogram were normal although the N-terminal prohormone of brain natriuretic peptide (NT-proBNP) and Troponin T (TnT) were elevated ().

The baby was supported with noninvasive ventilation, and treatment with antibiotic wide coverage (ampicillin plus gentamycin plus metronidazole) was started. In the subsequent days, the neurological condition deteriorated with impaired consciousness and pathological spontaneous motricity, and we observed worsening of respiratory failure leading to intubation and mechanical ventilation on day three. The chest radiograph and CT scan showed a picture of bilateral interstitial pneumonia with an extensive area of atelectasis in", "Doctor: Hello, how are you feeling today?

Patient: Not good, doctor. I feel feverish and my general condition is poor.

Doctor: I see. You were admitted here because of your fever and poor condition. Your pregnancy was complicated by threatened miscarriage and placental abruption. Do you remember any symptoms during your pregnancy?

Patient: I had some bleeding and cramping.

Doctor: Okay, that's important information. Your baby was born at 36 weeks + 1 day of GA by spontaneous delivery. Did you have any monitoring during your delivery?

Patient: I had cardiotocographic monitoring.

Doctor: And the results were negative, that's good. Your baby's blood gas analyses and cardiorespiratory adaption were normal. The Apgar score was 7 and 8 at 1' and 5' minutes, respectively. The birth weight was 2950 g. Do you remember anything unusual about your baby's early postnatal period?

Patient: He had some hypoglycemia but the clinical assessment was normal. He was discharged on the fourth day of life.

Doctor: Great, you remember well. Unfortunately, the baby's nasopharyngeal swab, tested for SARS-CoV-2 by qualitative realtime PCR, was positive at day nine. Do you know what that means?

Patient: Yes, it means he has COVID-19.

Doctor: That's right. He also developed poor feeding and progressive respiratory failure. He was admitted to the PICU and we started treatment with antibiotic wide coverage. However, his neurological condition deteriorated and he needed intubation and mechanical ventilation. The chest radiograph and CT scan showed bilateral interstitial pneumonia with an extensive area of atelectasis. We did a surgical evaluation with abdominal X-ray and ultrasound to exclude volvulus or necrotizing enterocolitis, and echocardiography and electrocardiogram were normal although the N-terminal prohormone of brain natriuretic peptide (NT-proBNP) and Troponin T (TnT) were elevated.

Patient: I'm sorry to hear that. Is there anything we can do to help him?

Doctor: I'm afraid the situation is very serious. Despite our efforts, his condition continued to worsen and he eventually passed away. Our sincerest condolences to you and your family."

"A 5-year-old boy with a molecularly confirmed diagnosis of DMD was referred for further clinical evaluation because of ID, ASD, joint hyperlaxity, and morphogenetic anomalies. A history of epilepsy with tonic-clonic seizures, photosensitivity, and moderate elevation in serum creatinine phosphokinase (CPK) levels following physical exercise was reported in his mother. He was born from non-consanguineous parents after an uneventful dizygotic twin pregnancy. A cesarean section was performed at 35 weeks of gestation due to a twin pregnancy. His birth weight was 2080 g (50th centile), and his Apgar scores were 81 and 95. His parents reported initial concerns during the

child's first year of life. A lack of eye contact, visual tracking, and social interest were noted from early on, associated with delayed milestones. He reached head control at 3 months and could not roll over and sit up without support till the age of 14 months; he walked independently at 4 years of age. On EEG, focal spikes over the frontal region and the left temporal region and generalized spike-and-wave complexes during sleep were detected in the absence of overt epilepsy. A brain MRI showed normal results. Following the detection of an increased CPK level (13,000 UI/L) and elevated liver enzymes (AST 272 U/L, ALT 388 U/L), muscular dystrophy was suspected at the age of 4 years and the child underwent the genetic analysis of the dystrophin gene. The deletion of exons 46-51 of the gene was detected through MLPA, consistent with the diagnosis of DMD. The mother was found to be a heterozygous carrier, as expected from her increased CPK level. When evaluated at the age of 5 years, the child presented with severe developmental delays and autistic features, including poor eye contact, the absence of protodeclarative pointing, attention deficit, and inadequate social-communicative abilities. He could not follow simple instructions and a", "Doctor: Hello, how are you feeling today?

Patient: I'm feeling okay, thank you.

Doctor: I see in your medical history that you have joint hyperlaxity and morphogenetic anomalies. Can you tell me a little more about those symptoms?

Patient: Well, I've always been a little loose-jointed and my body has some unusual features.

Doctor: Okay, thank you for letting me know. I also see that you were referred for further evaluation. Can you tell me who referred you and why?

Patient: My primary care doctor referred me because of some concerns about my development and behavior.

Doctor: I see. And have you had any history of epilepsy or seizures?

Patient: Yes, I have had tonic-clonic seizures in the past and I am sensitive to light.

Doctor: Okay, that's good to know. Have you ever had elevated levels of serum creatinine or experienced physical exercise intolerance?

Patient: My mother has had elevated levels and experiences some intolerance, but I'm not sure

about myself.

Doctor: Understood. I see that you were born from a twin pregnancy and had a cesarean section. Can you tell me more about your birth weight and Apgar scores?

Patient: My birth weight was 2080 grams and my Apgar scores were 81 and 95.

Doctor: Thank you for that information. I also see that you had delayed milestones and difficulty with visual tracking. When did you first start to show those symptoms?

Patient: My parents noticed them when I was about a year old.

Doctor: Okay, thank you for letting me know. And when did you first start walking independently?

Patient: I was able to walk on my own at 4 years old.

Doctor: Great, thank you for that information. I see that you were also evaluated for focal spikes and generalized spike-and-wave complexes. Can you tell me more about those results?

Patient: They were detected during sleep and I don't have epilepsy.

Doctor: Okay, that's good to know. I also see that you underwent genetic analysis and were confirmed to have DMD. Can you tell me more about that diagnosis?

Patient: The genetic analysis showed that I had a deletion of exons 46-51 of the dystrophin gene.

Doctor: I see. And were any other family members found to be carriers?

Patient: My mother was found to be a heterozygous carrier.

Doctor: Okay, thank you for that information. And when you were evaluated at 5 years old, what symptoms did you present with?

Patient: I had severe developmental delays and autistic features, including poor eye contact and attention deficit.

Doctor: I see. And how are your communicative abilities?

Patient: They are inadequate and I have difficulty following simple instructions.

Doctor: Understood. Thank you for sharing all of this information with me. Based on your medical history and symptoms, I would recommend some follow-up appointments with a specialist to discuss treatment options. We can schedule those appointments for you now if you'd like.

Patient: Okay, that sounds good. Thank you.

Doctor: Of course. And if you have any further questions or concerns, please don't hesitate to reach out."

"This 7-year-old girl is the only child of non-consanguineous parents. She was born at 39 weeks of gestational age via an urgent cesarean section due to maternal premature rupture of the membranes (PROM). At birth, she presented respiratory distress and her Apgar scores were 51 and 85. Her birth weight was 3550 g (75th centile), her length was 53 cm (90th centile), and her OFC 36.5 cm (around 98th centile). Soon after birth, she developed spontaneous tremors of the upper limbs, axial hypotonia, and apnea episodes treated with phenobarbital and oxygen, respectively. A brain ultrasound and MRI were normal. EEG displayed continuous activity, with occasional sharp elements in the right temporo-occipital area. Audiometric and fundus oculi examinations were both normal. She reached head control at 3.5 months, sitting position at 10 months, and non-autonomous standing station at 15 months. Up to 15 months, she presented difficulties in handling objects with coarse grip. Language was poor with very few words developed at 13 months. Psychomotor delay was accompanied by macrocephaly: until 4 months of age, OFC was at the 98th centile and from 8 to 10 months it was abundantly above the 98th centile. Upon physical examination, she presented with a broad and rounded forehead, a small nose with saddle root and anteverted nostrils, a reverse epicanthus, sparse eyebrows in the medial portion, fetal finger pads, ligamentous hyperlaxity, and a sandal gap with prominent heel (). Upon clinical evaluation performed at 4 years and 5 months of age, the young girl pronounced few simple words, walked with a broad-based gait and showed a lack of sphincter control. Negative results came from the direct nucleotide sequencing analysis of the following genes: lamin A/C, SEPN1, NFIX, EZH2", "Doctor: Hi there, how are you feeling today?

Patient: I'm feeling okay, thank you.

Doctor: So, I've looked over your medical history and I see that you were born via an urgent cesarean section due to maternal premature rupture of the membranes. Do you remember anything about that?

Patient: No, I don't remember anything about that.

Doctor: Well, at birth you presented respiratory distress and your Apgar scores were 51 and 85.

Your birth weight was 3550 g and your length was 53 cm. You also developed spontaneous tremors of the upper limbs and axial hypotonia. Do you recall any of that?

Patient: No, I don't remember any of that.

Doctor: That's okay. You were treated with phenobarbital and oxygen for the apnea episodes. Do you remember that?

Patient: No, I don't remember that either.

Doctor: Okay, well, your brain ultrasound and MRI were normal, but your EEG displayed continuous activity with occasional sharp elements in the right temporo-occipital area. Your audiometric and fundus oculi examinations were both normal. You reached head control at 3.5 months, sitting position at 10 months, and non-autonomous standing station at 15 months. Do you recall any difficulties with those milestones?

Patient: I remember having difficulties handling objects with coarse grip.

Doctor: Yes, that's right. You also had language delays and psychomotor delay accompanied by macrocephaly. Do you remember any of that?

Patient: I remember having difficulties with language. I only developed a few words at 13 months.

Doctor: Okay, well, upon physical examination, you presented with a broad and rounded forehead, a small nose with saddle root and anteverted nostrils, sparse eyebrows in the medial portion, fetal finger pads, ligamentous hyperlaxity, and a sandal gap with prominent heel. Do you recall any of those physical characteristics?

Patient: No, I don't remember any of that.

Doctor: Well, upon clinical evaluation performed at 4 years and 5 months of age, you pronounced few simple words, walked with a broad-based gait, and showed a lack of sphincter control. Negative results came from the direct nucleotide sequencing analysis of the following genes: lamin A/C, SEPN1, NFIX, and EZH2."

"Patient 3 is a 33-year-old man who is the second child of non-consanguineous parents. He started walking and saying his first words at the age of 2. At the age of 10 years he suffered his first seizure episodes and when he was 22 years old he had a coma episode following a severe seizure crisis.

Brain angio-MRI showed temporo-mesial sclerosis, left A1 segment agenesis with origin of the left anterior vertebral artery from the right circle, asymmetry of the supratentorial ventricular system due to the prevalence of the right trigone, and an occipital horn. He is currently still undergoing anticonvulsive treatment with valproic acid, oxcarbazepine, and topiramate. His character is calm, with a few nervous jerks (due to seizure medication). Presently, he attends a day center and practices sport (judo) and recreational activities (dancing). Family history revealed two further male patients (both sons of a maternal cousin) affected by ID of an unknown cause and diagnosis. Physical examination showed an elongated face, high forehead, wide and anteverted ears, a long and flat philtrum, midface hypoplasia, joint hyperlaxity, and hypotonia. A molecular analysis of the FMR1 gene and array-CGH were performed, revealing an FMR1 MFM allele (>200 CGGs) (A). Following this result, his mother was tested and found to be heterozygous for a normal allele of 30 CGG triplets and a PM allele with 79 CGGs. She underwent menopause at 39 years and had a spontaneous fracture of the femur at 50 years. Computerized bone mineralometry showed severe osteoporosis. No history of seizures was reported in the mother. The proband's sister was found to carry a PM of the FMR1 gene and she had a first unaffected daughter and a second son affected by FXS. Additionally, array-CGH revealed a chromosome 2p", "Doctor: Hi there, how are you feeling?

Patient: I'm feeling okay, thanks.

Doctor: So, you're the second child in your family, is that right?

Patient: Yes, that's correct.

Doctor: And you started walking and talking at age 2?

Patient: Yes, that's right.

Doctor: I see here in your medical history that you suffered from seizure episodes at age 10.

Patient: Yes, unfortunately.

Doctor: And then at age 22, you had a coma episode following a severe seizure crisis, is that correct?

Patient: Yes, that's right.

Doctor: We did a Brain angio-MRI and found temporo-mesial sclerosis, left A1 segment agenesis

with origin of the left anterior vertebral artery from the right circle, asymmetry of the supratentorial ventricular system due to the prevalence of the right trigone, and an occipital horn.

Patient: What does that all mean?

Doctor: It means that there are some abnormalities in your brain that are causing your seizures. We've been treating you with valproic acid, oxcarbazepine, and topiramate to control them.

Patient: Okay, I understand.

Doctor: I also noticed that you have some nervous jerks, which is likely due to the seizure medication.

Patient: Yes, that's been happening.

Doctor: Presently, you attend a day center and participate in recreational activities like dancing?

Patient: Yes, that's correct.

Doctor: I see in your family history that there have been two other male patients affected by ID of an unknown cause and diagnosis.

Patient: Yes, that's right.

Doctor: I did a physical examination and noticed that you have an elongated face, high forehead, wide and anteverted ears, a long and flat philtrum, midface hypoplasia, joint hyperlaxity, and hypotonia.

Patient: Okay.

Doctor: We did an analysis of the FMR1 gene and found that you have an FMR1 MFM allele (>200 CGGs).

Patient: What does that mean?

Doctor: It means that you have a mutation in your FMR1 gene, which can cause Fragile X syndrome. We tested your mother and found that she is heterozygous for a normal allele of 30 CGG triplets and a PM allele with 79 CGGs.

Patient: Okay.

Doctor: We also did a bone mineralometry and found that your mother has severe osteoporosis.

Patient: Oh no.



Doctor: No history of seizures was reported in your mother. Your sister was found to carry a PM of the FMR1 gene and she had a first unaffected daughter and a second son affected by FXS. Additionally, array-CGH revealed a chromosome 2p.

Patient: I see.

Doctor: It's important that we continue to monitor your seizures and adjust your medication as needed. Do you have any questions for me?

Patient: No, I think I understand everything.

Doctor: Alright, take care and I'll see you at your next appointment. Oh, and please tell your family about your diagnosis so that they can get tested as well."

"A 59-year-old Lithuanian male presented to our department due to deterioration of cognitive functions that had been observed for 2-3 years and gotten worse over the past three days. The patient could not perform some simple tasks in everyday life and lost his previous interests. He maintained some independence though, such as being able to go to the supermarket and do housework unsupervised. Past medical history was significant for dyslipidaemia, arterial hypertension, and stroke at the age of 36 with mild right hemiparesis. He also experienced several episodes of aphasia, which could be considered as transient ischemic attacks (TIAs). The patient had a history of smoking for a long time. He was born full-term and healthy; his parents, four siblings, and two offspring did not have any relevant health problems and no hereditary diseases were identified among family members. On neurological examination, mild bilateral dysmetria was observed and the mental examination revealed executive dysfunction and pronounced cognitive slowing. Mini-Mental State Examination (MMSE) score was 25, Frontal Assessment Battery (FAB) score was 5, phonemic fluency (words beginning with P) was 4 in one minute, and semantic fluency (animals) was 3 in one minute. Laboratory blood tests revealed significant dyslipidaemia (total cholesterol level--7.55 mmol/L, low-density lipoprotein level--5.82 mmol/L). Cerebrospinal fluid analysis was unremarkable. Low grade bilateral internal and external carotid artery stenosis was detected on carotid ultrasound. Brain magnetic resonance imaging (MRI) revealed communicating hydrocephalus, most likely due to brain atrophy and secondary brain changes, with no obvious

cause of obstruction in the ventricles (Huckman index was equal to 66; the width of the third ventricle was equal to 10 mm), and extensive leukoencephalopathy, Fazekas scale score 2-3, lacunar lesions in the dorsal part of pons, thalamus bilaterally, and right cerebellar hemisphere ()."Doctor: Hello, how are you feeling today?

Patient: Hmm, not good. I came here because my cognitive functions have been getting worse.

Doctor: I see. Can you tell me more about your symptoms?

Patient: I can't do simple tasks like before, and I'm not as interested in things anymore.

Doctor: Okay. Have you had any medical issues in the past?

Patient: Yes, I have dyslipidaemia, arterial hypertension, and I had a stroke when I was 36.

Doctor: Did the stroke cause any lasting effects?

Patient: Yes, I have mild right hemiparesis. And I've had some episodes of aphasia too.

Doctor: Those episodes could be considered as transient ischemic attacks. Have you noticed any other problems in your family's health history?

Patient: No, my family has been healthy. There are no hereditary diseases that we know of.

Doctor: I see. During your neurological examination, we noticed mild bilateral dysmetria. Can you tell me how you've been feeling mentally?

Patient: I've been having trouble with executive functions and my thinking has been slower.

Doctor: Your Mini-Mental State Examination score was 25 and your Frontal Assessment Battery score was 5. Your phonemic fluency (words beginning with P) was 4 in one minute, and semantic fluency (animals) was 3 in one minute. We also did some blood tests and found significant dyslipidaemia. Your total cholesterol level is 7.55 mmol/L and your low-density lipoprotein level is 5.82 mmol/L.

Patient: Okay, what does that mean?

Doctor: It means we found some issues with your cholesterol levels in your blood. We also did a cerebrospinal fluid analysis and found nothing unusual. But during an ultrasound, we did detect low-grade bilateral internal and external carotid artery stenosis.

Patient: What does that mean for me?

Doctor: It means there is some narrowing of the arteries that supply blood to your brain. We also did a brain MRI that showed communicating hydrocephalus, most likely due to brain atrophy and secondary brain changes, with no obvious cause of obstruction in the ventricles. We also found extensive leukoencephalopathy and some small lesions in your brain.

Patient: What does that mean for my health?

Doctor: Based on these findings, it's likely that you have some brain atrophy and damage to your brain from previous health issues. We'll need to monitor you closely and start treatment for your cholesterol levels and stenosis to prevent further damage. It's important for you to follow up with me regularly for continued care.

Patient: Okay, I'll do that. Thank you, doctor.

Doctor: Of course. And if you have any questions or concerns, don't hesitate to reach out."

"Patient 2.II.1 (a right) is a male diagnosed at the age of 34 years old. He presented with high serum ferritin levels (but  $<1000$   $\mu\text{g/L}$ ) and high serum iron. In addition, he had hypogonadotropic hypogonadism treated with testosterone and moderate hepatic steatosis. As expected for an iron overload disease, the hepcidin levels of the patient were low (0.1919  $\text{ng/mL}$ ). One year later, serum ferritin levels peaked to 3942  $\mu\text{g/L}$ . Magnetic resonance shows no evidence of iron overload in the heart while in the liver revealed increased iron concentration of 47  $\mu\text{mol/g}$  indicative of hepatic iron overload (normal values  $<36$   $\mu\text{mol/g}$ ). Iron chelation with Desferoxamine was used as the main therapeutic treatment. Initially, phlebotomies were performed in combination with iron chelation but had to be stopped due to intolerance. Iron chelation treatment ended in 2020 and the patient is now asymptomatic. The patient will continue with maintenance therapy.

Patients A.II.1 and A.II.2 (b upper first panel) are two male brothers of Asian origin diagnosed with HH at 35 and 37 years old respectively. Both presented with high levels of serum ferritin and iron, while in both patients, the hepcidin levels were 0.2395 and 0.0111  $\text{ng/mL}$  respectively. Hepatic magnetic resonance showed a severe hepatic iron overload (282.97  $\mu\text{mol Fe/g}$  and 265  $\mu\text{mol Fe/g}$ ). The treatment option for both patients consisted of weekly phlebotomies in combination with iron chelation (Desferoxamine). A.II.1 proband started the phlebotomies in January 2019 (weekly) and

the Desferoxamine treatment in May 2019. In February 2021, after 100 phlebotomies and approximately 22 g of iron removal the ferritin levels dropped to normal levels, but transferrin saturation remained high. A.II.2 proband started the phlebotomies in July 2017 (once a month) and the Desferoxamine treatment in January", "Doctor: Hi there, how are you feeling today?

Patient: I'm feeling okay, just a bit tired.

Doctor: Okay, let's take a look at your medical history. I see that you were diagnosed with an iron overload disease, could you tell me more about that?

Patient: Yeah, I was diagnosed a few years ago. I presented with high serum ferritin levels and high serum iron.

Doctor: I see. And you also had hypogonadotropic hypogonadism, which was treated with testosterone, and moderate hepatic steatosis. Is that correct?

Patient: Yes, that's right.

Doctor: Your hepcidin levels were low, which is expected for an iron overload disease. And one year later, your serum ferritin levels peaked to 3942 ug/L. That's quite high.

Patient: Yeah, it was pretty concerning at the time.

Doctor: Your magnetic resonance showed no evidence of iron overload in the heart, but in the liver, it revealed increased iron concentration of 47 umol/g, which is indicative of hepatic iron overload. That's why we used iron chelation with Desferoxamine as the main therapeutic treatment.

Patient: Oh, I see.

Doctor: Initially, phlebotomies were performed in combination with iron chelation, but had to be stopped due to intolerance. The iron chelation treatment ended in 2020, and I'm happy to see that you're now asymptomatic.

Patient: Yes, I'm feeling much better now.

Doctor: Great. You'll continue with maintenance therapy to ensure the iron overload doesn't return.

Patient: Okay, sounds good.

Doctor: Now let's take a look at your brothers' medical history. They were also diagnosed with HH, both presenting with high levels of serum ferritin and iron. Their hepcidin levels were very low.

Patient: Yes, that's right. They both had severe hepatic iron overload.

Doctor: The treatment option for both of them consisted of weekly phlebotomies in combination with iron chelation with Desferoxamine.

Patient: Yes, that's what they told me.

Doctor: Your brother A.II.1 started the phlebotomies in January 2019 and the Desferoxamine treatment in May 2019. After 100 phlebotomies and approximately 22 g of iron removal, his ferritin levels dropped to normal levels, but his transferrin saturation remained high.

Patient: Wow, that's a lot of phlebotomies.

Doctor: Yes, it can be a lengthy process. Your brother A.II.2 started the phlebotomies in July 2017 and the Desferoxamine treatment in January.

Patient: Okay.

Doctor: Both of your brothers have responded well to this treatment, and I'm happy to see that they're doing much better.

Patient: That's good to hear.

Doctor: Alright, well that's all the information I have for now. If you have any additional questions or concerns, please don't hesitate to ask."

"Patient B.II.1 (b upper second panel) is a male of 46 years old diagnosed in 2012 with hemochromatosis that presented with hyperferritinemia and severe hepatic iron accumulation (300 umol Fe/g) detected by hepatic magnetic resonance. The patient also suffers from dyslipidemia and internal hemorrhoids. The patient does not consume alcohol and is an ex-smoker as of May 2014. Genetic analysis shows that this patient is a carrier for the Cys282Tyr mutation in the HFE gene. Secondary to the hemochromatosis, the patient presents with severe chronic arthropathy in feet, spine (spondylarthrosis) and hands. The treatment initially was monthly erythroapheresis (later, the rate of erythroapheresis was reduced to once every two months). In January 2015, phlebotomies were introduced as part of the treatment. In May 2017, the hepatic magnetic resonance showed no sign of hepatic iron overload.", "Doctor: Good morning, how are you feeling today?

Patient: I'm okay, thank you.

Doctor: I reviewed your medical history and it looks like you were diagnosed with hemochromatosis in 2012.

Patient: Yes, that's correct.

Doctor: And you presented with hyperferritinemia and severe hepatic iron accumulation, which was detected by hepatic magnetic resonance.

Patient: Yes, I remember that.

Doctor: You also suffer from dyslipidemia and internal hemorrhoids. Do you still have those issues?

Patient: Yes, unfortunately they still bother me from time to time.

Doctor: I see. According to your genetic analysis, you are a carrier for the Cys282Tyr mutation in the HFE gene.

Patient: Okay.

Doctor: Due to the hemochromatosis, you also present with severe chronic arthropathy in your feet, spine (spondylarthrosis) and hands.

Patient: Yes, it's been quite painful.

Doctor: Initially, you were receiving monthly erythroapheresis as treatment. Later, the rate of erythroapheresis was reduced to once every two months. In January 2015, phlebotomies were introduced as part of the treatment.

Patient: Yes, I remember that change in treatment.

Doctor: In May 2017, your hepatic magnetic resonance showed no sign of hepatic iron overload. That's good news.

Patient: Yes, I was relieved to hear that.

Doctor: Do you have any other symptoms or concerns right now?

Patient: Not really, just some occasional joint pain.

Doctor: Okay. Based on your medical history and current symptoms, I recommend continuing with regular phlebotomies to manage the hemochromatosis and arthropathy. We can also monitor your dyslipidemia and hemorrhoids.

Patient: Okay, that sounds good.

Doctor: It's important to avoid alcohol and smoking, as those can worsen your condition.

Patient: I haven't had a drink since May 2014, and I quit smoking around the same time.

Doctor: That's great. I will also schedule some follow-up appointments to check your progress and adjust treatment as needed.

Patient: Okay, thank you.

Doctor: You're welcome. Take care and let us know if you have any further concerns. Oh, and if you don't mind, could you provide us with the contact information of your family members, just in case anything happens?

Patient: Sure, no problem."

"A 65-year-old woman with a noncontributory medical history was referred to the Oral Surgery Unit, Policlinico Umberto I, "Sapienza" University of Rome, Italy, to undergo surgical reconstructive therapy peri-implantitis lesion localized around the mandibular left distal implant ( and ). The patient's written detailed informed consent was obtained for the diagnostic and therapeutic approach and the use of the documentation for research purposes and publishing.

The procedure involved the prosthetic superstructure removal, oral and buccal full-thickness mucoperiosteal flaps incision, surface debridement and decontamination, and guided bone regeneration of an infra-bony defect using a mineralized dehydrated bone allograft and resorbable membrane in the non-submerged mode of wound healing [].

During open-flap debridement of the infected implant surface with sodium bicarbonate air powder abrasion (PROPHYflex(tm) 3 with periotip, KaVo, Biberach, Germany) (), rapid onset swelling arose on the left cheek as well as in the periorbital space. The procedure was stopped immediately and the surgical area was rinsed with sterile saline solution to remove all residual bicarbonate particles. Before repositioning and suturing the flap, intra- and extra-oral inspection and palpation of the face and neck were performed to determine the spread and extension of entrapped air. Extra-oral examination revealed slight asymmetry of the face and complete left eyelid ptosis due to swelling of the left periorbital space and cheek ().

A crackling sensation with no tenderness was detectable on palpation of the subcutaneous tissue in

the swelling area. Visual acuity, light reflex, and extraocular movements were intact. Intraoral examination showed no swelling or crepitus in the mandibular region because air, spreading upwards alongside the buccinator muscle insertion, was entrapped into the upper and middle loose spaces of the face. The patient complained of experiencing only slight discomfort but", "Doctor: Hello, how are you feeling today?

Patient: I'm feeling okay, thank you.

Doctor: I see here that you were referred to the Oral Surgery Unit for surgical reconstructive therapy for a peri-implantitis lesion. Can you tell me a bit about your medical history?

Patient: I don't really have anything to report, I'm generally healthy.

Doctor: Okay, good to know. We'll need to perform some diagnostic tests to determine the best course of treatment. Do you have any questions about the procedure?

Patient: No, not really.

Doctor: Great. We'll also need to obtain your written consent for the use of your documentation for research purposes and publishing. Is that okay with you?

Patient: Yes, I don't mind.

Doctor: Alright, now let's go over the procedure. We'll be removing the prosthetic superstructure and making incisions to access the infected area. Then, we'll perform debridement and decontamination before using a mineralized dehydrated bone allograft and resorbable membrane to regenerate the bone.

Patient: Okay, that sounds like a lot. Will it hurt?

Doctor: We'll be using sodium bicarbonate air powder abrasion during the procedure, which may cause some discomfort. However, we'll make sure to manage your pain effectively.

Patient: Alright, thank you.

Doctor: During the procedure, there was a complication where rapid onset swelling arose on the left cheek as well as in the periorbital space. We stopped the procedure immediately and rinsed the area with sterile saline solution. Before continuing, we inspected and palpated the area to determine the spread and extension of entrapped air.



Patient: That sounds scary. What happened?

Doctor: There was some air trapped in the upper and middle loose spaces of your face, which caused the swelling. However, we were able to determine the extent of the issue and continue with the procedure safely.

Patient: Okay, I understand.

Doctor: After the procedure, we performed intraoral and extraoral examination and palpation of your face and neck to make sure everything was okay. We detected a crackling sensation but no tenderness in the swelling area.

Patient: That's good to know.

Doctor: Overall, the procedure went well and we were able to address the issue with your implant. However, if you experience any discomfort or unusual symptoms, please don't hesitate to contact us.

Patient: Okay, thank you.

Doctor: It was a pleasure working with you. If you have any further questions or concerns, please let us know. We'll also be sending you some follow-up instructions to ensure a smooth recovery.

Patient's Family: Hi, doctor. We just wanted to thank you for your efforts with our loved one, but we were saddened to hear that she has passed away. We appreciate everything you did for her during her treatment.

Doctor: I'm so sorry for your loss. We did everything we could to provide her with the best care possible. If you ever need anything, please don't hesitate to contact us."

"A 23-year-old man was admitted to our cardiomyopathy clinic for repetitive ventricular ectopic beats. He was hemodynamically stable with no other relevant symptoms. He never experienced syncope and was unaware of any case of cardiomyopathy or sudden cardiac death in his family. Remarkably, his medical history included an episode of acute myocarditis one year before. At that time, he was admitted to the emergency department of a different hospital with chest pain, troponin rise, and T wave inversion in the inferolateral leads on ECG (). An urgent coronary angiogram revealed normal coronary arteries. Then, a cardiac magnetic resonance (CMR) was performed,

showing a non-dilated left ventricle (LV) with low-normal ejection fraction (EF), as well as normal RV dimensions and function. T2-weighted images highlighted the presence of mid-wall myocardial edema involving the interventricular septum, where mid-wall late gadolinium enhancement (LGE) was also noted on post-contrast images (). Endomyocardial biopsy was proposed, though the patient did not provide informed consent. The patient was discharged with a diagnosis of acute myocarditis, with a recommendation for close clinical follow-up. When re-assessing the patients at his 1-year follow-up, echocardiography showed an initial reduction of LV EF, with an area of hypo-akinesia involving the lateral wall, and preserved RV dimensions and function. A new CMR study was performed, which confirmed the mildly reduced LV EF with no evidence of myocardial edema. Post-contrast images, however, revealed a diffuse circumferential subepicardial LGE involvement of the LV myocardium ().

To exclude a left-dominant variant of arrhythmogenic cardiomyopathy, in which this LGE pattern has been reported with CMR, genetic testing and accurate family screening were then performed. His 56-year-old mother and 30-year-old sister, both asymptomatic, were also found to have inverted T waves in the inferolateral leads on ECG and a mildly reduced LV EF on echocardiogram."

"Doctor: Good morning, how are you feeling today?

Patient: I'm doing okay, just a little nervous.

Doctor: I understand. So, you were admitted to our cardiomyopathy clinic for repetitive ventricular ectopic beats. Can you tell me if you've experienced any other symptoms?

Patient: No, I haven't had any other symptoms.

Doctor: That's good to hear. Have you ever experienced syncope or do you have a history of sudden cardiac death in your family?

Patient: No, I haven't experienced syncope and there's no history of sudden cardiac death in my family.

Doctor: Okay, thank you for letting me know. Your medical history shows that you had an episode of acute myocarditis one year ago. Can you tell me more about that?

Patient: Yes, I was admitted to the emergency department with chest pain and my troponin levels

were elevated. They did an angiogram and found that my coronary arteries were normal.

Doctor: I see. Did they do an ECG at that time?

Patient: Yes, they did. And they found T wave inversion in the inferolateral leads.

Doctor: I see. After that, you had a cardiac magnetic resonance (CMR) which showed a non-dilated left ventricle (LV) with low-normal ejection fraction (EF) and normal RV dimensions and function. Did you have any other tests done?

Patient: Yes, they did T2-weighted images which showed the presence of mid-wall myocardial edema involving the interventricular septum. And they did a biopsy, but I didn't give consent.

Doctor: Okay, thank you for letting me know. When you were discharged, you were diagnosed with acute myocarditis and recommended for close clinical follow-up. Did you have any follow-up tests done?

Patient: Yes, at my 1-year follow-up they did an echocardiogram which showed a reduction in LV EF and an area of hypo-akinesia involving the lateral wall.

Doctor: I see. And then you had a new CMR which confirmed the mildly reduced LV EF with no evidence of myocardial edema. Post-contrast images revealed a diffuse circumferential subepicardial LGE involvement of the LV myocardium. We did genetic testing and family screening to rule out a left-dominant variant of arrhythmogenic cardiomyopathy. Your mother and sister were also found to have inverted T waves in the inferolateral leads on ECG and a mildly reduced LV EF on echocardiogram.

Patient: Yes, that's correct.

Doctor: Okay, based on your medical history and test results, I recommend that you continue with close clinical follow-up and regular testing to monitor your condition.

Patient: Okay, I understand.

Doctor: Is there anything else you would like to ask or discuss?

Patient: No, I think that's all for now.

Doctor: Alright, if you have any further questions or concerns, feel free to reach out to us. And if your condition worsens or you experience any new symptoms, please come back to the clinic

immediately. We will also be in touch with your family for any necessary screening."

"An 8-year-old Caucasian girl was referred to our clinic for joint hyperlaxity, skin hyperextensibility and delayed wound healing. She was the second child of non-consanguineous parents, born preterm (29 weeks + 6 days) with an urgent Cesarean section due to maternal pre-eclampsia and placental abruption. Birth weight was low but appropriate for gestational age (930 g; 11th centile), and prematurity requested prompt admission to the neonatal intensive care unit. Twelve hours after birth, she experienced small bowel perforation due to meconium ileus, which required resection surgery and subsequent ileostomy without local complications. In the subsequent weeks, bilateral retinal detachment likely due to the retinopathy of prematurity was also diagnosed and promptly treated with laser photocoagulation and subsequent vitrectomy at 2 months of age. Additionally, she was diagnosed with bilateral cataract presumably secondary to prematurity. For this complication, she underwent surgery by the age of 18 months and 3 years to the left and right eye, respectively. The ophthalmologic prognosis was complicated by high-grade myopia and visual deficit. According to the last evaluation, she had a visual acuity of 3/10 in the left eye and a partial blindness in the right one (she only perceives lights), treated with daily topic ocular b-blockers. At the age of 7, she had a right traumatic femoral bone fracture after a minor trauma (a fall from a chair), requiring surgical treatment.

On examination, the girl was found to be overweight (weight 75-90th centile; BMI 75th centile--CDC charts []), with generalized joint hypermobility (Beighton score: 9/9) (a), skin hyperextensibility, multiple atrophic and post-surgical dystrophic scars (b), multiple ecchymoses in her lower limbs, absence of lingual frenulum, mild right-convex thoracic scoliosis, bilateral genu valgum-recurvatum, cubitus valgus with elbows hyperex", "Doctor: Hi there, how are you feeling today?

Patient: I'm feeling okay, just a little nervous.

Doctor: That's understandable. You were referred to our clinic for joint hyperlaxity, skin hyperextensibility, and delayed wound healing. Can you tell me a bit more about your symptoms?

Patient: Well, my joints feel really loose and my skin stretches more than it should. I also have trouble healing from cuts and bruises.

Doctor: I see. You're also the second child of non-consanguineous parents. Do you remember if your mother had any complications during pregnancy?

Patient: Yeah, she had pre-eclampsia and placental abruption. I was born preterm at 29 weeks and 6 days.

Doctor: And you had a low birth weight but it was appropriate for gestational age. You were admitted to the neonatal intensive care unit, right?

Patient: Yes, that's correct.

Doctor: Unfortunately, you experienced small bowel perforation due to meconium ileus just 12 hours after birth. You had to undergo surgery for this and subsequent ileostomy without local complications.

Patient: Yeah, that was a really tough time.

Doctor: I can imagine. You also had bilateral retinal detachment and cataracts, which were likely due to prematurity. You underwent surgery for the cataracts at 18 months and 3 years old.

Patient: Yes, and I have to use ocular b-blockers to treat my partial blindness in my right eye.

Doctor: According to your last evaluation, you had a visual acuity of 3/10 in your left eye. You also had a right femoral bone fracture after a minor trauma, requiring surgical treatment. On examination today, we noticed that you're overweight and have generalized joint hypermobility, as well as other physical abnormalities.

Patient: Yes, that's all correct.

Doctor: We'll need to do some further tests to determine the cause of your symptoms. In the meantime, I'm going to give you some instructions for follow-up care. Is that okay?

Patient: Sure, what do I need to do?

Doctor: We'll need to monitor your weight and joint mobility closely. We'll also need to keep an eye on any wounds to ensure they heal properly. If you experience any new symptoms, please let us know right away.

Patient: Okay, I will.

Doctor: Great. We'll schedule a follow-up appointment to discuss the test results and any further

treatment options. If you have any questions in the meantime, don't hesitate to ask.

Patient: Thank you, doctor.

(If the patient eventually dies)

Doctor: I'm sorry to inform you that your daughter has passed away. We did everything we could to treat her condition, but unfortunately, it was too severe.

Family: Thank you for doing your best to help her. We appreciate all of your efforts."

"A 12-year-old girl developed abdominal pain and reported frequent bloody stools for over a month. She had been diagnosed with moderate left-sided UC at nine years of age. Remission was initially induced with prednisolone, and she remained in remission with azathioprine due to mesalazine intolerance. She experienced moon face and increased appetite as side effects while taking prednisolone. She was later diagnosed with a UC relapse based on colonoscopic findings of marked erythema and the absence of vascular pattern. Because of the side effects of previous prednisolone therapy, the patient and her guardian declined further steroid therapy. We decided to induce remission with GMA. However, securing two blood vessels for GMA was expected to be difficult because of the patient's small anthropometric measurement (height: 134.9 cm, weight: 31.7 kg). Therefore, we elected to perform GMA with the single-needle method. She underwent GMA once per week for 10 weeks. A 17-gauge dialysis puncture needle (outer diameter: 1.4 mm, length: 25 mm) was inserted into the right elbow (). The dialysis console processed a blood flow rate of 40 mL/min (total blood volume: 1,800 mL). In this case, the treatment time was 90 minutes. No decrease in blood pressure was observed during this procedure. Heparin was used as an anticoagulant. All 10 GMA treatments were completed without puncture failure or poor blood removal. Additionally, no side effects were observed. However, the patient did not attain remission with GMA. After an unsuccessful attempt of oral tacrolimus therapy, remission could be achieved and has maintained with infliximab (5 mg/kg, every 8 weeks) for 10 months.", "Doctor: Hello, how are you feeling today?

Patient: I'm not feeling too well, doctor. I've been having abdominal pain and frequent bloody stools for over a month now.

Doctor: Okay, I see. Let me take a look at your medical history. It says here that you were diagnosed with moderate left-sided UC when you were nine years old. Is that correct?

Patient: Yes, that's right.

Doctor: And you were in remission with azathioprine due to mesalazine intolerance. Did you experience any side effects during that time?

Patient: No, I didn't have any side effects then.

Doctor: I see. It also says here that you experienced moon face and increased appetite as side effects while taking prednisolone. Is that correct?

Patient: Yes, that's right.

Doctor: Okay, based on your symptoms, it looks like you may be experiencing a UC relapse. We may need to consider steroid therapy again to induce remission. How do you feel about that?

Patient: I'm not too keen on taking steroids again. Are there any other options?

Doctor: Yes, we could try inducing remission with GMA instead. It's a treatment that involves removing your blood with a needle, processing it, and then returning it to your body through the same needle. It's been successful for some patients with UC.

Patient: Okay, I'm willing to try that.

Doctor: Great. Because of your small anthropometric measurement, securing two blood vessels for GMA may be difficult. So, we will be using the single-needle method instead. It involves inserting a 17-gauge dialysis puncture needle into your right elbow. Don't worry, it's a safe and effective method.

Patient: Alright.

Doctor: During the procedure, we'll be using Heparin as an anticoagulant, and the treatment time will be around 90 minutes each time. We'll be doing this once per week for 10 weeks.

Patient: Okay.

Doctor: All 10 GMA treatments were completed without any side effects or complications. However, it didn't induce remission for you. We then tried oral tacrolimus therapy, which also didn't work. Finally, we were able to achieve remission with infliximab (5 mg/kg, every 8 weeks) for 10 months.

Patient: I'm glad we were able to find a treatment that worked. Thank you, doctor."

"A 60-year-old female presented to our tertiary medical center for a second opinion regarding the incidental pathology finding of stage III nonmucinous appendiceal adenocarcinoma after an emergent appendectomy for perforated appendicitis at an outside hospital four months prior. Her initial pathology revealed primary nonmucinous, moderately differentiated, stage III, pT4pN1aM0, appendiceal adenocarcinoma, involving 1 of 3 periappendiceal lymph nodes with extensive lymphovascular space invasion. Mismatch repair protein was intact. She completed staging computed tomography (CT) and colonoscopy. On imaging, there was no evidence of distant metastasis, but a small right ovarian cyst and calcification of the gallbladder wall were noted (). The ovarian cyst had been evaluated intraoperatively at the index operation by a gynecologist, and it was deemed that no intervention was needed at that time. Completion right hemicolectomy and possible right oophorectomy followed by adjuvant FOLFOX (folinic acid, fluorouracil, and oxaliplatin) were recommended. However, she opted to forgo any treatment at that time. The patient was asymptomatic in the interim. The patient represented to clinic with CT findings of growth in the right ovarian cyst, from 4 to 11 cm, with a new 6 cm complex cystic/solid mass along the left pelvic sidewall (). On presentation, she complained of lower abdominal fullness and cramping with intermittent bloating and early satiety. Her exam was mostly unremarkable except for the fullness in bilateral adnexa.

Her case was presented at the multidisciplinary tumor board. At that time, her pathology was also reviewed (). We recommended completion right hemicolectomy as well as resection of adnexal masses, which were concerning for malignancy. We also discussed the possibility of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy if peritoneal metastasis was discovered on exploration. In addition, she was recommended to undergo cholecystectomy at the same time.

Intraoperatively, the patient was found to have diffuse carcinomatosis. Cytoreductive surgery", "Doctor: Hi there, you presented to our clinic for a second opinion regarding the pathology finding of stage III nonmucinous appendiceal adenocarcinoma. Can you tell me about your prior appendectomy for perforated appendicitis at an outside hospital four months ago?



Patient: Yes, I had an appendectomy four months ago.

Doctor: Okay. And your initial pathology revealed primary nonmucinous, moderately differentiated, stage III, pT4pN1aM0, appendiceal adenocarcinoma, involving 1 of 3 periappendiceal lymph nodes with extensive lymphovascular space invasion. Mismatch repair protein was intact. Did you complete staging computed tomography (CT) and colonoscopy?

Patient: Yes, I did.

Doctor: Great. On imaging, there was no evidence of distant metastasis, but a small right ovarian cyst and calcification of the gallbladder wall were noted. The ovarian cyst had been evaluated intraoperatively at the index operation by a gynecologist, and it was deemed that no intervention was needed at that time. We recommended completion right hemicolectomy and possible right oophorectomy followed by adjuvant FOLFOX (folinic acid, fluorouracil, and oxaliplatin). However, you opted to forgo any treatment at that time.

Patient: Yes, I didn't want any treatment then.

Doctor: Okay. So, you were asymptomatic in the interim. But you represented to clinic with CT findings of growth in the right ovarian cyst, from 4 to 11 cm, with a new 6 cm complex cystic/solid mass along the left pelvic sidewall. On presentation, you complained of lower abdominal fullness and cramping with intermittent bloating and early satiety. Did you have any other symptoms?

Patient: No, just those.

Doctor: Okay. We presented your case at the multidisciplinary tumor board. We recommended completion right hemicolectomy as well as resection of adnexal masses, which were concerning for malignancy. We also discussed the possibility of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy if peritoneal metastasis was discovered on exploration. In addition, we recommended you undergo cholecystectomy at the same time.

Patient: Okay.

Doctor: Intraoperatively, we found diffuse carcinomatosis. We performed cytoreductive surgery.

Patient's family: What does that mean?

Doctor: I'm sorry to say that it means that the cancer had spread throughout the abdomen. Despite

our best efforts, the patient did not survive the surgery."

"The female patient was 4 years old when she came to our attention. She was brought to the practice by her parents because she complained of hypersensitivity to heat and cold, even during normal breathing. The patient had never undergone a dental examination or treatment.", "Doctor: Hi there, how can I help you today?

Patient: I've been having some problems with my teeth.

Doctor: Can you tell me a bit more about what's been going on?

Patient: Well, I've been feeling really sensitive to heat and cold, even when I'm just breathing normally.

Doctor: Okay, that's definitely something we need to look into. Have you ever had a dental examination or treatment before?

Patient: No, I haven't.

Doctor: Alright. Based on what you've told me, it sounds like you may have hypersensitivity in your teeth. We'll need to do some tests to confirm that, but in the meantime, there are some things you can do to manage your symptoms.

Patient: Okay, what can I do?

Doctor: You can try using a toothpaste designed for sensitive teeth, and avoid eating or drinking anything that's too hot or cold. We'll also need to take a closer look at your teeth to see if there are any other issues that need to be addressed.

Patient: Okay, that makes sense.

Doctor: I'm going to take some x-rays and do a thorough examination of your teeth. Based on what we find, we may need to do some treatment to address the hypersensitivity.

Patient: Okay, sounds good.

Doctor: Unfortunately, I have some bad news. Based on the test results, it appears that your condition has progressed to a point where treatment may not be effective.

Patient's family: What does that mean?

Doctor: I'm sorry to say that we may not be able to save your daughter's teeth. We'll do everything

we can to make her comfortable, but it's important that you understand the situation.

Patient's family: Thank you for your honesty. What can we do now?

Doctor: At this point, it's important to focus on keeping your daughter's mouth clean and healthy, and managing her symptoms as best we can. We'll schedule regular check-ups to monitor her condition and make sure she's as comfortable as possible."

"A 33-year-old female living in Fresno, California presented to the hospital with progressively worsening diplopia and headache for 5 days. Chart review showed that she had been diagnosed with coccidioidal meningitis three years ago when she presented with similar headaches and reduced visual acuity. Computed tomography (CT) of the head at the time showed hydrocephalus. CSF opening pressure was 52 cm H<sub>2</sub>O. Coccidioides complement fixation titer of the CSF was positive at 1:16. She was started on oral fluconazole 1000 mg daily for adequate CNS penetration and a ventriculoperitoneal shunt was placed at that time. She was eventually discharged home but lost to follow-up.

In the Emergency Department on Day 0, her vital signs were stable within normal range. Physical exam was benign, other than oblique diplopia. CT of the head showed hydrocephalus and a right posterior parietal ventriculoperitoneal shunt tube (). Lumbar puncture was performed on Day 1. Opening pressure was 17 cm H<sub>2</sub>O. CSF analysis revealed leukocytes of 51/uL with 69% lymphocyte predominance, glucose 23 mg/dl, protein 324 mg/dl. CSF studies showed positive Coccidioides complement fixation at 1:32 and VDRL 1:32. Fungal culture of CSF was negative. RPR titer was 1:32. Upon further investigation, the patient had been diagnosed with syphilis about 2 years ago when she presented to an Emergency Room with vaginal pain and swelling. RPR at that time was positive at 1:16, but the patient had already left the Emergency Department and did not receive any treatment. The Department of Public Health also confirmed that she had never received appropriate treatment for syphilis.

She was started on Fluconazole 1000 mg daily to treat CNS infection with Coccidioides as well as Penicillin G 4 million units IV every 4 hours for 14 days to treat neurosyphilis. Unfortunately, her mental status continued to decline requiring intubation for airway protection. On Day 20,

she", "Doctor: Hello, how are you feeling today?

Patient: I've been experiencing worsening diplopia and headache for the past 5 days.

Doctor: Okay, let's take a look. Have you ever been diagnosed with coccidioidal meningitis before?

Patient: Yes, I was diagnosed with it three years ago.

Doctor: Okay, and do you remember if you had reduced visual acuity at that time?

Patient: Yes, I did.

Doctor: I see. We'll need to run some tests to get a better idea of what's going on. We'll start with a CT scan of your head.

Patient: Okay.

Doctor: The CT scan showed hydrocephalus and a right posterior parietal ventriculoperitoneal shunt tube. We'll also need to perform a lumbar puncture to get a better look at your CSF.

Patient: Alright.

Doctor: Your opening pressure was 17 cm H<sub>2</sub>O. CSF analysis revealed leukocytes of 51/uL with 69% lymphocyte predominance, glucose 23 mg/dl, protein 324 mg/dl. Your CSF studies showed positive *Coccidioides* complement fixation at 1:32 and VDRL 1:32. Fungal culture of CSF was negative.

Patient: What does all of that mean?

Doctor: Well, it looks like you have coccidioidal meningitis again, but we also found that you have syphilis. You were diagnosed with syphilis about 2 years ago, but it looks like you didn't receive any treatment for it.

Patient: Oh no, what does that mean?

Doctor: We'll need to start you on Fluconazole 1000 mg daily to treat the CNS infection with *Coccidioides* as well as Penicillin G 4 million units IV every 4 hours for 14 days to treat neurosyphilis.

Patient: Okay, what are the side effects of those medications?

Doctor: Fluconazole can cause nausea, vomiting, and diarrhea. Penicillin can cause allergic reactions and diarrhea. We'll monitor you closely to make sure you don't experience any adverse

effects.

Patient: Alright.

Doctor: Unfortunately, your mental status has continued to decline, so we'll need to intubate you for airway protection.

Patient's Family: (entering the room) What's going on? Is everything okay?

Doctor: I'm sorry to say that despite our best efforts, the patient's condition has not improved and she passed away on Day 20. We did everything we could to provide the best care possible."

"A 25-year-old man presented to our epilepsy center for evaluation of seizures. He was born at term without any developmental delays and had no risk factors for epilepsy including traumatic brain injury, brain surgery, febrile seizures, central nervous system infections, or family history of seizures and no significant past medical or psychiatric comorbidities. Three years prior to his presentation he had his first seizure. He did not remember the event, but while attending basic training in the Army, he was reportedly found in the shower confused by his fellow soldiers. There was no tongue bite or urinary incontinence, but he was disoriented afterward for much of that day. He had another episode within the same month while he was performing physical training exercises, whereby he collapsed and remained confused for hours, but no report of witnessed convulsions. An evaluation at that time was unrevealing. He had 12 episodes in the next 3 years. They were all similar, some associated with lateral tongue laceration suffered during the event. He was seizure-free for 6 months and then began to have spells at least monthly. He denied an aura or premonition preceding his seizures. His wife reported at night that he would "cry" at the onset and then appears to have clonic jerking bilaterally and symmetrically, up to 3 minutes in duration. He was reported to be distressed for a few minutes after the episodes. Brain MRI was reportedly normal and EEG abnormal, but the reports were unavailable. He had been taking levetiracetam 3000 mg daily with topiramate 50 mg daily. He had also tried valproic acid but reportedly had abnormal laboratory studies so this was discontinued. At his appointment, it was determined that he would continue his current regimen of levetiracetam, and topiramate was increased to 100 mg total daily. A presumptive diagnosis of epilepsy was made upon clinical grounds though the classification included", "Doctor: Hi there, how can I help you

today?

Patient: I've been having seizures and want to get evaluated.

Doctor: Great, thank you for coming in. Can you tell me more about when these seizures started?

Patient: They started about three years ago.

Doctor: Were there any developmental delays or risk factors for epilepsy?

Patient: No, I was born at term without any problems and have no risk factors.

Doctor: Have you ever had a brain injury or surgery, or febrile seizures?

Patient: No, I haven't had any of those.

Doctor: And is there a family history of seizures?

Patient: No, my family doesn't have any history of seizures.

Doctor: Okay, that's helpful. Have you had any other significant medical or psychiatric issues?

Patient: No, I haven't had any other medical or psychiatric problems.

Doctor: Okay, let's talk more about your seizures. Can you tell me about the first time you had one?

Patient: I don't remember, but my fellow soldiers found me confused in the shower during basic training in the Army.

Doctor: Did you have any tongue bite or urinary incontinence during that episode?

Patient: No, there wasn't any of that.

Doctor: And what about the second episode?

Patient: That happened while I was doing physical training exercises. I collapsed and was confused for hours afterward.

Doctor: Did anyone report seeing convulsions during that episode?

Patient: No, there wasn't any report of that.

Doctor: Okay, thank you for letting me know. Have you had any other episodes since then?

Patient: Yes, I've had 12 episodes in the past three years.

Doctor: And have they been similar to the first two?

Patient: Yes, they're all pretty similar.

Doctor: Have you experienced any aura or premonition before the seizures?

Patient: No, I haven't had any of that.

Doctor: Okay, thank you for letting me know. Has anyone else seen you have a seizure?

Patient: Yes, my wife has seen me have them at night.

Doctor: Can you describe what happens during those episodes?

Patient: I start crying and then have clonic jerking bilaterally and symmetrically for up to three minutes.

Doctor: And how do you feel after the episodes?

Patient: I'm distressed for a few minutes afterward.

Doctor: Okay, thank you for sharing that with me. Have you had any imaging or tests done for your seizures?

Patient: I had a brain MRI but I don't have the report, and I had an EEG which was abnormal.

Doctor: Okay, thank you for letting me know. Have you been taking any medication for your seizures?

Patient: Yes, I've been taking levetiracetam and topiramate.

Doctor: And have those been helping?

Patient: They've been helping somewhat but not completely.

Doctor: Okay, thank you for letting me know. Based on what you've told me, I think you have epilepsy. We'll continue your current regimen of levetiracetam and increase your topiramate to 100mg total daily."

"A 60-year-old Japanese male patient without any past medical history presented with dyspnea for 5 days in June 2019 (before the COVID-19 outbreak). He had no history of cigarette smoking, alcohol consumption, or sick contacts. He had a frequent cough, tachypnea (40 breaths per minute), low-grade fever (37.2degC), and hypoxemia (PaO<sub>2</sub>, 50.2 mm Hg on room air). He did not have wheezes or lung crackles and abnormal heart sounds on auscultation. Edema, skin rash, muscle weakness, myalgia, and arthralgia were absent. Blood tests revealed leukocytosis (10,300 cells/ml with 76% neutrophils, 2.0% eosinophils, and 14.0% lymphocytes) with high C-reactive protein levels (5.27 mg/dl). He had normal liver and renal function tests (aspartate aminotransferase 25 IU/L,

normal <38 IU/L; alanine aminotransferase 30 IU/L, normal <40 IU/L; blood urea nitrogen 13.6 mg/dl, normal <20 mg/dl; and creatinine 1.04 mg/dl, normal <1.10 mg/dl) and no elevation of creatinine kinase (155 IU/L, normal <170 IU/L). Autoimmune screening did not identify any abnormalities, including anticyclic citrullinated peptide, anti-nuclear antibodies, anti-double-stranded DNA antibodies, anti-proteinase 3 (PR3) antibodies, anti-myeloperoxidase (MPO) antibodies, anti-Scl-70 antibodies, anti-Sjogren's syndrome-related antigen A (SSA/Ro52) antibodies, anti-aminoacyl-transfer RNA synthetase (ARS) antibodies, anti-Jo-1 antibodies, and anti-melanoma differentiation-associated gene 5 (MDA5) antibodies. Chest X-ray and computed tomography (CT) scan showed diffuse ground-glass opac", "Doctor: Good morning! How are you feeling today?

Patient: Not great, I'm having trouble breathing.

Doctor: I see. Can you tell me a little about your past medical history?

Patient: I don't have any history of medical issues.

Doctor: Okay. When did you first start experiencing dyspnea?

Patient: It's been about 5 days now.

Doctor: Have you ever smoked cigarettes or consumed alcohol?

Patient: No, I haven't.

Doctor: Do you have a frequent cough?

Patient: Yes, I've been coughing a lot lately.

Doctor: And have you noticed any wheezes or lung crackles when you breathe?

Patient: No, I haven't noticed anything like that.

Doctor: I see. During your physical exam did you have any abnormal heart sounds?

Patient: No, everything seemed normal.

Doctor: Did you experience any edema, skin rash, muscle weakness, myalgia, or arthralgia?

Patient: No, none of that.

Doctor: Your blood tests showed leukocytosis with high C-reactive protein levels. Do you have any questions about that?

Patient: What does that mean?



Doctor: It means that you have an elevated white blood cell count and inflammation in your body.

Patient: I see.

Doctor: Your chest X-ray and computed tomography scan showed diffuse ground-glass opacities. This is indicative of lung disease.

Patient: Okay, what does that mean for me?

Doctor: Based on your symptoms and test results, it appears that you have pneumonia. We will need to treat this with antibiotics and monitor your oxygen levels.

Patient: Okay, what else do I need to do?

Doctor: We will need to perform follow-up tests to ensure that the antibiotics are working and monitor your condition closely. If your oxygen levels continue to drop, we may need to admit you to the hospital for more advanced treatment.

Patient: Okay, thank you for your help.

Doctor: Of course. Please take care and let us know if you experience any changes in your symptoms."

"A 70-year-old Caucasian woman with medical history significant for stage III chronic kidney disease, transitional cell ureteral cancer status post-left-sided nephroureterectomy, and three-year history of Waldenstrom's macroglobulinemia (WM) presented with complaints of right-sided weakness associated with paresthesias, dysarthria, and blurry vision of three weeks duration. Magnetic resonance (MRI) imaging of the brain demonstrated an enhancing, hypercellular mass centered in the left thalamus with additional foci of signal abnormality and enhancement in the cortex of the left frontal lobe and subcortical white matter (Figure ). These findings were concerning for an intracranial neoplastic process, especially given her history of WM.

Regarding her oncological history, she was initially diagnosed with WM at the age of 67 after workup for complaints of chronic fatigue revealed elevated IgM levels (3370 mg/dl) as well as serum hyperviscosity. Bone marrow biopsy showed a low-grade B-cell lymphoma with plasmacytic differentiation and 60%-70% bone marrow involvement. Neoplastic cells were found to be lambda restricted and negative for CD5, CD10, and CD23 by flow cytometry. An increased number of

lambda predominant cells were confirmed by flow cytometry and CD138 immunostaining. The patient was started on first-line therapy with the Bruton tyrosine kinase inhibitor ibrutinib; however, due to worsening adverse effects after 6 months of therapy she transitioned to rituximab, an anti-CD20 monoclonal antibody. Unfortunately, the patient was found to have worsening IgM levels and serum viscosity while on rituximab monotherapy over the next 6 months. Thus, she was restarted on ibrutinib while continuing rituximab every 3 months and had significant improvement on this combination of therapy.

She completed two years of maintenance rituximab and reduced-dose ibrutinib (140 mg) at time of presentation with the most recent IgM levels of 299 mg/dl prior to the onset of her previously", "Doctor: Good afternoon, how are you feeling today?

Patient: Hi doctor, I'm not feeling well, I have been experiencing weakness on my right side, paresthesias, dysarthria, and blurry vision for the past three weeks.

Doctor: I see, do you have any previous medical history?

Patient: Yes, I have stage III chronic kidney disease, transitional cell ureteral cancer, and Waldenstrom's macroglobulinemia.

Doctor: Ok, thank you for letting me know. We conducted an MRI of your brain, and the results showed an enhancing, hypercellular mass centered in the left thalamus with additional foci of signal abnormality and enhancement in the cortex of the left frontal lobe and subcortical white matter.

Patient: What does that mean, doctor?

Doctor: These findings are concerning for an intracranial neoplastic process, especially given your history of Waldenstrom's macroglobulinemia.

Patient: Is it serious?

Doctor: Unfortunately, yes. According to the clinical note, you were initially diagnosed with Waldenstrom's macroglobulinemia three years ago and have had a history of worsening IgM levels and serum viscosity while on treatment.

Patient: Yes, that's right.

Doctor: You were started on first-line therapy with the Bruton tyrosine kinase inhibitor ibrutinib, but

due to worsening adverse effects, you transitioned to rituximab, an anti-CD20 monoclonal antibody.

You had significant improvement on this combination of therapy.

Patient: Yes, that's correct.

Doctor: However, the most recent MRI showed that the neoplastic process has progressed despite treatment.

Patient: What can we do now?

Doctor: We will need to conduct further tests to determine the next course of action. I will refer you to an oncologist who will provide you with more information and guidance.

Patient: Ok, thank you, doctor.

Doctor: In the meantime, please keep track of any changes in your symptoms and report them to your oncologist.

Patient: Sure, I will do that.

Doctor: Thank you, and please take care."

"The case study is devoted to investigating of penile pain in a 41-year-old married man. According to medical evaluation, the pain extended to the perineal and inguinal regions and it was reported to be more acute during erection. The patient was referred by urologist for sonographic evaluation of penis and testes. The pain had started 3 days before the urologist examination, following his first full erection for intercourse, after his positive COVID-19 polymerase chain reaction (PCR) test.

The patient did not have any other urologic symptoms such as discharge, hematuria, or dysuria. He denied any trauma to the penis, previous pelvic tumor, pelvic surgery and history of recent immobilization. He did not use vasoconstrictive drugs. The patient reported positive nasopharyngeal swab test for COVID-19 three weeks earlier. He had mild symptoms of COVID-19 infection including muscle pain, fever, cough, and fatigue. He had received conservative treatment and had not taken any anti-coagulants, antivirals, and corticosteroids. His medical history did not show any significant underlying disease and any risk factor for cardiovascular disease. He also did not have history of previous deep vein thrombosis. In physical examination of the penis and testes, no pathologic finding was detected such as skin tissue changes, discoloration, edema, tenderness, or palpable

nodularity.

Ultrasound evaluation showed thrombosis of deep dorsal penile vein while the superficial dorsal penile vein, iliac veins, and inferior vena cava were intact (Figures ,,).

Laboratory tests revealed slightly increased D-dimer level(may be due to inflammatory process of COCID-19 infection), normal levels of fibrinogen, anti-thrombin III, protein S, Protein C, anti-cardiolipin antibodies and normal count of platelets and white blood cell counts. Also Tests were negative for anti-phospholipid-IgG, IgM, and lupus anti-coagulant (Table ).

Immediately after sonographic diagnose of deep dorsal penile vein", "Doctor: Hello, how are you feeling today?

Patient: I'm not doing too well, doctor. I'm experiencing some pain.

Doctor: Can you tell me more about the pain? When did it start?

Patient: It started a few days ago and it's mostly in my penis, perineal, and inguinal regions.

Doctor: Did you notice any other symptoms along with the pain?

Patient: No, I didn't experience any discharge, hematuria, or dysuria.

Doctor: I see. Were you referred by a urologist for a sonographic evaluation of your penis and testes?

Patient: Yes, that's correct.

Doctor: Okay, and before that, did you test positive for COVID-19 polymerase chain reaction (PCR) test?

Patient: Yes, I did.

Doctor: I'm sorry to hear that. Did you experience any other symptoms of COVID-19 infection?

Patient: Yes, I had muscle pain, fever, cough, and fatigue.

Doctor: Alright. Did you take any anti-coagulants, antivirals, or corticosteroids?

Patient: No, I only received conservative treatment.

Doctor: I see. Did you have any previous history of pelvic tumor, pelvic surgery, or recent immobilization?

Patient: No, I don't have any of those.

Doctor: Okay, and did you use any vasoconstrictive drugs?

Patient: No, I didn't.

Doctor: Alright. Based on your sonographic evaluation, we have found thrombosis of the deep dorsal penile vein. Do you understand what that means?

Patient: Not really, doctor. Can you explain it to me?

Doctor: Of course. Thrombosis means a blood clot has formed in one of your veins. The deep dorsal penile vein is located inside the penis and it's responsible for carrying blood away from the penis. In your case, it's blocked by a blood clot.

Patient: Oh, I see.

Doctor: We also conducted laboratory tests and found slightly increased D-dimer level, which may be due to the inflammatory process of COVID-19 infection. However, your fibrinogen, anti-thrombin III, protein S, Protein C, and anti-cardiolipin antibodies levels are all normal. Your platelets and white blood cell counts are also normal. We also tested for anti-phospholipid-IgG, IgM, and lupus anti-coagulant and the results were negative.

Patient: Okay.

Doctor: Based on our findings, we will need to prescribe some medication for you to take. Additionally, we will need to monitor your condition closely. Do you have any questions?

Patient: No, I don't think so.

Doctor: Alright. I'll give you a prescription for the medication and we'll schedule a follow-up appointment. If you experience any worsening of symptoms, please contact us immediately."

"A 45-year-old male was admitted to the emergency department with postural instability and dysarthria. To lessen his instability and avoid to fall, the patient widened his support polygon. He had also reported dyspnea at effort, which occurred 3 days prior to his admission. He had a history of rheumatic mitral stenosis, since 2005, for which he benefited from a percutaneous mitral dilation in the same year. He also reported a Penicillin allergy.

Initial examination found the patient conscious. His heart rate was 125 b/m, blood pressure was 135/85 mm Hg. He was polypneic and orthopneic with a respiratory rate of 28 breaths/min, an O2

saturation of 96% on ambient air with the presence of bilateral crackles. He had a fever measured at 39.5C. Cardiac

auscultation revealed a low-pitched diastolic rumble, well heard at the apex. The neurologic examination revealed unsteady gait and the patient was unable to perform Romberg's test.

The ECG showed coarse-mesh atrial fibrillation with an average ventricular rate of 90 cycles per minute (). No abnormalities were detected on the chest x-ray. Transthoracic echocardiogram (TTE) found rheumatic changes of the mitral valve including: commissural fusion and thickening, producing "dog leg deformity" of the anterior mitral leaflet (-A). The mitral valve area was 0,8 cm<sup>2</sup> (-B) and the pressure gradient across the mitral valve was 22 mmhg (-E). We noted a mobile vegetation measuring 11,7 mm of length, located in the posterior leaflet of the mitral valve (-C). The left atrium was dilated at 47 cm<sup>2</sup> while size and function of the left ventricle was normal. Pulmonary arterial systolic pressure (PASP) was important (-F) and the filling pressures of the left ventricle were elevated. In addition to that, we reported moderate aortic stenosis and regurgitation and mitral regurgitation", "Doctor: Good morning, how are you feeling today?

Patient: Not so good, I feel very unstable and my speech is slurred.

Doctor: I see you were admitted to the emergency department due to postural instability and dysarthria. Have you been experiencing any other symptoms?

Patient: Yes, I've been having trouble breathing when I exert myself for the past 3 days.

Doctor: Okay, that's important to note. I see you have a history of rheumatic mitral stenosis. When was the last time you had a procedure for that?

Patient: I had a percutaneous mitral dilation back in 2005.

Doctor: And do you have any allergies to medications?

Patient: Yes, I'm allergic to Penicillin.

Doctor: Understood. Let's do a quick examination. Are you conscious right now?

Patient: Yes, I am.

Doctor: Your heart rate is currently at 125 beats per minute and your blood pressure is 135/85 mm Hg. You're also breathing rapidly at 28 breaths per minute and have a fever of 39.5C. I hear a

low-pitched diastolic rumble in your cardiac auscultation, and you have bilateral crackles in your lungs.

Patient: Okay.

Doctor: We also found a mobile vegetation measuring 11.7mm on your mitral valve during a Transthoracic echocardiogram. Your left atrium is dilated at 47cm<sup>2</sup> and your Pulmonary arterial systolic pressure is elevated.

Patient: What does that mean?

Doctor: The dilation of your left atrium and elevated Pulmonary arterial systolic pressure indicates that there is pressure building up in your heart and lungs. This can lead to difficulty breathing and other complications. We also found moderate aortic stenosis and regurgitation and mitral regurgitation.

Patient: What's the next step?

Doctor: We will need to monitor your condition and determine the best course of treatment. We may need to perform additional tests or procedures to stabilize your heart and lungs. I will also prescribe medication to help manage your symptoms in the meantime.

Patient: Okay, thank you.

Doctor: You're welcome. Just remember to follow up with any appointments and take your medication as prescribed. If you experience any changes in your symptoms, please contact us immediately.

Patient: Will do.

(If patient dies) Doctor: I'm sorry to inform you that we were unable to save your loved one. We did everything we could to stabilize his condition, but unfortunately, his heart and lungs were too compromised. Our condolences to you and your family during this difficult time."

"A 29-year-old female patient, gravida 1, para 1, with no significant pathological history, had presented herself in consultation complaining of a left cervical swelling that had been evolving for 11 months in a context of general state conservation. The mass was increased in size rapidly after the end of the breastfeeding period (three months). The clinical examination at admission found normal

vital signs, and Body mass index of 26.3 kg/m<sup>2</sup>. Family history was unremarkable for cancer. The patient was using a combined oral contraceptive for menstrual regulation.

The cervical examination showed a postero-lateral mass of the left neck measuring 6 cm in diameter, painless, of firm consistency, unilobed, soft, adherent to the superficial and deep plane. There was no palpable cervical lymphadenopathy or inflammatory signs of the adjacent skin.

A cervical magnetic resonance imaging (MRI) was performed, revealing a mass of the left posterior cervical soft parts, at the expense of the trapezium muscle, tissue, oval, of regular contours, well-defined, measuring 41 x 68 x 81 mm, enhanced after injection of Gadolinium, with multiple homolateral supraclavicular and lateral cervical lymph nodes ( ). The Mantoux test, in the absence of an IRD tuberculin skin intradermoreaction, was negative.

A biopsy of the mass with Tru-cut(r) was performed, concluding a desmoid tumor. Abdominopelvic and thoracic computed tomography, indicated for staging, showed the absence of other progressive lesions elsewhere.

In view of these clinical, radiological and pathological findings, a large resection of the tumor was indicated. The patient was installed in the supine position. Access to the posterior neck area was via a direct surgical approach (Fusiform incision). The mass was found to originate from the trapezius muscle without local infiltration of surrounding structures. A sharp dissection over the mass of the tumor away from the muscle was not possible. Complete excision of the mass was accomplished involving", "Doctor: Good afternoon, how can I help you today?

Patient: Hi, I'm a gravida 1 and I have a left cervical swelling that's been growing for 11 months.

Doctor: Okay, thank you for letting me know. Have you been to a doctor before for this issue?

Patient: No, this is my first consultation.

Doctor: I see. Do you have any significant pathological history that I should know about?

Patient: No, I don't.

Doctor: Alright. I'm going to perform a clinical examination, is that okay with you?

Patient: Yes, sure.

Doctor: During the examination, I found a postero-lateral mass of the left neck measuring 6 cm in



diameter. It's painless, of firm consistency, unilobed, soft, adherent to the superficial and deep plane. There's no palpable cervical lymphadenopathy or inflammatory signs of the adjacent skin.

Patient: Okay.

Doctor: I'll need to perform a cervical magnetic resonance imaging (MRI) to determine the cause of the mass.

Patient: Okay.

Doctor: The MRI revealed a mass of the left posterior cervical soft parts, measuring 41 x 68 x 81 mm, enhanced after injection of Gadolinium, with multiple homolateral supraclavicular and lateral cervical lymph nodes.

Patient: What does that mean?

Doctor: Based on these findings, I performed a biopsy and concluded that you have a desmoid tumor.

Patient: Is it cancerous?

Doctor: No, your family history is unremarkable for cancer. Additionally, abdominopelvic and thoracic computed tomography showed the absence of other progressive lesions elsewhere.

Patient: That's a relief.

Doctor: Yes, it's good news. In view of these clinical, radiological and pathological findings, I recommend a large resection of the tumor.

Patient: What does that entail?

Doctor: You'll need to be installed in the supine position, and access to the posterior neck area will be via a direct surgical approach (Fusiform incision). The mass will be removed, involving complete excision of the mass and any local infiltration.

Patient: Okay, I understand. When can we schedule the surgery?

Doctor: We'll need to schedule it soon. I'll give you more details on the procedure and the follow-up requirements after the surgery."

"The participant in this study was a 24-year-old man who was in a motor vehicle accident that led to a severe TBI two years ago. According to the report of the spiral brain CT scan, the primary lesion

was located in the left frontotemporal area due to contusion, and a few lacunar infarcts were seen in the left basal ganglia. Before the accident, he was an active member of a music band and was involved in bodybuilding activities. He was hospitalized for 48 days after the accident. Following discharge from the hospital, he received regular rehabilitation, including electrical stimulation of the wrist and knee extensors and ankle dorsiflexors, resistance training, and aerobic and endurance conditioning (e.g., walking on treadmill and stationary bike). At the time of the first visit to the research clinic, he could not independently walk or stand up from a chair and was using a wheeled walker for mobility and an ankle foot orthosis to prevent drop foot.

The clinical examination was performed by an experienced physical therapist. The participant had right (RT) hemiplegia with full and strong grasping and gripping but without the ability to write. Other impairments were aphasia, bradykinesia, and dyscoordination of movements of RT upper (i.e., finger to nose) and lower (i.e., heel to shin) extremities. Also, deep tendon reflexes were increased with no spasticity in his muscles. He was dependent in some activities of daily living (ADL) (e.g., dressing, toilet use, and feeding).", "Doctor: Hello, how are you feeling today?

Patient: I'm okay, I guess.

Doctor: I see that you were in a motor vehicle accident a couple of years ago. Can you tell me more about that?

Patient: Yeah, it was pretty severe. I sustained a TBI.

Doctor: I see. According to the report of your spiral brain CT scan, the primary lesion was located in the left frontotemporal area due to contusion, and a few lacunar infarcts were seen in the left basal ganglia. Do you remember anything about that?

Patient: No, not really.

Doctor: Before the accident, you were an active member of a music band and were involved in bodybuilding activities. Did you enjoy those activities?

Patient: Yeah, they were a big part of my life.

Doctor: After the accident, you were hospitalized for 48 days. Following discharge from the hospital, you received regular rehabilitation, including electrical stimulation of the wrist and knee extensors

and ankle dorsiflexors, resistance training, and aerobic and endurance conditioning (e.g., walking on treadmill and stationary bike). How did that go for you?

Patient: It was tough, but I knew I had to do it.

Doctor: At the time of your first visit to the research clinic, you could not independently walk or stand up from a chair and were using a wheeled walker for mobility and an ankle foot orthosis to prevent drop foot. How have things been since then?

Patient: I can walk a little now, but I still need the walker.

Doctor: The clinical examination was performed by an experienced physical therapist. You had right hemiplegia with full and strong grasping and gripping but without the ability to write. Other impairments were aphasia, bradykinesia, and dyscoordination of movements of RT upper (i.e., finger to nose) and lower (i.e., heel to shin) extremities. Also, deep tendon reflexes were increased with no spasticity in your muscles. You were dependent in some activities of daily living (ADL) (e.g., dressing, toilet use, and feeding). Do you have any questions about these findings?

Patient: No, not really.

Doctor: Okay. I'm going to recommend some follow-up requirements for you, including regular physical therapy and occupational therapy to help you improve your mobility and independence. We'll also need to monitor your progress closely to make sure you're improving. Is there anything else you want to discuss?

Patient: No, I think that's it.

Doctor: Alright, I'll make sure to schedule your appointments and get you set up with the therapy you need. Thank you for coming in today. If you have any questions, don't hesitate to call us.

Patient: Thank you, doctor. (The patient's family is notified later of the patient's death due to complications from the TBI.)"

"A 53-year-old man presented with a pruritic rash on the trunk as well as on the upper and lower extremities. Examination was notable for lichenified papules throughout the trunk and extremities, most notably on the back. Biopsies of the rash showed mild spongiosis with an underlying superficial and deep perivascular infiltrate (). Due to failure of topical halobetasol, topical tacrolimus, oral

antihistamines, prednisone, and mycophenolate mofetil, dupilumab was initiated at standard dosing. Within 3 months, the patient noticed a dramatic improvement of his rash and pruritus, complaining only of mild pruritus between injections and minimal residual post-inflammatory hyperpigmented macules. Dupilumab was stopped after 1 year due to insurance reasons, and the initial pruritic rash returned. After insurance reapproval, dupilumab was restarted with complete resolution of his rash and pruritus."

Doctor: Hello, how are you feeling today?

Patient: I'm doing okay, thanks for asking.

Doctor: I see that you presented with a pruritic rash on your trunk and extremities. Can you tell me more about that?

Patient: Yeah, I've been dealing with this rash for a while now. It's really itchy and has spread to different parts of my body.

Doctor: I understand. During your examination, we noticed lichenified papules throughout your trunk and extremities, with the most notable being on your back. Biopsies of the rash showed mild spongiosis with an underlying superficial and deep perivascular infiltrate.

Patient: Okay, I'm not sure what that means.

Doctor: Basically, we found some inflammation and cellular changes in the skin under the rash. We tried several treatments such as topical halobetasol, topical tacrolimus, oral antihistamines, prednisone, and mycophenolate mofetil, but they didn't work.

Patient: That's frustrating.

Doctor: Yes, it can be. However, we then initiated a treatment called dupilumab at standard dosing. Within 3 months, you noticed a dramatic improvement of your rash and pruritus, complaining only of mild pruritus between injections and minimal residual post-inflammatory hyperpigmented macules.

Patient: That's true. The dupilumab really helped.

Doctor: Unfortunately, we had to stop the dupilumab after 1 year due to insurance reasons, and the initial pruritic rash returned. But, after insurance reapproval, we restarted dupilumab with complete resolution of your rash and pruritus.

Patient: Yes, I'm so glad it's working again.

Doctor: It's important that you continue with this treatment as prescribed to ensure that the rash doesn't come back. We'll schedule a follow-up appointment to check on your progress."

"A 48-year-old woman presented with a 5-year history of intense pruritus and rash significantly impacting her daily life. Examination showed few excoriated papules and subtle lichenification on the upper back, elbows, dorsal forearms, thighs, and fingers. Biopsy revealed mild epidermal spongiosis with a perivascular lymphocytic infiltrate containing rare eosinophils, consistent with DHR (). After failing multiple therapies including topical betamethasone, topical tacrolimus, and oral mycophenolate mofetil, dupilumab was initiated with improvement in severity and duration of flares within the first 6 months. Due to slight progression of her baseline blurry vision and headaches, the dose was decreased to 200 mg every 2 weeks. The patient experienced subsequent flaring of her rash, so the dose was increased back to 300 mg every 2 weeks with resolution of her pruritus and rash and no further exacerbation of her ocular symptoms. Ultimately her ocular symptoms were evaluated by an ophthalmologist and deemed to not be consistent with dupilumab-induced conjunctivitis nor glaucoma.","Doctor: Hi there, what brings you in today?

Patient: I've been dealing with intense itching and a rash for the past five years, and it's really impacting my daily life.

Doctor: Okay, can you tell me more about your history with these symptoms?

Patient: Well, I've tried multiple therapies like betamethasone and tacrolimus, but nothing has really worked.

Doctor: I see. During the examination, we noticed some excoriated papules and subtle lichenification on your upper back, elbows, dorsal forearms, thighs, and fingers.

Patient: Yes, that sounds about right.

Doctor: We did a biopsy, and it revealed mild epidermal spongiosis with a perivascular lymphocytic infiltrate containing rare eosinophils, consistent with DHR.

Patient: What does that mean?

Doctor: It's a type of skin inflammation that can cause itching and a rash. We started you on dupilumab, and it's been helping with the severity and duration of your flares. However, we did have

to decrease the dose due to some blurry vision and headaches.

Patient: Oh, I see.

Doctor: But when we increased the dose back up, your rash and itching resolved and your ocular symptoms didn't worsen. We did evaluate your eyes with an ophthalmologist, and they determined that your symptoms weren't consistent with dupilumab-induced conjunctivitis or glaucoma.

Patient: That's good to know. What should I do now?

Doctor: Continue taking the medication as prescribed and follow up with us regularly. If you notice any changes in your symptoms or if you have any concerns, don't hesitate to reach out to us."

"A healthy 43-year-old woman presented with a 1-year history of a pruritic rash affecting her legs and abdomen. On exam, the patient was noted to have erythematous, blanchable papules coalescing into small plaques on her abdomen and distal part of the legs. Biopsy of the rash revealed an unremarkable epidermis and superficial perivascular lymphocytes with abundant interstitial eosinophils consistent with DHR. Patch testing was performed, which was 2+ for nickel sulfate and 1+ for p-tert-butylphenol formaldehyde resin, but the rash was persistent even with allergen avoidance. After failing multiple topical regimens, including triamcinolone and clobetasol, as well as oral prednisone, the patient was initiated on mycophenolate mofetil therapy, with excellent control but poor gastrointestinal tolerance. Her rash subsequently recurred, so dupilumab was started at standard dosing, and 5 months after starting dupilumab the patient's rash and pruritus had resolved without any side effects.", "Doctor: Hello, how are you feeling today?

Patient: I'm doing okay, thanks for asking.

Doctor: I see from your medical history that you presented with a pruritic rash affecting your legs and abdomen. Can you describe the rash to me?

Patient: It was red and itchy, with small bumps that joined together to form larger patches.

Doctor: Based on your description, it sounds like you had erythematous, blanchable papules coalescing into small plaques on your abdomen and legs. We did a biopsy of the rash and found superficial perivascular lymphocytes with abundant interstitial eosinophils consistent with DHR.

Patient: Okay, I didn't know that.

Doctor: We also performed patch testing, which was positive for nickel sulfate and p-tert-butylphenol formaldehyde resin. We advised you to avoid these allergens, but the rash persisted.

Patient: Yeah, I remember that.

Doctor: We tried several topical regimens, including triamcinolone and clobetasol, as well as oral prednisone, but unfortunately, none of them worked.

Patient: That's right.

Doctor: That's when we initiated mycophenolate mofetil therapy, which provided excellent control, but you experienced poor gastrointestinal tolerance.

Patient: Yeah, I had some stomach issues.

Doctor: After your rash recurred, we started you on dupilumab, which you've been taking for 5 months now. How has that been working for you?

Patient: It's been great. My rash and itching have completely resolved.

Doctor: That's fantastic to hear. Have you experienced any side effects from the dupilumab?

Patient: No, I haven't had any side effects.

Doctor: That's great news. We'll continue to monitor your condition, and please don't hesitate to contact us if you have any concerns."

"A 68-year-old man presented with a 6-month history of a pruritic rash that began on his back and legs and spread to his knees, elbows, shoulders, and chest. Patch testing showed 1+ positivity for both sodium laurel sulfate and benzaprene #4, which were deemed not clinically relevant. On examination, he had scattered erythematous scaly patches on the upper chest, shoulders, and back with overlying excoriation. Biopsy of the right shoulder showed an unremarkable epidermis and a sparse perivascular and interstitial mixed infiltrate containing scattered interstitial eosinophils, consistent with a DHR (). Oral prednisone initially cleared the rash, but it recurred on discontinuation. The rash was also recalcitrant to trials of topical steroids, oral antihistamines, and topical tacrolimus; therefore, he was transitioned to dupilumab at standard dosing. After 3 months, the patient reported complete clearing of the rash and pruritus. He did note occasional eye dryness, which was well-managed with artificial tears.", "Doctor: Good afternoon! What brings you in today?

Patient: Hi! I've been dealing with a pruritic rash for about six months now.

Doctor: Okay, can you tell me more about your rash? When did it first appear, and where on your body did it start?

Patient: It started on my back and legs, and then it spread to my knees, elbows, shoulders, and chest. It's been really itchy and uncomfortable.

Doctor: I see. We'll need to do a thorough examination to determine the cause. Have you tried any treatments so far?

Patient: Yes, I've tried topical steroids, oral antihistamines, and even topical tacrolimus, but nothing seems to work for very long.

Doctor: Hmm, that's not uncommon with pruritic rashes. We may need to do some patch testing to determine if there's an underlying allergy causing your symptoms.

Patient: Okay, that sounds good. What does the patch testing involve?

Doctor: We'll place small patches on your skin with different substances, including sodium laurel sulfate and benzaprene #4. We'll then check the patches after a few days to see if there's any reaction. From there, we can determine if there's an allergy present.

Patient: Okay, I'm willing to try that.

Doctor: Great, we'll get that scheduled. In the meantime, I'll also perform a physical examination to assess the extent of your rash and any overlying excoriation.

Patient: Okay, thank you.

Doctor: After examining your rash, I'll likely perform a biopsy to get a better understanding of what's going on beneath the surface. From there, we can determine the best course of treatment.

Patient: Okay, I trust your professional judgment.

Doctor: Thank you. Based on the biopsy results, it looks like you have a DHR, which means there's a mixed infiltrate of cells that's causing your rash. We'll need to treat this with oral prednisone to start.

Patient: Okay, I'm willing to try that. How long will I need to take it for?

Doctor: We'll start with a short course of a few weeks, but we may need to extend that depending on



the results. It's important to follow the prescribed dosage and not discontinue it without consulting me first.

Patient: Okay, I understand.

Doctor: After taking the prednisone, we'll likely try some other treatments, such as dupilumab. This is a newer medication specifically designed to treat DHR, and it has shown promising results.

Patient: Okay, that sounds good. What are the potential side effects?

Doctor: Some patients have reported eye dryness, but that can be managed with artificial tears. Other than that, it's generally well-tolerated.

Patient: Okay, that's good to know. After starting the dupilumab, how long until I should start seeing results?

Doctor: It can vary from patient to patient, but typically after about three months, you should start to see complete clearing of your rash and pruritus.

Patient: That's great news! Thank you for your help, doctor.

Doctor: Of course, it's my pleasure. Just make sure to follow up with me regularly and let me know if you experience any side effects or changes in your symptoms.

Patient: Okay, I will. Thank you again.

(If the patient eventually dies) Doctor: I'm sorry to inform you that your loved one has passed away. We did everything we could to treat his condition, but unfortunately, it was not enough. Please let me know if there's anything I can do to support you during this difficult time."

"A 75-year-old man presented with a 1-year history of recurrent diffuse, pruritic rash. Examination revealed a generalized eruption of erythematous papules with minimal scale on the extremities and trunk particularly the flanks. Initial differential diagnosis included hypersensitivity dermatitis, contact dermatitis, non-bullous pemphigoid, atopic dermatitis, and Grover disease. A biopsy was performed on the left part of the chest and revealed a predominantly perivascular inflammatory infiltrate with occasional eosinophils consistent with DHR. A direct immunofluorescence test was negative. The patient failed multiple therapies, including topical triamcinolone, clobetasol, and hydroxyzine. Oral prednisone helped but was discontinued due to steroid-induced diabetes. The patient was started

on dupilumab 300 mg injections every 14 days and within 4 months, his dermatitis and pruritus resolved. Due to cost, the injections were spaced to every 30 days, and he continued to experience resolution of his symptoms without any side effect from the medication.", "Doctor: Hi there, how can I help you today?

Patient: I have a rash that won't go away. It's been bothering me for a whole year now.

Doctor: Okay, tell me more about your history with this rash.

Patient: It's pruritic and appears all over my body. There are red papules and minimal scale on my arms, legs, and trunk.

Doctor: I see. Examination reveals a generalized eruption of erythematous papules with minimal scale on the extremities and trunk particularly the flanks. Have you had any other symptoms like hypersensitivity or contact dermatitis?

Patient: No, not that I'm aware of.

Doctor: Based on your history and examination, we need to rule out non-bullous pemphigoid, atopic dermatitis, and Grover disease. We will need to perform a biopsy to be sure.

Patient: Okay, I'm willing to do that.

Doctor: The biopsy showed a predominantly perivascular inflammatory infiltrate with occasional eosinophils consistent with DHR. The direct immunofluorescence test was negative.

Patient: What does that mean?

Doctor: It means you have dermatitis with a perivascular inflammatory infiltrate, but it's not an autoimmune condition. We will need to try different therapies to see what works for you.

Patient: I've already tried topical triamcinolone, clobetasol, and hydroxyzine.

Doctor: I see. Since oral prednisone helped, but was discontinued due to steroid-induced diabetes, I recommend we try dupilumab 300 mg injections every 14 days. This medication has helped many patients with similar symptoms and has minimal side effects.

Patient: Okay, I'm willing to try it.

Doctor: After 4 months of treatment, your dermatitis and pruritus resolved. Due to cost, we spaced the injections to every 30 days, and you continued to experience resolution of your symptoms

without any side effect from the medication.

Patient: That's great news. Thank you so much, doctor.

Doctor: You're welcome. Please continue to monitor your symptoms and let us know if anything changes."

"A 78-year-old man presented with a 5-year history of extreme pruritus. No significant dermatitis was observed aside from faint pink patches on the upper chest and lower back with mild lichenification. Patch testing was performed and revealed 1+ positivity to potassium dichromate, but no culprit allergens were identified. A biopsy taken from the right part of the chest revealed mild acanthosis and minimal spongiosis with a perivascular lymphocytic infiltrate containing rare eosinophils in the presence of a negative direct immunofluorescence test, consistent with a DHR. The patient failed multiple therapies including topical corticosteroids, antihistamines, doxepin, narrow-band UV-B light, doxepin, gabapentin, butorphanol, and aprepitant. Azathioprine was poorly tolerated due to fatigue. The patient was then started on dupilumab with dramatic improvement in his pruritus and a 50%-60% reduction of the rash within the first 2 months with no associated side effects. His condition remains stable on this medication.

Additional clinical information is summarized in .","Doctor: Hi there, how can I help you today?

Patient: I've been experiencing extreme itching for the past five years.

Doctor: Okay, when did it first start?

Patient: It started five years ago.

Doctor: Have you noticed any rashes or dermatitis?

Patient: I have faint pink patches on my upper chest and lower back with mild lichenification.

Doctor: We'll need to do some testing to figure out what's causing your symptoms. We'll start with patch testing to see if there are any allergens that might be causing your symptoms.

Patient: Okay.

Doctor: The patch testing revealed 1+ positivity to potassium dichromate, but we couldn't identify any culprit allergens.

Patient: I see.

Doctor: We performed a biopsy on the right part of your chest which revealed mild acanthosis and minimal spongiosis with a perivascular lymphocytic infiltrate containing rare eosinophils in the presence of a negative direct immunofluorescence test, consistent with a DHR.

Patient: What does that mean?

Doctor: It means that you have a type of skin condition called a drug hypersensitivity reaction.

Patient: What treatments are available?

Doctor: We've tried multiple therapies including topical corticosteroids, antihistamines, doxepin, narrow-band UV-B light, doxepin, gabapentin, butorphanol, and aprepitant. Azathioprine was poorly tolerated due to fatigue. However, we've had success with dupilumab which has dramatically improved your pruritus and reduced the rash by 50%-60% within the first 2 months with no associated side effects.

Patient: That's great to hear. How is my condition now?

Doctor: Your condition remains stable on this medication. We'll need to schedule follow-up appointments to monitor your progress."

"A 31-year-old gravida 4 para 0 African American woman at 22-weeks gestation presented with vaginal bleeding to an outside hospital. Her obstetric history was significant for 2 therapeutic abortions and 1 spontaneous abortion. During prenatal care, the fetus was noted to have a unilateral dysplastic kidney. The patient's family history was significant for two family members with cervical cancer and two family members with endometrial cancer. She was placed on bedrest with inpatient admission. 48 h after admission she developed pelvic pain and uterine contractions. She expelled a mass vaginally measuring 11 x 9 x 5 cm with no fetal contents. The pathology from the outside facility showed a highly cellular tumor composed of spindle-shaped cells and bizarre multinucleated giant cells with focal myxomatous change with mitotic count is greater than 50 per 10 high power field (Positive for CD10, SMA, ER, PR, EMA) with the differential diagnosis including endometrial stromal sarcoma and undifferentiated uterine sarcoma. The patient underwent examination under anesthesia, demonstrating a 3 x 3 cm defect of the posterior vaginal wall with active bleeding, which was sutured for hemostasis. The cervix was long, closed, and high with no

evidence of bleeding and the fetus was intact with normal heart tones. She was discharged in stable condition.

At 27-weeks, the patient was referred to our institution for maternal-fetal medicine, and gynecology oncology consultation. On initial evaluation, she reported no prior abnormal gynecology history and no history of infertility issues. She denied dyspareunia and bulk symptoms prior to or during pregnancy, and her periods before pregnancy were normal. A pap smear at 27-weeks gestation was normal and negative for human papilloma virus. Her intake physical exam at our institution revealed a normal pelvic exam with no evidence of residual vaginal mass, and an ultrasound revealed no intrauterine myomas.

Given the differential diagnosis included an endometrial stromal sarcoma, an undifferentiated uterine sarcoma, and a primary vaginal sarcoma, the patient underwent magnetic resonance imaging", "Doctor: Hello, how are you feeling today?

Patient: I'm doing okay, thank you.

Doctor: So, I see from your clinical note that you are a gravida 4 para 0 African American woman at 22-weeks gestation and presented with vaginal bleeding. Is that correct?

Patient: Yes, that's correct.

Doctor: Okay, can you tell me about your obstetric history? I see you've had 2 therapeutic abortions and 1 spontaneous abortion.

Patient: Yes, that's right.

Doctor: During your prenatal care, your fetus was noted to have a unilateral dysplastic kidney. Did you experience any symptoms related to that?

Patient: No, I didn't have any symptoms related to that.

Doctor: I also see that your family history is significant for two family members with cervical cancer and two family members with endometrial cancer.

Patient: Yes, that's correct.

Doctor: After your admission, you developed pelvic pain and uterine contractions. Can you tell me more about that?

Patient: It was pretty painful, and I was having contractions for a few hours.

Doctor: You expelled a mass vaginally measuring 11 x 9 x 5 cm with no fetal contents. That must have been difficult for you.

Patient: Yes, it was pretty scary.

Doctor: The pathology showed a highly cellular tumor composed of spindle-shaped cells and bizarre multinucleated giant cells with focal myxomatous change with mitotic count is greater than 50 per 10 high power field (Positive for CD10, SMA, ER, PR, EMA) with the differential diagnosis including endometrial stromal sarcoma and undifferentiated uterine sarcoma.

Patient: I didn't understand most of that, but it sounds serious.

Doctor: It is serious, but we will do everything we can to help you. You underwent examination under anesthesia, demonstrating a 3 x 3 cm defect of the posterior vaginal wall with active bleeding, which was sutured for hemostasis. The cervix was long, closed, and high with no evidence of bleeding and the fetus was intact with normal heart tones.

Patient: Okay.

Doctor: You were discharged in stable condition, but at 27 weeks, you were referred to our institution for maternal-fetal medicine and gynecology oncology consultation.

Patient: Yes, that's right.

Doctor: On initial evaluation, you reported no prior abnormal gynecology history and no history of infertility issues. You denied dyspareunia and bulk symptoms prior to or during pregnancy, and your periods before pregnancy were normal. A pap smear at 27-weeks gestation was normal and negative for human papilloma virus. Her intake physical exam at our institution revealed a normal pelvic exam with no evidence of residual vaginal mass, and an ultrasound revealed no intrauterine myomas.

Patient: Okay.

Doctor: Given the differential diagnosis included an endometrial stromal sarcoma, an undifferentiated uterine sarcoma, and a primary vaginal sarcoma, you underwent magnetic resonance imaging.

Patient: Yes, that's correct.

Doctor: We will need to monitor you closely and schedule follow-up appointments to ensure the best possible outcome for you and your fetus. If you have any questions or concerns, please don't hesitate to reach out.

Patient's family: Thank you, doctor. We appreciate your help and will do everything we can to support our loved one."

"A 55-year-old male with a history of type 1 diabetes mellitus (T1DM) and unspecified autoimmune disease who presented with acute onset of confusion as well as concrete visual hallucinations and behavioral change. There were no reports of any headache, fever, or stroke-like symptoms. His only outpatient medications were insulin and low-dose steroids.

The patient was initially admitted to an outside hospital where magnetic resonance imaging (MRI) of the brain revealed multifocal areas of restricted diffusion with areas of corresponding T2 hyperintensities on fluid-attenuated inversion recovery (FLAIR) sequences (Figure ). There was a concern for stroke in multiple vascular territories with concern for vasculitis. Initial workup was unremarkable, and the patient was started on methylprednisolone for presumed primary central nervous system (CNS) vasculitis. He was transferred to our institution for further management by the Neurology service.

His initial neurologic exam was notable for encephalopathy, manifesting as inattention, disorientation to place and time, and stupor. He was only able to follow simple appendicular commands. Cranial nerve exam revealed left lower facial droop. He had full strength in bilateral upper extremities and 4/5 strength in bilateral lower extremities. Initial differential diagnosis included autoimmune vasculopathies, primary CNS vasculitis, and infectious meningoencephalitis given his mental status changes, reported visual hallucinations, and multifocal strokes.

Steroids were initially held on admission to our institution until further workup could be performed. Extensive rheumatologic labs were ordered, and only rheumatoid factor and anti-CCP were found to be mildly elevated. A contrast-enhanced MRI of the brain demonstrated evolving areas of restricted diffusion with multifocal new areas of restricted diffusion in multiple vascular territories (Figure ).

There was also incomplete suppression of CSF signal on FLAIR with multiple areas of abnormal leptomeningeal enhancement, suggestive of a superimposed inflammatory process affecting the meninges (Figures , ). In addition, there was abnormal vessel", "Doctor: Good afternoon, how are you feeling today?

Patient: I'm not feeling well, doctor.

Doctor: Okay, can you tell me what brought you here today?

Patient: I had an acute onset of confusion, visual hallucinations, and behavioral change.

Doctor: I see. Do you have a history of any medical conditions?

Patient: Yes, I have type 1 diabetes mellitus and an unspecified autoimmune disease.

Doctor: Okay. Have you experienced any headaches or fever?

Patient: No, I haven't.

Doctor: That's good to know. Can you tell me what medications you're currently taking?

Patient: I'm taking insulin and low-dose steroids.

Doctor: I see. You were admitted to an outside hospital previously, correct?

Patient: Yes, that's right.

Doctor: They performed a magnetic resonance imaging (MRI) of your brain and found multifocal areas of restricted diffusion with areas of corresponding T2 hyperintensities on fluid-attenuated inversion recovery (FLAIR) sequences. Did you experience any stroke-like symptoms?

Patient: No, I didn't.

Doctor: They were concerned for stroke in multiple vascular territories with concern for vasculitis. They started you on methylprednisolone for presumed primary CNS vasculitis. You were then transferred to our institution for further management by the Neurology service. How has your mental status been since then?

Patient: I've been experiencing encephalopathy, inattention, disorientation to place and time, and stupor.

Doctor: I see. They also noted left lower facial droop during your cranial nerve exam. Have you been experiencing any other symptoms?



Patient: No, just those.

Doctor: They initially considered autoimmune vasculopathies, primary CNS vasculitis, and infectious meningoencephalitis given your mental status changes, reported visual hallucinations, and multifocal strokes. We held off on the steroids until further workup could be performed. We ordered extensive rheumatologic labs and only rheumatoid factor and anti-CCP were found to be mildly elevated. We then performed a contrast-enhanced MRI of the brain and found evolving areas of restricted diffusion with multifocal new areas of restricted diffusion in multiple vascular territories. There was also incomplete suppression of CSF signal on FLAIR with multiple areas of abnormal leptomeningeal enhancement, suggestive of a superimposed inflammatory process affecting the meninges.

Patient: Okay, what does that mean?

Doctor: It means that we have found some abnormalities in your tests, which may indicate that you have an inflammatory process affecting your meninges. We will need to perform further tests and possibly start you on treatment to manage this condition.

Patient: Alright, what's the next step?

Doctor: We will need to monitor your condition closely and perform further tests to determine the best course of treatment. We may need to start you on more aggressive therapy, depending on how you respond to the treatment. In the meantime, we will continue to manage your symptoms and keep you comfortable.

Patient: Okay, thank you.

Doctor: You're welcome. Is there anyone you would like us to contact regarding your condition?

Patient: Yes, please contact my family."

"A 35-year-old male with a history of hyperlipidemia and seizure disorder presented to an outside hospital following a breakthrough seizure, where he was incidentally also found to have punctate areas of acute cerebral infarcts in multiple vascular territories. Additional workup revealed the presence of a left atrial thrombus and newly diagnosed atrial fibrillation. He was ultimately discharged to home on apixaban. The patient then re-presented a month later for evaluation of

transient diplopia, expressive aphasia, daily right temporal headaches, and right facial and left leg weakness. MRI of the brain showed new areas of diffusion restriction in the left cerebellar hemisphere and left medial occipital lobe (Figure ). CTA showed no signs of carotid occlusion or stenosis. The etiology of his multifocal strokes was thought to be related to his newly diagnosed atrial fibrillation and left atrial thrombus.

The patient was then transferred to our hospital for further evaluation. His initial NIH stroke scale was 8 (primary deficits were including unilateral facial palsy, bilateral lower extremity pronator drift and ataxia). Stroke labs, including lipid panel and hemoglobin A1C, were unremarkable. MRI of the brain with contrast showed a new infarct in the splenium of the corpus callosum in addition to prominent generalized meningeal enhancement (Figure ). MRI of the spine with contrast showed possible meningeal enhancement as well as punctate areas of encephalomalacia in the C3-4, C7, and T3 spinal levels. A bedside LP revealed a mildly elevated opening pressure of 24 cm H<sub>2</sub>O, lymphocytic pleocytosis (WBC 150 K/cumm, 61% lymphocytes), protein 170 mg/dl, hypoglycorrhachia of 15 mg/dl, and presence of cryptococcal antigen. Other notable CSF labs included the presence of 11 oligoclonal bands. He was diagnosed with cryptococcal meningoencephalitis and started on a four-week course of amphotericin B and flucytosine. A repeat LP after several days of treatment showed a normal opening pressure of 14 cm H<sub>2</sub>O, mildly improved ple", "Doctor: ""Hello, how are you feeling today?""

Patient: ""I'm feeling okay, thanks for asking.""

Doctor: ""Can you tell me about your medical history, particularly any history of hyperlipidemia or seizure disorder?""

Patient: ""Yes, I have a history of hyperlipidemia and seizure disorder.""

Doctor: ""I see. And when did you first present with cerebral infarcts?""

Patient: ""I presented to an outside hospital following a breakthrough seizure.""

Doctor: ""Okay, and were you also found to have a left atrial thrombus and newly diagnosed atrial fibrillation?""

Patient: ""Yes, I was discharged home on apixaban.""

Doctor: ""I see. And then you re-presented with transient diplopia, expressive aphasia, daily right temporal headaches, and right facial and left leg weakness?""

Patient: ""Yes, that's correct.""

Doctor: ""And the MRI showed new areas of diffusion restriction in the left cerebellar hemisphere and left medial occipital lobe, but CTA showed no signs of carotid occlusion or stenosis?""

Patient: ""Yes, that's what they told me.""

Doctor: ""The etiology of your multifocal strokes was thought to be related to your newly diagnosed atrial fibrillation and left atrial thrombus.""

Patient: ""Okay.""

Doctor: ""When you were transferred to our hospital, your initial NIH stroke scale was 8. Can you tell me more about your symptoms at that time?""

Patient: ""I had unilateral facial palsy, bilateral lower extremity pronator drift, and ataxia.""

Doctor: ""I see. And were your stroke labs, including lipid panel and hemoglobin A1C, unremarkable?""

Patient: ""Yes, they were.""

Doctor: ""But MRI of the brain with contrast showed a new infarct in the splenium of the corpus callosum in addition to prominent generalized meningeal enhancement. And MRI of the spine with contrast showed possible meningeal enhancement as well as punctate areas of encephalomalacia in the C3-4, C7, and T3 spinal levels?""

Patient: ""Yes, that's what they found.""

Doctor: ""And a bedside LP revealed a mildly elevated opening pressure of 24 cm H2O, lymphocytic pleocytosis, protein, and hypoglycorrhachia of 15 mg/dl, and presence of cryptococcal antigen. Other notable CSF labs included the presence of 11 oligoclonal bands.""

Patient: ""Okay.""

Doctor: ""Based on these results, you were diagnosed with cryptococcal meningoencephalitis and started on a four-week course of amphotericin B and flucytosine. A repeat LP after several days of treatment showed a normal opening pressure of 14 cm H2O and mildly improved pleocytosis.""

Patient: "Okay, what happens now?"

Doctor: "We will continue to monitor your progress and adjust your treatment as needed. It's important to follow up regularly to ensure that you are responding well to the medication." (If the patient has died, the doctor may add: "I'm sorry to inform you that despite our best efforts, your loved one has passed away. We will provide support and grief counseling for you and your family during this difficult time.")"

"A 71-year-old male presented with a two-week history of painless right submandibular swelling that was not associated with fever. The patient had underlying hypertension and diabetes mellitus that were regularly treated.

On examination, a right submandibular swelling with normal overlying skin measuring 6 x 5 cm that was non-tender, mobile, and firm in consistency was noted (Figure , ). The swelling is ballotable by bimanual palpation. There was no other swelling palpable in the neck region. Intraorally, pus was noted at the Wharton's duct orifice, and no sialolith was palpable.

Preoperative blood investigations (complete blood count, serum urea and electrolytes, and serum uric acid), electrocardiography, and chest radiographs were normal. Computed tomography (CT) of the neck was performed as part of the preoperative assessment, which showed opacity in the right submandibular gland and duct (Figure , , ). A diagnosis of right submandibular stone was made. The patient subsequently underwent excision of the right submandibular gland under general anesthesia. Intraoperatively, the right submandibular gland was indurated (Figure ). During the excision, the surgeon noted another firm bulge along the submandibular duct that turned out to be a few smaller pieces of stones within the duct (Figure ). The size of the largest stone was 25 mm. Postoperative recovery was uneventful. Histopathology examination revealed severe acute-on-chronic sialadenitis with multiple calculi."

Doctor: Good morning, how can I help you today?

Patient: Hi, I presented with a painless swelling on the right side of my neck two weeks ago.

Doctor: I see. Can you tell me more about the history of this swelling? Was it associated with fever?

Patient: No, it wasn't associated with fever. I have underlying hypertension and diabetes that are

regularly treated.

Doctor: Okay, let's take a look. During the examination, I noted a non-tender, mobile, and firm swelling on the right side of your neck. There was no other swelling palpable in the neck region. Did you notice any pus in the mouth?

Patient: Yes, I noticed pus at the Wharton's duct orifice.

Doctor: Ah, I see. There's no sialolith palpable. We need to do some tests to further assess the swelling. We'll do some preoperative blood investigations, electrocardiography, and chest radiographs.

Patient: Okay, that sounds good.

Doctor: The blood investigations, electrocardiography, and chest radiographs all came back normal. However, we still need to do a computed tomography (CT) of the neck as part of the preoperative assessment.

Patient: Alright.

Doctor: The CT scan showed opacity in the right submandibular gland and duct. It's a right submandibular stone. We need to excise the right submandibular gland under general anesthesia.

Patient: Okay, I understand.

Doctor: During the excision, the surgeon noted another firm bulge along the submandibular duct. It turned out to be a few smaller pieces of stones within the duct. The size of the largest stone was 25 mm.

Patient: That's a relief to know.

Doctor: Postoperative recovery was uneventful. However, the histopathology examination revealed severe acute-on-chronic sialadenitis with multiple calculi.

Patient: Is there anything I need to do for follow-up?

Doctor: Yes, we need to monitor your blood pressure and blood sugar levels regularly, as well as follow up with any recommended appointments."

"A seven-year-old otherwise healthy female sustained bilateral elbow trauma after a fall with outstretched elbows and landing with force on the floor (kindergarten facility at the climbing frame).

The neurovascular status of both upper extremities was intact upon the arrival of the patient to the Trauma Unit. Clinical examination revealed loss of any active movement in both elbow joints in every plane. The joint was locked in a relatively extended position with the forearm neutral to a slightly supinated position. The patient had no sign of swelling or hematoma. Clinical suspicion was guided to a complex elbow injury, possibly with the participation of various bony structures.

A gross estimation of the patient's potential hyperlaxity was performed except for the elbow joints using the Beighton scale without significant clinical findings []. Neurovascular status of the upper limbs was thoroughly re-examined, but no sign of neural or vascular impairment or compromise was found.

Plain radiographs with standard projections (anteroposterior [AP] and lateral views) confirmed posterolateral elbow dislocation bilaterally with no signs of evident fractures. Identification of the bony structures was performed, and meticulous control and confirmation of the secondary ossification centers expected for the patient's age was done to exclude any secondary damage (Figures -).

In the emergency department, the upper limbs were immobilized in a provisional plaster with the elbows in a light hyperextension and neutral rotation of the forearms to reduce any movement and relieve the pain. The reduction was achieved under sedation in the operating theater and muscle relaxation with the patient in the beach chair position and with access to fluoroscopy during the whole procedure. The maneuver included gentle manipulation of the joints by slightly rotating, distracting and giving a flexion jerk to the joint. The audible and palpable "click" sign and the complete restoration of the arch of motion with the appropriate imaging confirmed the reduction as well as achievement of ligamentotaxis. Postoperatively, the

Doctor: Hello there, how are you feeling today?

Patient: I'm feeling a bit sore, doctor.

Doctor: I see. Can you tell me what happened to you?

Patient: I fell off the climbing frame at kindergarten and hurt my elbows.

Doctor: I'm sorry to hear that. We suspect you have a complex elbow injury, possibly involving

various bony structures. We'll need to perform a clinical examination to confirm.

Patient: Okay, doctor. What does that involve?

Doctor: We'll need to check your joint's position, as it appears to be locked in a relatively extended position with the forearm neutral to a slightly supinated position. Is there any swelling or hematoma in the area?

Patient: No, doctor.

Doctor: Okay, that's good to hear. We'll also perform a gross estimation of your potential hyperlaxity using the Beighton scale without significant clinical findings. We need to exclude any secondary damage, so we'll thoroughly examine your neurovascular status of the upper limbs.

Patient: Alright, I understand.

Doctor: We'll also need to take some plain radiographs to confirm the extent of the injury. Have you had any X-rays taken yet?

Patient: Yes, doctor. They confirmed posterolateral elbow dislocation bilaterally with no signs of evident fractures.

Doctor: I see. We'll need to immobilize your upper limbs in a provisional plaster with the elbows in a light hyperextension and neutral rotation of the forearms to reduce any movement and relieve the pain. We will perform the reduction under sedation in the operating theater and muscle relaxation with you in the beach chair position and with access to fluoroscopy during the whole procedure. The maneuver includes gentle manipulation of the joints by slightly rotating, distracting and giving a flexion jerk to the joint. The complete restoration of the arch of motion with the appropriate imaging confirmed the reduction as well as achievement of ligamentotaxis.

Patient: That sounds complicated, doctor.

Doctor: It is, but we need to ensure that your elbows heal properly. After the procedure, we'll need to monitor your progress and schedule follow-up appointments to make sure everything is healing as it should be.

Patient: Alright, I'll make sure to follow all your instructions, doctor.

Doctor: That's great to hear. Is there anything else you'd like to ask me about your injury?

Patient: No, doctor. Thank you for your help.

Doctor: You're welcome. We'll make sure to keep you and your family updated on your progress."

"We present the case of a 42-year-old man who presented to the emergency department with a complaint of abdominal pain and diarrhea for 3 days. The abdominal pain started in the periumbilical region and was shifted to the right lower quadrant of the abdomen. The pain started gradually and had been progressing in severity. He described the pain as a stabbing in nature. It was exacerbated by movement and food intake. The pain was partially relieved by oral analgesic medications like paracetamol. The pain was associated with low-grade fever and decreased appetite. The patient also complained of diarrhea with five bowel motions/day. The stools were watery with no mucus or blood. He reported that diarrhea developed after he received an oral antibiotic therapy (cefuroxime) for a recent upper respiratory tract infection.

The past medical history of the patient was remarkable for diabetes mellitus that was well-controlled with oral antidiabetic agents. He did not undergo any previous abdominal surgeries. He had a smoking history of 15 pack-years. He had never drunk alcohol before. He worked as a taxi driver. The family history was unremarkable for any inherited gastrointestinal disorders.

Upon examination, the patient appeared sick. He was not pale, jaundiced, or cyanosed. Vital signs revealed tachycardia (115 bpm), low-grade fever (37.5), normal respiratory rate (14 bpm), and maintained blood pressure (122/80 mmHg). The oxygen saturation was 99% on room air. Abdominal examination revealed a soft abdomen with diffuse tenderness. However, the tenderness was more pronounced in the right iliac fossa with a positive rebound sign. Further, the Rovsing sign was positive. Initial laboratory investigation revealed elevated leukocyte count and elevated inflammatory markers, including erythrocyte sedimentation rate and C-reactive protein. The renal and hepatic profiles were within the normal limits (Table ).

In light of the aforementioned clinical information, the patient was diagnosed as having acute appendicitis. A CT scan with intravenous", "Doctor: Hello, how are you feeling today?

Patient: I'm not feeling well. I presented to the emergency department with abdominal pain and diarrhea for 3 days.



Doctor: I see. Can you describe the pain for me?

Patient: The pain started gradually in the periumbilical region and shifted to the right lower quadrant of the abdomen. It was stabbing in nature and exacerbated by movement and food intake.

Doctor: Okay, and did you take any medications for the pain?

Patient: Yes, I took oral analgesic medications like paracetamol which partially relieved the pain.

Doctor: I understand. Did you experience any other symptoms with the pain?

Patient: Yes, I had low-grade fever and decreased appetite.

Doctor: Did you notice any changes in your bowel movements?

Patient: Yes, I had watery diarrhea with no mucus or blood. I reported that the diarrhea developed after I received an oral antibiotic therapy (cefuroxime) for a recent upper respiratory tract infection.

Doctor: I see. Based on your past medical history, are you currently taking any medications or have any medical conditions?

Patient: I have diabetes mellitus that is well-controlled with oral antidiabetic agents. I did not undergo any previous abdominal surgeries. I have a smoking history of 15 pack-years and have never drunk alcohol before. I work as a taxi driver.

Doctor: Thank you for the information. Upon examination, we found tenderness in the right iliac fossa with a positive rebound sign and a positive Rovsing sign. Your Vital signs revealed tachycardia, low-grade fever, normal respiratory rate, and maintained blood pressure. Your oxygen saturation was 99% on room air. We also found elevated leukocyte count and elevated inflammatory markers. Based on this information, we have diagnosed you with acute appendicitis. We will need to perform a CT scan with intravenous contrast to confirm the diagnosis.

Patient: Okay, what are the next steps?

Doctor: We will schedule the CT scan as soon as possible. In the meantime, we will provide you with pain relief medication and antibiotics to prevent further infection. Once the CT scan results come back, we will determine if surgery is necessary to remove the inflamed appendix. It's important to follow up with us and keep us informed of any changes in your symptoms.

Patient's family: Thank you, doctor. We will make sure to keep you updated and follow all of your

instructions."

"A 29-year-old, non-lactating, and non-gravid woman presented with a complaint of a lump in her right breast. The patient also complained of low-grade fever and unilateral pain in breast tissue. The general physical examination showed a one-centimeter erythematous and tender mass in the right breast tissue. There was no nipple discharge, axillary lymphadenopathy, or external draining sinuses. The primary care physician evaluated the patient and called for a USG for the assessment of the affected breast, which demonstrated an ill-defined lesion with thin fluid streaks in the lower outer quadrant, suggesting an inflammatory lesion (Figure ).

At the same time, cystic fluid from her breast was aspirated, and the bacterial culture test showed no growth of any microorganisms after 48 hours. The cytology revealed predominantly neutrophils and degenerating cells in a hemorrhagic background, which suggested an acute suppurative inflammatory process of the affected breast as shown in Figure .

Based on the clinical features, imaging findings, and cytology reports, a presumptive diagnosis of acute mastitis with underlying bacterial abscess was established. Subsequently, she was being prescribed a course of antibiotics and antipyretics for one week. However, instead of improving, her condition worsened over time. Therefore, the physician decided to repeat the ultrasound-guided fine-needle aspiration and cytology (FNAC). The sonomammogram of the right breast revealed an ill-demarcated hypoechoic irregular lesion involving the parenchyma of the right breast in the outer lower and adjoining upper quadrants. The lesion measured 34.4 millimeters on a long axis with no fluid components as shown in Figure .

The repeated cytological examination also showed cellular clusters comprising histiocytes and epithelioid-like cells. Hence, based on these findings, the treating physician concluded that the ongoing clinical picture was more suggestive of tuberculosis of the breast. Therefore, after discussing with the patient, a therapeutic trial of an anti-tuberculosis therapy (ATT),"Doctor: Hello, how can I help you today?

Patient: Hi, I have a lump in my right breast and I've been having a low-grade fever and unilateral pain.

Doctor: Okay, let's take a look. During the physical examination, we found a one-centimeter erythematous and tender mass in the right breast tissue. Did you notice any nipple discharge, axillary lymphadenopathy, or external draining sinuses?

Patient: No, I didn't experience any of those symptoms.

Doctor: Based on your symptoms, we did an ultrasound-guided assessment of the affected breast and it demonstrated an ill-defined lesion with thin fluid streaks in the lower outer quadrant, suggesting an inflammatory lesion.

Patient: Oh, I see.

Doctor: We also aspirated cystic fluid from your breast and the bacterial culture test showed no growth of any microorganisms after 48 hours. However, the cytology revealed predominantly neutrophils and degenerating cells in a hemorrhagic background, which suggested an acute suppurative inflammatory process of the affected breast.

Patient: Okay, what does that mean?

Doctor: We've established a presumptive diagnosis of acute mastitis with underlying bacterial abscess and prescribed you with a course of antibiotics and antipyretics for one week. However, instead of improving, your condition worsened over time.

Patient: That's worrying.

Doctor: Yes, that's why we repeated the ultrasound-guided fine-needle aspiration and cytology. The sonomammogram of the right breast revealed an ill-demarcated hypoechoic irregular lesion involving the parenchyma of the right breast in the outer lower and adjoining upper quadrants.

Patient: What does that indicate?

Doctor: The repeated cytological examination also showed cellular clusters comprising histiocytes and epithelioid-like cells. Based on these findings, we suspect that your condition is more suggestive of tuberculosis of the breast.

Patient: Tuberculosis? Is it curable?

Doctor: Yes, it is treatable. We've discussed with you and decided to start a therapeutic trial of an anti-tuberculosis therapy (ATT). It's important to follow the medication and come back for follow-up

appointments.

Patient: Okay, thank you for explaining everything to me.

Doctor: Of course, if you have any other concerns or questions, don't hesitate to reach out."

"A 58-year-old man, with no relevant medical history, presented with a history of an enlarging painless mass at his right groin region for the past three months (Figure ). The patient did not have any other complaints or symptoms. Physical examination revealed a firm, skin-colored and mobile tumor with well-defined margins (5 cm largest diameter). There were no palpable adenomegalies.

The patient was referred to the General Surgery department by a urologist, with suspicion of a soft-tissue tumor. An MRI described a "focal subcutaneous lesion with nodular morphology of 4.7 cm and no malignancy features". Based on clinical and image findings, it was decided to perform an excisional biopsy.

Despite the apparent benign characteristics, the lesion was surgically removed along with the surrounding adipose tissue, preserving the margins. There were no complications related to the procedure.

Grossly, it was a subcutaneous nodular non-capsulated solid lesion, multilobulated, well-circumscribed, greyish-yellowish, without necrotic areas (Figure ). Microscopically, a variable amount of atypical bland spindle cells and mature adipocytes were seen, with multinucleated floret-like cells in a myxoid stroma with ropey collagen bundle cells. Sclerosing areas were not disclosed (Figure ). On immunohistochemistry, the tumor was stained for CD34, S100, and MDM2 (focal-weak), whereas CDK4 expression was absent (Figure ). Based on these findings, an atypical pleomorphic lipomatous tumor was diagnosed.", "Doctor: Hello, how are you feeling today?

Patient: I'm okay, just worried about this mass on my right groin.

Doctor: I see in your medical history that you presented with an enlarging painless mass on your right groin region for the past three months. Is that correct?

Patient: Yes, that's right.

Doctor: During the physical examination, we found a firm, skin-colored, and mobile tumor with well-defined margins. There were no palpable adenomegalies. Did you have any other complaints or

symptoms?

Patient: No, I didn't have any other issues.

Doctor: Based on the clinical and image findings, you were referred to the General Surgery department with suspicion of a soft-tissue tumor. An MRI described a "focal subcutaneous lesion with nodular morphology of 4.7 cm and no malignancy features". It was decided to perform an excisional biopsy.

Patient: Okay, what does that mean?

Doctor: We surgically removed the lesion along with the surrounding adipose tissue, preserving the margins. There were no complications related to the procedure.

Patient: That's good to hear.

Doctor: The gross findings showed it was a subcutaneous nodular non-capsulated solid lesion, multilobulated, well-circumscribed, greyish-yellowish, without necrotic areas. Microscopically, a variable amount of atypical bland spindle cells and mature adipocytes were seen, with multinucleated floret-like cells in a myxoid stroma with ropey collagen bundle cells.

Patient: Hmmm, that sounds complicated.

Doctor: On immunohistochemistry, the tumor was stained for CD34, S100, and MDM2 (focal-weak), whereas CDK4 expression was absent. Based on these findings, you were diagnosed with an atypical pleomorphic lipomatous tumor.

Patient: Is that a serious condition?

Doctor: It can be concerning, but it is typically a benign tumor. We will need to monitor it closely and possibly consider further treatment if it grows or changes.

Patient: Okay, thank you for explaining everything to me.

Doctor: Of course, please make sure to follow up with us regularly to ensure we catch any changes early. If you have any concerns or symptoms, don't hesitate to contact us.

Patient: Will do, thank you.

Family (if patient died): What happened to our loved one? Can you explain the cause of death?

Doctor: I'm sorry to inform you that despite our efforts, your loved one passed away due to

complications related to the lipomatous tumor. We did everything we could to treat the condition, but unfortunately, it was too advanced. Please accept our deepest condolences."

"A 15-year-old female patient was referred by a pediatric cardiologist to our pediatric cardiac surgery clinic with a confirmed diagnosis of CCL syndrome since birth by a dermatologist. Her cardiovascular symptoms started one month before the presentation with a history of recurrent episodes of shortness of breath, palpitations, and chest pain. The severity of the symptoms has increased in the past few weeks. At the time of referral, she was on furosemide 10 mg twice daily and enalapril 10 mg once daily. Her parents are phenotypically normal. All her siblings, five brothers and two sisters, are free from the disorder. Also, the patient has a remarkable family history, as her cousin is a 20-year-old male with the same disorder. There is consanguinity between parents in the family. On general examination, she had a senile appearance with generalized inelastic, loose, and sagging skin. Vital signs revealed a heart rate of 114 beats per minute, respiratory rate of 20 breaths per minute, blood pressure of 123/73 mmHg, oxygen saturation (SpO<sub>2</sub>) of 100% in room air, and temperature of 36 degC. On cardiac examination, the precordium was hyperactive, the first and second heart sounds were obscured, and pansystolic murmur grade III/VI radiating to the axilla was detected. The hematological studies were within normal limits. Electrocardiogram (ECG) showed sinus tachycardia with right atrial enlargement and right ventricular hypertrophy (Figure ). Chest x-ray showed cardiomegaly with subsegmental atelectasis (Figure ). For more assessment and operative plan, transesophageal echocardiogram (TEE) revealed severe mitral and tricuspid valve prolapse with malcoaptation causing severe regurgitation of both valves with pulmonary hypertension and severe dilatation of both right and left atria (Figures -). After the patient's condition was discussed in the heart team meeting, the plan was set for mitral and tricuspid valve", "Doctor:

Good morning, how are you feeling today?

Patient: Hi, doctor. I'm not feeling well recently.

Doctor: I see. You were referred to us by a pediatric cardiologist. Can you tell me more about your symptoms?

Patient: Yes, I have been experiencing shortness of breath, palpitations, and chest pain for about a

month now.

Doctor: I see. And have these symptoms increased recently?

Patient: Yes, they have become more severe in the past few weeks.

Doctor: Okay, thank you for letting me know. You were diagnosed with CCL syndrome since birth, is that correct?

Patient: Yes, that's right. A dermatologist confirmed it.

Doctor: And you are currently taking furosemide and enalapril?

Patient: Yes, 10 mg of furosemide twice a day and 10 mg of enalapril once a day.

Doctor: I see. Your parents are phenotypically normal, but there is consanguinity in your family. Do you have any siblings with the same disorder?

Patient: No, all my siblings are free from the disorder.

Doctor: Okay. On general examination, you have a senile appearance with loose skin. Your vital signs are stable, but your heart rate is elevated. On cardiac examination, we detected a pansystolic murmur grade III/VI radiating to the axilla.

Patient: Okay.

Doctor: We conducted some tests, and your hematological studies were within normal limits. However, your ECG showed sinus tachycardia with right atrial enlargement and right ventricular hypertrophy. Your chest x-ray showed cardiomegaly with subsegmental atelectasis.

Patient: Okay.

Doctor: For further assessment, we conducted a transesophageal echocardiogram, which revealed severe mitral and tricuspid valve prolapse with malcoaptation causing severe regurgitation of both valves with pulmonary hypertension and severe dilatation of both right and left atria.

Patient: I see.

Doctor: After discussing your condition in the heart team meeting, the plan is to perform mitral and tricuspid valve surgery. I will have our team provide you with more information on the surgery and what to expect."

"An 11-year-old boy was diagnosed with Crohn's disease at the age of nine years. Since then, he

was on a regular infliximab transfusion regimen at monthly intervals at a dose of 5 mg/kg for maintenance of remission of disease as symptoms relapse by the end of each month. He presented to the Maternity and Children Hospital in Al-Ahsa, Eastern Province in Saudi Arabia, complaining of palpitation for one year. The palpitations were intermittent at the beginning of the year but then worsen progressively over the last month. They were associated with easy fatigability and chest discomfort, with no history of cyanosis or chest pain. There was no history of a similar condition or history of cardiac disease or sudden death in the family. In addition, these symptoms occur with the manifestation of tachycardia during infliximab transfusion with no respiratory or mucocutaneous involvement or other signs of anaphylaxis. This transfusion reaction is managed by slowing the transfusion rate and premedication with steroids and antihistamines.

Upon examination of the child, he appeared pale, underweight (with weight of 18 kg below the third centile) but not distressed. He had sinus tachycardia (150-160 beats/min) with maintained blood pressure (98/59 mmHg). chest examination revealed hyperdynamic precordium with pan-systolic murmur grade III out of VI at the apex with radiation to left mid-axillary line with no thrill. Rest of the examinations were unremarkable. Laboratory investigations showed microcytic hypochromic anemia related to the drop of iron profile and thrombocytosis, with positive anti-Saccharomyces cerevisiae antibodies for Crohn's disease and negative antibodies for infliximab (Table ). ECG and Holter 24 hours monitor were done and showed intermittent sinus tachycardia with no dysrhythmias (Figure ). Echocardiography showed dilated left ventricle with ejection fraction of 21% and fraction of shortening of 10% associated with severe mitral regurgitation (Figure and Video", "Doctor: Hi there, I see that you were diagnosed with Crohn's disease a couple of years ago.

Patient: Yes, that's correct.

Doctor: And you've been on a regular infliximab infusion regimen for maintenance of remission of the disease?

Patient: Yes, I get an infusion every month.

Doctor: I see. Well, you presented to the hospital with palpitations. Can you tell me more about that?



Patient: Yeah, they started about a year ago and have been getting worse over the past month.

Doctor: Were they intermittent at first?

Patient: Yes, they were.

Doctor: And have you been experiencing any easy fatigability or chest discomfort?

Patient: Yes, actually.

Doctor: Have you ever had cyanosis or chest pain with these symptoms?

Patient: No, I haven't.

Doctor: Do you have any family history of a similar condition or cardiac disease?

Patient: No, I don't.

Doctor: I see. Now, have you noticed if these symptoms occur during your infliximab transfusion?

Patient: Yes, they seem to manifest with the tachycardia during the infusion.

Doctor: I see. Well, we manage this transfusion reaction by slowing the rate and giving you premedication with steroids and antihistamines.

Patient: Okay.

Doctor: Now, upon examination, you appeared pale and underweight.

Patient: Yeah, I haven't been eating much lately.

Doctor: And you had sinus tachycardia with maintained blood pressure.

Patient: Yes, that's right.

Doctor: I also noticed on chest examination that you had a pan-systolic murmur grade III out of VI at the apex with radiation to the left mid-axillary line but no thrill.

Patient: Oh, okay.

Doctor: We did some laboratory investigations and found microcytic hypochromic anemia related to the drop of iron profile and thrombocytosis.

Patient: Okay.

Doctor: We also found positive anti-Saccharomyces cerevisiae antibodies for Crohn's disease and negative antibodies for infliximab.

Patient: Oh, I see.

Doctor: We did some further testing with an ECG and a 24-hour Holter monitor, which showed intermittent sinus tachycardia with no dysrhythmias.

Patient: Okay.

Doctor: And an echocardiography showed that your left ventricle was dilated with an ejection fraction of 21% and fraction of shorting of 10% associated with severe mitral regurgitation.

Patient: Wow, that sounds serious.

Doctor: Yes, it is. We will need to take some further action to treat this condition."

"In September 2020, a 42-year-old male was referred to our Department of Internal Medicine because of a finding in a chest X-ray. The patient was healthy with no previous hospitalizations and worked as a nurse at our institution. He was not taking any medications, had no smoking history, and was presenting no malignancy-related symptoms (fatigue, unintended weight loss, or changes in bowel habits). He had seen an anesthesiologist before being seen by a surgeon due to an inguinal hernia, a minor condition. The anesthesiologist noticed the pulmonary lesion. A chest X-ray showed a solitary pulmonary nodule in the right mid-lung that was 2 cm in diameter (Figure ). The patient was asymptomatic, as mentioned above, and had a previous chest X-ray that was normal.

In a physical examination, his temperature was 36.7degC, blood pressure was 138/78 mm Hg, heart rate was 76 beats per minute, and oxygen saturation was 98% in room air. In auscultation, heart and lung sounds were normal. Both oropharyngeal and abdominal examinations were normal, and he had no periodontal disease. The patient was admitted to the hospital for further investigation.

Blood tests were normal, with a white blood cell count of 9,430 leucocytes/mm<sup>3</sup> with 63% neutrophils, hemoglobin level of 153 g/L, and platelet count of 205 x 10<sup>9</sup>/L. C-reactive protein was 83 mg/dL (normal range: <5 mg/dL). A reverse-transcription polymerase chain reaction (RT-PCR) test was negative on hospitalization day 1 (Table ). As mentioned, a chest X-ray showed a solitary pulmonary nodule in the right upper lobe.

Our patient presented with a solitary pulmonary nodule, which raised the suspicion of a primary lung tumor or metastasis of unknown origin. For further radiological characterization and assessment of the pulmonary node, the patient underwent a thoracic CT scan, which revealed ground glass

opacities that", "Doctor: Good morning, how are you feeling today?

Patient: I'm okay, thank you.

Doctor: I see that you were referred to our Department of Internal Medicine due to a finding in a chest X-ray. Can you tell me more about that?

Patient: Yes, I had a chest X-ray and they found a solitary pulmonary nodule in the right mid-lung.

Doctor: I see. Were you experiencing any symptoms related to malignancy such as fatigue, unintended weight loss, or changes in bowel habits?

Patient: No, I was not.

Doctor: That's good to hear. I see that you had no previous hospitalizations and were not taking any medications. Do you have a smoking history?

Patient: No, I do not smoke.

Doctor: Okay, thank you. Now, let's move on to your physical examination. Can you tell me what your temperature, blood pressure, heart rate, and oxygen saturation were?

Patient: My temperature was 36.7degC, blood pressure was 138/78 mm Hg, heart rate was 76 beats per minute, and oxygen saturation was 98% in room air.

Doctor: Great, thank you. And how were your heart and lung sounds during auscultation?

Patient: They were normal.

Doctor: That's good to hear. Were there any abnormalities found during your oropharyngeal and abdominal examinations?

Patient: No, they were normal.

Doctor: Okay, thank you. Did you have any periodontal disease?

Patient: No, I did not.

Doctor: Thank you for letting me know. You were admitted to the hospital for further investigation. Can you tell me more about what happened during your hospitalization?

Patient: Blood tests were done, and they were normal except for a high C-reactive protein level. I also had a chest X-ray that showed the solitary pulmonary nodule.

Doctor: I see. Did you undergo any other tests while you were hospitalized?

Patient: Yes, I had a reverse-transcription polymerase chain reaction (RT-PCR) test, which was negative.

Doctor: Okay, thank you for letting me know. Based on your symptoms and test results, you presented with a solitary pulmonary nodule. This raises the suspicion of a primary lung tumor or metastasis of unknown origin. Did you undergo a thoracic CT scan for further assessment?

Patient: Yes, I did.

Doctor: And what did the CT scan reveal?

Patient: It revealed ground glass opacities.

Doctor: Okay, thank you for letting me know. Based on your results, we will need to conduct further tests to determine the cause of your symptoms. I will instruct you on follow-up requirements. If you have any questions, please feel free to ask.

(Patient's family is informed of the patient's death due to complications related to the pulmonary nodule)"

"A female patient aged 27 years presented with a slow-growing abdominal lump of nine months duration. There were no other symptoms except for fullness of the abdomen after taking food and weight loss. Clinical examination revealed large, non-tender, soft cystic swelling occupying the entire upper abdomen.

On radiological investigations, ultrasonogram (USG)-complex cystic mass with internal septation was present. Contrast-enhanced computed tomography (CECT) abdomen showed a large multiseptated cystic lesion occupying almost the entire abdomen and adhered to the pancreas with mass effect. The lesion was well defined, lobulated, hypodense in nature, and associated with main pancreatic duct dilatation. There was also portal vein thrombosis with portal cavernoma on the CECT abdomen (Figure ).

USG-guided FNAC revealed straw-colored aspirate with mature lymphocytes; no atypical cells were noted. Cyst amylase and carcinoembryonic antigen (CEA) were within the normal range (Figure ).

After complete preoperative workup, the patient underwent surgical exploration. On exploration, there was a large multiloculated cystic lesion extending through gastrosplenic omentum, pushing the

stomach up and transverse colon downwards with hundreds of cystic spaces containing lymphatic fluid (Figure ).

Cysts were decompressed, and the entire lesion was excised. The anterior surface of the pancreas was forming the base of the lesion. Postoperatively patient had continued lymphatic discharge from the abdominal drain, and the patient was discharged with it (Figure ).

Final histopathological examination showed unremarkable pancreatic tissue with attached lesion consisting of dilated lymphatic spaces with lymphatic follicles in the wall, with congested blood vessels and fibrocollagenous tissue with chronic inflammatory infiltrate. Cytocentrifuged smears from fluid show lymphocytes, and no malignant or atypical cell was seen. The patient was followed regularly in outpatient department, and drain output gradually decreased over two weeks and was removed (Figure ).", "Doctor: Good morning, how are you feeling today?

Patient: I'm okay, thank you.

Doctor: So, you are a 27-year-old female who presented with a slow-growing abdominal lump of nine months duration, is that correct?

Patient: Yes, that's right.

Doctor: Were there any other symptoms besides fullness of the abdomen after taking food and weight loss?

Patient: No, there were no other symptoms.

Doctor: During the clinical examination, was there any swelling or tenderness in the abdominal area?

Patient: Yes, there was a large, non-tender, soft cystic swelling occupying the entire upper abdomen.

Doctor: Okay, and on radiological investigations, a complex cystic mass with internal septation was present on the ultrasonogram, correct?

Patient: Yes, that's correct.

Doctor: Did the contrast-enhanced computed tomography (CECT) also show a large multiseptated cystic lesion occupying almost the entire abdomen and adhered to the pancreas with mass effect?

Patient: Yes, that's right.

Doctor: And there was also portal vein thrombosis with portal cavernoma on the CECT?

Patient: Yes, that's correct.

Doctor: The USG-guided FNAC revealed straw-colored aspirate with mature lymphocytes, and no atypical cells were noted. Were the cyst amylase and carcinoembryonic antigen (CEA) within the normal range?

Patient: Yes, they were within the normal range.

Doctor: After complete preoperative workup, the patient underwent surgical exploration, correct?

Patient: Yes, that's right.

Doctor: On exploration, there was a large multiloculated cystic lesion extending through gastrocolic omentum, pushing the stomach up and transverse colon downwards with hundreds of cystic spaces containing lymphatic fluid, is that correct?

Patient: Yes, that's correct.

Doctor: Cysts were decompressed, and the entire lesion was excised. The anterior surface of the pancreas was forming the base of the lesion. Postoperatively, did the patient have continued lymphatic discharge from the abdominal drain?

Patient: Yes, that's correct.

Doctor: The final histopathological examination showed unremarkable pancreatic tissue with attached lesion consisting of dilated lymphatic spaces with lymphatic follicles in the wall, with congested blood vessels and fibrocollagenous tissue with chronic inflammatory infiltrate. Cytocentrifuged smears from fluid show lymphocytes, and no malignant or atypical cell was seen. The patient was followed regularly in the outpatient department, and the drain output gradually decreased over two weeks and was removed. How are you feeling now?

Patient: I'm feeling much better now, thank you.

Doctor: That's great to hear. Please continue to follow up regularly with us to ensure that you are recovering well."

"A 58-year-old woman with a past medical history of diabetes and hypertension presented to our

clinic for evaluation of an enlarging left breast mass that she first noticed three years ago. She stated that the mass started to progressively increase in size in the past few months. She also reported a weight loss of 34 pounds over the last nine months. On physical exam, she had a palpable breast mass of approximately 3 centimeters in the tail of the left breast. Rest of physical exam was unremarkable. Review of labs showed WBC of 8.8/mL with absolute lymphocyte count of 4400/mL, hemoglobin of 12g/dl and platelet count of 316K. Prior mammograms and ultrasounds had revealed stable intramammary lymph nodes at the site of the present lesion on the left breast over the last three years with no suspicious calcifications or architectural distortions. There were no palpable ipsilateral or contralateral axillary lymphadenopathy. The mass was subsequently percutaneously biopsied. Histopathology showed diffuse atypical small lymphocytic cells (Figure ). Immunohistochemical staining revealed neoplastic lymphoma cells positive for CD20 (Figure ), CD5 (Figure ), CD23 (Figure ), PAX5, CD4, BCL2 and negative for CD3, CD10, BCL1, and BCL6. The final pathologic diagnosis was consistent with primary small lymphocytic lymphoma of the breast rather than chronic lymphocytic leukemia. This was unexpected. Bone marrow biopsy was done and histopathology revealed diffuse involvement with small lymphocytic lymphoma (Figure ). Fluorescence in situ hybridization (FISH) studies revealed trisomy 12 cytogenetic abnormality. Computed tomography (CT) imaging revealed extensive mediastinal lymphadenopathy (Figure ) and retroperitoneal lymphadenopathy (Figure ). The final clinicopathologic diagnosis was small lymphocytic lymphoma (Stage 4) with breast and bone marrow involvement. She was subsequently treated with the FCR regimen comprising of fludarabine, cyclophosphamide and rituximab which resulted in clinical and radiologic remission. The breast mass was no longer palpable and repeat CT", "Doctor: Good morning, Mrs. Johnson. I see from your past medical history that you have diabetes and hypertension.

Patient: Yes, that's correct.

Doctor: You presented to our clinic for evaluation of an enlarging left breast mass that you first noticed three years ago. Can you tell me more about that?

Patient: Yes, the mass started to progressively increase in size in the past few months.

Doctor: You also reported a weight loss of 34 pounds over the last nine months. Is that correct?

Patient: Yes, that's right.

Doctor: On physical exam, you had a palpable breast mass of approximately 3 centimeters in the tail of the left breast. The rest of your physical exam was unremarkable.

Patient: Okay.

Doctor: Review of your labs showed a WBC of 8.8/mL with an absolute lymphocyte count of 4400/mL, hemoglobin of 12g/dl, and platelet count of 316K.

Patient: Okay.

Doctor: Your prior mammograms and ultrasounds had revealed stable intramammary lymph nodes at the site of the present lesion on the left breast over the last three years with no suspicious calcifications or architectural distortions. There were no palpable ipsilateral or contralateral axillary lymphadenopathy.

Patient: Okay.

Doctor: The mass was subsequently percutaneously biopsied and histopathology showed diffuse atypical small lymphocytic cells.

Patient: Oh no.

Doctor: Immunohistochemical staining revealed neoplastic lymphoma cells positive for CD20, CD5, CD23, PAX5, CD4, and BCL2, and negative for CD3, CD10, BCL1, and BCL6. The final pathologic diagnosis was consistent with primary small lymphocytic lymphoma of the breast rather than chronic lymphocytic leukemia.

Patient: What does that mean?

Doctor: This means that you have small lymphocytic lymphoma (Stage 4) with breast and bone marrow involvement. Bone marrow biopsy was done and histopathology revealed diffuse involvement with small lymphocytic lymphoma. Fluorescence in situ hybridization (FISH) studies revealed trisomy 12 cytogenetic abnormality. Computed tomography (CT) imaging revealed extensive mediastinal lymphadenopathy and retroperitoneal lymphadenopathy.

Patient: What are the next steps?



Doctor: You will need to be treated with the FCR regimen comprising of fludarabine, cyclophosphamide, and rituximab which resulted in clinical and radiologic remission. The breast mass was no longer palpable and repeat CT imaging showed no evidence of disease.

Patient: Thank you, doctor.

Doctor: You're welcome. Please come back for follow-up appointments to monitor your condition."

"This is a case of 41-month-old infant girl who presented with weight loss and intractable diarrhea associated with oral feeding. She is a product of full-term pregnancy, delivered through spontaneous vaginal delivery, with a birth weight of 2 kg, and she did not require admission to the neonatal intensive care unit (NICU). The pregnancy was uneventful. Parents are first-degree cousins, and the patient has two older healthy siblings.

At the age of six months, she presented to another hospital afebrile with a loss of weight and had watery, non-bloody diarrhea, six to seven times per day. Both endoscopy and biopsy from the duodenum were normal according to the mother. The patient was initially misdiagnosed with cow milk protein allergy, so hypoallergenic formula was given but there was no improvement, then after two months, she was switched to amino acid-based infant formula 200 ml five times per day. In the beginning, there was an improvement, but with time, she stopped gaining weight again. At the age of 10 months, she came to the gastroenterology and genetics teams at our facility with chronic diarrhea, poor growth, and abnormal hair. Her weight and height were 5.30 kg (<3rd percentile) and 61 cm (<3rd percentile), respectively. The diagnosis of THES was confirmed by whole exons sequence (WES) analysis, which identified the homozygous variant (c.1201G > A) p. (Glu401Lys) in the SKIV2L gene. Upon literature review, we did not find the mentioned variant mutation in any previous literature (Table ).

At 12 months of age, she was admitted for dehydration and nasogastric tube (NGT) feeding due to poor weight gain. Her body measurements upon admission were 5.64 kg (<3rd percentile) for the weight, and her height was 63 cm (<3rd percentile). Upon examination, she had some dysmorphic features such as a depressed nasal bridge", "Doctor: Hello, how can I help you today?

Patient: I've been having some problems with my weight and diarrhea.

Doctor: Can you tell me more about your symptoms? When did they first appear?

Patient: I presented with weight loss and intractable diarrhea associated with oral feeding when I was 41 months old.

Doctor: Okay, and were you a product of a full-term pregnancy and delivered through spontaneous vaginal delivery?

Patient: Yes, that's correct. And I didn't require admission to the neonatal intensive care unit (NICU).

Doctor: I see. And do you have any family history of medical conditions?

Patient: Well, my parents are first-degree cousins, but my two older siblings are healthy.

Doctor: Thank you for letting me know. At six months of age, you had watery, non-bloody diarrhea, is that correct?

Patient: Yes, that's right.

Doctor: And were you initially misdiagnosed with cow milk protein allergy?

Patient: Yes, I was. But even after switching to hypoallergenic formula, there was no improvement.

Doctor: I see. And then you were switched to amino acid-based infant formula and there was some improvement, but with time, you stopped gaining weight again?

Patient: Yes, that's correct.

Doctor: At 10 months of age, you came to our facility with chronic diarrhea, poor growth, and abnormal hair. And the diagnosis of THES was confirmed by whole exons sequence (WES) analysis?

Patient: Yes, that's right. The homozygous variant (c.1201G > A) p. (Glu401Lys) in the SKIV2L gene was identified.

Doctor: Thank you for confirming that. And at 12 months of age, you were admitted for dehydration and nasogastric tube (NGT) feeding due to poor weight gain. Is that correct?

Patient: Yes, that's correct.

Doctor: Thank you for letting me know. And upon examination, you had some dysmorphic features such as a depressed nasal bridge?

Patient: Yes, that's right."

"A 49-year-old female patient was admitted with complaints of fever, abdominal bloating, and losing weight for one year. She was diagnosed with cirrhosis and was treated at a local hospital. Three months ago, the patient deteriorated; thus, peripheral blood test, bone marrow (BM) aspiration, and bone marrow biopsy were performed. The results showed lymphocytosis in the marrow. Therefore, the patient was referred to our center. On physical examination, she had a fever (about 38degC), mild pallor, swollen legs, mild hepatomegaly, and huge splenomegaly. There was no purpura and no peripheral lymphadenopathy. There were no clinical infections and no joint damage.

Complete hemogram revealed hemoglobin of 117 g/L, platelet count of 82 G/L, total leukocyte count of 12.63 G/L with 65% lymphocytes, and 30% neutrophils. The peripheral blood smear showed lymphocytosis and thrombocytopenia (Figure ). The lymphocytes were predominantly large lymphocytes, which were having abundant cytoplasm containing coarse azurophilic granules and clumped chromatin. Her biochemical examination was fairly normal. Serological examination revealed no evidence of HIV, HBV, HCV, EBV, CMV, or dengue infection. The results of cultures of fungi and bacteria in blood were negative. The ultrasound of the abdomen confirmed mild hepatomegaly and huge splenomegaly.

Bone marrow imprint smears showed 33% lymphocytes (lymphocytosis) (Figure ). The lymphocytes displayed a medium to large size with a moderate amount of cytoplasm containing numerous azurophilic granules and a round nucleus with clumped chromatin. Bone marrow biopsy displayed an increasing level of cell density and lymphocytic infiltration in hematopoietic compartments with nonuniform size and similar morphology lymphocytes seen in peripheral smear (Figure ). The erythroid, myeloid, and megakaryocytic series were suppressed.

Cytogenetics revealed a normal karyotype. Flow cytometric analysis of the bone marrow showed that 49.5% of cells were of lymphoid origin. These lymphoid cells were positive for", "Doctor: Hello, Mrs. Smith. How are you feeling today?

Patient: Hmm, not so good, doctor. I've been having fever, abdominal bloating, and I've lost a lot of weight in the past year.

Doctor: I see. When were you admitted to the hospital?

Patient: About a year ago. I was diagnosed with cirrhosis and was treated at a local hospital.

Doctor: Did your condition deteriorate after that?

Patient: Yes, doctor. About three months ago, my condition got worse, and I was referred to your center.

Doctor: Okay, let's do a physical examination. Can you tell me if you have any purpura or peripheral lymphadenopathy?

Patient: No, doctor. I don't have those symptoms.

Doctor: I see. I noticed that you have mild pallor, swollen legs, mild hepatomegaly, and huge splenomegaly. We'll need to run some tests to determine the cause of your symptoms. We'll start with a complete hemogram.

Patient: Okay, doctor.

Doctor: The results of your complete hemogram show a hemoglobin level of 117 g/L, a platelet count of 82 G/L, and a total leukocyte count of 12.63 G/L. Your lymphocyte count is at 65%, and your neutrophil count is at 30%. We also found lymphocytosis in your peripheral blood smear.

Patient: What does that mean, doctor?

Doctor: Lymphocytosis is a condition where there are too many lymphocytes in your blood. Your lymphocytes are predominantly large lymphocytes with abundant cytoplasm containing coarse azurophilic granules and clumped chromatin.

Patient: Hmm, I see.

Doctor: We also did a bone marrow aspiration and biopsy, which showed lymphocytosis and an increasing level of cell density and lymphocytic infiltration in hematopoietic compartments with nonuniform size and similar morphology lymphocytes seen in peripheral smear. The erythroid, myeloid, and megakaryocytic series were suppressed.

Patient: Okay, doctor. What's next?

Doctor: We also did a serological examination and cultures of fungi and bacteria in your blood, which were both negative. We also did an ultrasound of your abdomen, which confirmed mild hepatomegaly and huge splenomegaly.

Patient: I see.

Doctor: We also did a cytogenetic test and flow cytometric analysis of your bone marrow, which showed a normal karyotype and 49.5% of cells were of lymphoid origin, respectively. These lymphoid cells were positive for...

Patient: Doctor, what does all of this mean? Am I going to be okay?

Doctor: Mrs. Smith, based on your test results, we have found that you have a type of cancer called chronic lymphocytic leukemia. We will need to start treatment right away to manage your condition. I will explain the treatment options to you and answer any questions you may have. If you have any family members with you, I would also like to speak with them about your condition and treatment plan.

(Family members enter the room and the doctor explains the patient's condition and treatment plan to them.)"

"A 34-year-old man with no previous history of chronic illness and a non-smoker presented with a history of headache, fatigue, diarrhea, vomiting, and insomnia for three days. During the initial examination, he was conscious and alert. His blood pressure (BP) was 111/71, pulse rate (PR) 40, respiration rate (RR) 14/min, body temperature 36.7, and oxygen saturation (SpO2) 96% under ambient oxygen conditions. The patient had a clear chest, without any crepitating sounds in the cardiovascular system (CVS; S1+S2+0). An abdominal exam showed a soft and lax abdomen, and both lower limbs were normal. The status of the central nervous system (CNS) was normal, all cranial nerves were intact, and chest X-ray and chest CT scans were performed (Figures -). EKG showed sinus rhythm, first-degree heart block with prolonged QT interval, and bigeminy (Figure ). Echo revealed a normal echo study (Figure ). General clinical and blood parameters of the patients are shown in Table . Due to the COVID-19 pandemic, all patients reporting to the hospital with fever were routinely tested with the PCR test for COVID-19. Also, a nasopharyngeal swab was tested by RT-PCR and proved to be positive for SARS-CoV-2.", "Doctor: Hi, how are you feeling today?

Patient: I'm not feeling too well. I have a headache, fatigue, diarrhea, vomiting, and insomnia.

Doctor: Okay, let's take a look. Can you tell me about your medical history? Have you ever had any

chronic illness before?

Patient: No, I've never had any chronic illness before.

Doctor: That's good to know. You mentioned that you've been experiencing these symptoms for three days. When did they start?

Patient: Three days ago.

Doctor: During the examination, you were conscious and alert. Your blood pressure was 111/71, pulse rate 40, respiration rate 14/min, body temperature 36.7, and oxygen saturation 96% under ambient oxygen conditions. Did you notice any difficulty breathing or shortness of breath?

Patient: No, I didn't.

Doctor: Okay, that's good. During the abdominal exam, I noticed that your abdomen was soft and lax. Did you experience any pain or discomfort in your abdomen?

Patient: No, I didn't.

Doctor: That's good to know. Your chest X-ray and chest CT scans came back normal. However, your EKG showed sinus rhythm, first-degree heart block with prolonged QT interval, and bigeminy. Did you experience any discomfort or chest pain?

Patient: No, I didn't.

Doctor: Alright. Your echo revealed a normal echo study. Your general clinical and blood parameters are all within normal range. However, your nasopharyngeal swab came back positive for SARS-CoV-2. Due to the COVID-19 pandemic, all patients reporting to the hospital with fever were routinely tested with the PCR test for COVID-19.

Patient: Okay.

Doctor: I'm going to prescribe you some medication to help with your symptoms. Please make sure to follow up with your primary care physician and self-isolate at home for at least 14 days. If your symptoms worsen, please come back to the hospital immediately. Do you have any questions or concerns?

Patient: No, I think I understand. Thank you, doctor.

Doctor: You're welcome. Take care of yourself. If you need anything, don't hesitate to contact us."

"Another 34-year-old male patient who smoked visited the hospital with a history of fever, runny nose, and diarrhea for seven days. There was no complaint of shortness of breath or chest pains. The patient was tested for central nervous system (CNS) response and reflexes and was alert and conscious. Examination of clinical vitals parameters was performed and recorded as BP: 126/76; PR: 43; RR: 21/min; body temperature: 36.6degC; oxygen saturation (SpO2): 98%; CVS: S1+S2+0; chest bilateral vesicular breathing, and no lower limbs edema. EKG reports showed sinus bradycardia with a prolonged PR interval and QT interval; a U wave was observed in V1 (Figure ). Chest X-ray and chest CT showed unremarkable findings (Figures -). Echocardiography also revealed a normal echo study (Figure ). General clinical and blood parameters of the patients are provided in Table .

Patient 2 was suspected of COVID-19 due to a non-symptomatic fever. The nasal swab of Patient 2 was tested by the same procedure as for Patient 1 and was SARS-CoV-2 positive.

#### Treatment

Both patients were admitted to the isolation room and treated conservatively without hydroxychloroquine and azithromycin. They were administered 1 mg IV atropine and showed a transient change from bradyarrhythmia to sinus rhythm.", "Doctor: Good morning, how are you feeling today?

Patient: I'm feeling quite unwell, doctor. I've been having a fever, runny nose, and diarrhea for the past seven days.

Doctor: Okay, I'll take your history. Have you experienced any shortness of breath or chest pains?

Patient: No, I haven't.

Doctor: Great, let's check your CNS response and reflexes. Are you alert and conscious?

Patient: Yes, I am.

Doctor: Good, let's examine your vitals parameters. Your BP is 126/76, PR is 43, and RR is 21/min. Your body temperature is 36.6degC, and your oxygen saturation is 98%. I also noticed that you have bilateral vesicular breathing and no lower limbs edema.

Patient: Hmm, okay.

Doctor: I see that your EKG reports show sinus bradycardia with a prolonged PR interval and QT interval. A U wave was observed in V1. Your Chest X-ray and chest CT showed unremarkable findings. Your echocardiography also revealed a normal echo study.

Patient: Uh-huh.

Doctor: Your general clinical and blood parameters are provided in this table. Based on your symptoms, you were suspected of COVID-19. Your nasal swab was tested, and it was SARS-CoV-2 positive.

Patient: Oh no, that's not good news.

Doctor: Don't worry, we will admit you to the isolation room and treat you conservatively without hydroxychloroquine and azithromycin. We will administer 1 mg IV atropine to help with your bradyarrhythmia.

Patient: Okay, thank you, doctor.

Doctor: You're welcome. We will monitor you closely and make sure you are comfortable. If you experience any changes, please inform us immediately."

"A 50-year-old Indian gentleman, a known case of diabetes and an active smoker, presented with a right eye painless inferior visual field defect upon waking up from sleep. At presentation, his right and left eyes' visual acuity (VA) were 6/24 and 6/9, respectively. Anterior segment examination was unremarkable in both eyes. Fundoscopy revealed swollen right optic disc with peripapillary splinter hemorrhage (Figure ). Humphrey visual field (HVF) showed right inferior altitudinal scotoma. Computed tomography of the brain and orbit proceeded to rule out compressive lesions. Thus, a diagnosis of right eye NAION was made. Three months later, he complained of a worsening visual field of the right eye. VA remained static with the right eye (VA 6/24) and left eye (VA 6/9). Examination showed right eye relative afferent pupillary defect (RAPD) with impaired red saturation and light brightness. His right optic disc was pale; however, the left was hyperemic and swollen with peripapillary splinter hemorrhage (Figure ). HVF showed right eye tunnel vision while the left eye displayed inferior arcuate scotoma (Figure ). The patient was admitted for further investigations and was co-managed by the neuro-medical team. The visual evoked potential test was suggestive of



right optic neuropathy. Serum glucose and serum hemoglobin A1c (HbA1c) levels were elevated, measuring 13.9 mmol/L and 9.1%, respectively. Serum total cholesterol (4.6 mmol/L) and low-density lipoprotein (LDL) cholesterol (2.1 mmol/L) were normal, but triglyceride level was high (3.3 mmol/L). Full blood count, erythrocyte sedimentation rate (2 mm/hour), and C-reactive protein (0.7 mg/dL) were all within normal limits. Serum anti-aquaporin-4, anti-"Doctor: Hello, how are you feeling today?

Patient: I'm not feeling well, doctor. I have a painless inferior visual field defect in my right eye.

Doctor: I see. Can you tell me more about your medical history? Are you diabetic or a smoker?

Patient: Yes, I have diabetes and I'm an active smoker.

Doctor: Okay, that information is important. At presentation, your right eye had a visual acuity of 6/24 and your left eye was 6/9. I conducted an anterior segment examination and it was unremarkable in both eyes.

Patient: Hmm.

Doctor: However, your fundoscopy showed a swollen right optic disc with peripapillary splinter hemorrhage. Your Humphrey visual field showed a right inferior altitudinal scotoma. We proceeded with a computed tomography of the brain and orbit to rule out compressive lesions and diagnosed you with right eye NAION.

Patient: Okay.

Doctor: Three months later, you complained of a worsening visual field in your right eye. Your VA remained static with the right eye at 6/24 and left eye at 6/9. Examination showed right eye relative afferent pupillary defect with impaired red saturation and light brightness. Your right optic disc was pale, however, the left was hyperemic and swollen with peripapillary splinter hemorrhage. HVF showed right eye tunnel vision while the left eye displayed inferior arcuate scotoma. We admitted you for further investigations and co-managed you with the neuro-medical team. The visual evoked potential test was suggestive of right optic neuropathy.

Patient: Oh no.

Doctor: Your serum glucose and serum hemoglobin A1c levels were elevated, measuring 13.9

mmol/L and 9.1%, respectively. Your serum total cholesterol and low-density lipoprotein cholesterol were normal, but your triglyceride level was high. Your full blood count, erythrocyte sedimentation rate, and C-reactive protein were all within normal limits.

Patient: Okay, what does that all mean?

Doctor: It means that your diabetes and smoking have contributed to the development of NAION, which has caused extensive damage to your optic nerve. This is a serious condition that requires ongoing monitoring and management.

Patient: What do I need to do next?

Doctor: We need to closely monitor your eyes and blood sugar levels. You'll need to make some lifestyle changes to control your diabetes and stop smoking. We'll also prescribe medications to help manage your condition."

"We present the case of a 30-month-old male who was brought to the family medicine clinic with a complaint of abdominal bloating and persistent diarrhea after every feeding for four months. His stools were foul-smelling and occurred more than four times a day. The diarrhea was associated with a failure to gain weight. The parents reported that the child has a normal appetite with no history of vomiting or feeding intolerance. There was no history of fever, night sweats, rash, cough, or joint pain. The child did not have any recent sick contact. The patient was seen by several general practitioners for the same complaint, but no diagnosis was obtained.

The patient had an unremarkable past medical history. He did not have any previous hospital admissions. He had no history of previous surgeries. He does not take any medications and was not known to have any food or drug allergies. Regarding the perinatal history, the child was full term with a birth weight of 3.5 kg. The labor and delivery were unremarkable for any complications. The child was up to date with his vaccination schedule. Regarding the developmental history, the child reached the developmental milestones at the appropriate ages, and there was no parental concern regarding his development. The social history was noncontributory. There was no history of diseases running in the family. The child was not born of a consanguineous marriage.

Upon examination, the child was awake and alert and did not appear sick. No dysmorphic features

were noted. The patient was below the second standard deviations for weight and height. He appeared pale, and there was no scleral icterus. His vital signs were as follows: heart rate of 90 bpm, blood pressure of 80/52 mmHg, respiratory rate of 22 bpm, and temperature of 36.8degC. Abdominal examination revealed a soft and non-tender abdomen with no organomegaly and had normal bowel sounds. Neurological examination, including hearing and vision tests", "Doctor: Hello, I'm Dr. Smith. What brings you here today?

Patient: Hi, I've been having a complaint of abdominal bloating and persistent diarrhea after every feeding.

Doctor: How long has this been going on for?

Patient: It's been going on for four months now.

Doctor: That's quite a while. How often do you experience the diarrhea?

Patient: More than four times a day.

Doctor: Have you noticed any other symptoms?

Patient: My stools are foul-smelling and I've had a failure to gain weight.

Doctor: Have you had a normal appetite?

Patient: Yes, I have a normal appetite with no history of vomiting or feeding intolerance.

Doctor: Have you experienced any fever, night sweats, rash, cough, or joint pain?

Patient: No, I haven't had any of those symptoms.

Doctor: Have you had any recent sick contact?

Patient: No, I haven't had any recent sick contact.

Doctor: I see. Have you seen any other doctors for this complaint?

Patient: Yes, I've seen several general practitioners, but no diagnosis was obtained.

Doctor: Okay, let's move on to your past medical history. Have you had any hospital admissions or surgeries before?

Patient: No, I haven't had any hospital admissions or surgeries.

Doctor: Do you take any medications or have any food or drug allergies?

Patient: No, I don't take any medications and I'm not known to have any food or drug allergies.

Doctor: That's good to know. Were you born full term?

Patient: Yes, I was born full term with a birth weight of 3.5 kg.

Doctor: Were there any complications during your labor and delivery?

Patient: No, there were no complications during my labor and delivery.

Doctor: Have you been up to date with your vaccination schedule?

Patient: Yes, I have been up to date with my vaccination schedule.

Doctor: That's great. Have your parents expressed any concerns about your development?

Patient: No, there have been no parental concerns regarding my development.

Doctor: Okay, let's move on to your social history. Is there anything you think I should know?

Patient: No, there's nothing I think you should know.

Doctor: Has anyone in your family had any diseases running in the family?

Patient: No, there's no history of diseases running in the family.

Doctor: Thank you for the information. Now, I'd like to examine you.

Patient: Okay.

Doctor: You appear awake and alert. I don't see any dysmorphic features. You're below the second standard deviations for weight and height. You appear pale, and there's no scleral icterus. Your vital signs are heart rate of 90 bpm, blood pressure of 80/52 mmHg, respiratory rate of 22 bpm, and temperature of 36.8degC. Your abdominal examination reveals a soft and non-tender abdomen with no organomegaly and normal bowel sounds. Your neurological examination, including hearing and vision tests, is normal.

Patient: Okay.

Doctor: Based on your symptoms and examination, I'm going to order some tests to help us make a diagnosis.

Patient: Okay, what tests will you order?

Doctor: I'm going to order some blood tests and stool samples to check for any infections or other issues that may be causing your symptoms.

Patient: Okay.

Doctor: I'll have the results in a few days. In the meantime, I want you to try to stay hydrated and avoid any foods that may exacerbate your symptoms.

Patient: Okay, I'll do that.

Doctor: If you start experiencing any fever, night sweats, rash, cough, or joint pain, please let me know immediately.

Patient: Okay, I will.

Doctor: Thank you for coming in today. I'll be in touch with you about your test results.

Patient: Thank you, doctor.

(If the patient dies)

Doctor: I'm sorry to inform you that despite our efforts, your child has passed away. We did everything we could to try and save him, but his condition was too severe.

Family: (sobbing) Thank you for everything you did for him.

Doctor: Of course, please let me know if you need any support during this difficult time."

"A 27-year-old male patient was admitted to a high-complexity institution due to a five-day clinical picture consisting of additive, symmetrical polyarticular pain, located in the wrists, knees, and left shoulder without other associated symptoms. The joint pain was continuous, permanent, and of great intensity that caused limitation of movement, mainly in the hands. In the systems review, no urinary or gastrointestinal symptoms were documented before the onset of joint symptoms. As the only relevant antecedent, he referred mild respiratory infection by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) confirmed by reverse transcription-polymerase chain reaction the month before hospitalization. The initial clinical examination confirmed the presence of bilateral carpal synovitis, left suprapatellar synovitis, and synovitis of the sternoclavicular joints (Figures , , ).

Magnetic resonance imaging of the different compromised anatomical compartments was performed, presenting as additional findings the presence of bursitis of the lateral collateral ligament of the left lower limb and a peritendinous inflammatory process of the triangular fibrocartilage in the right wrist. Mild lymphopenia associated with a marked elevation of acute-phase reactants was

documented in laboratory studies. Differential diagnoses of infectious etiology were sought, including a positive fourth-generation HIV enzyme-linked immunosorbent assay with a subsequent CD4 count of 98 cells/mm<sup>3</sup> and a viral load of 459,000 copies/mL. Treatment with prednisolone at a dose of 1 mg/kg and sulfasalazine (1 g per day) was initiated and no significant improvement in joint symptoms was noted despite sequential changes from disease-modifying antirheumatic drugs (DMARDs) such as methotrexate and leflunomide. Subsequently, the patient achieved a complete joint response when antiretroviral therapy (abacavir, dolutegravir/lamivudine) was initiated, thereby achieving a response to therapy resulting in gradual reduction of glucocorticoid doses and tapering to maintenance therapy solely with sulfasalazine. The description of the most", "Doctor: Good morning, how are you feeling today?

Patient: I'm feeling a lot of pain in my wrists, knees, and left shoulder.

Doctor: I see. When did the pain start?

Patient: It's been going on for five days now.

Doctor: That's quite a long time. Have you experienced any other symptoms?

Patient: No, just the pain.

Doctor: Okay. I'm going to admit you to the institution for further evaluation.

Patient: Alright.

Doctor: We've done some tests and found that you have symmetrical polyarticular pain. We also found synovitis in your joints.

Patient: What does that mean?

Doctor: It means that the lining of your joints is inflamed. This can cause continuous pain and limitation of movement.

Patient: I see.

Doctor: We also did some Magnetic Resonance Imaging and found some additional findings, including bursitis of the lateral collateral ligament of the left lower limb and a peritendinous inflammatory process of the triangular fibrocartilage in your right wrist.

Patient: That sounds serious.

Doctor: We tested for infectious etiology, including a positive fourth-generation HIV enzyme-linked immunosorbent assay. Your CD4 count was 98 cells/mm<sup>3</sup> and your viral load was 459,000 copies/mL.

Patient: Oh no.

Doctor: We've started you on treatment with prednisolone and sulfasalazine, but we haven't seen much improvement in your joint symptoms. We tried different disease-modifying antirheumatic drugs like methotrexate and leflunomide, but they didn't work either.

Patient: What can we do?

Doctor: We started you on antiretroviral therapy with abacavir, dolutegravir/lamivudine. This treatment resulted in a complete joint response, so we were able to gradually reduce your glucocorticoid doses and taper you to maintenance therapy solely with sulfasalazine.

Patient: That's good news.

Doctor: Yes, it's important to continue with your therapy to maintain your joint response. We'll monitor your progress and make adjustments as needed.

Patient: Okay, thank you, doctor.

Doctor: You're welcome. If you have any questions, don't hesitate to ask. We'll also have a discussion with your family about your progress."

"A 43-year-old-male with no known medical problems presented from an outside hospital with concern for intraabdominal hemorrhage. He was in an MVC three weeks prior and presented with complaints of right upper quadrant abdominal pain, left-sided chest pain, nausea, and vomiting. A CT scan showed fluid in the lesser sac, suggestive of pancreatic hemorrhage, so he was transferred to the University of Kentucky Medical Center for further management (Figure ).

Interventional radiology was consulted, and celiac angiogram showed an arterio-portal fistula in the liver which was embolized with 900 um particles Embozene (Palo Alto, CA: Varian Medical Systems, Inc.), as well as a few tiny rounded foci of contrast enhancement in the spleen which was managed conservatively without embolization (Figure ). Following the procedure, the patient developed an elevated white blood cell (WBC) count and increased abdominal distension. A repeat CT scan four

days later showed an increase in the size of the lesser sac hematoma and a pseudoaneurysm in the anterior spleen (Figure ). Surgery was discussed with the patient, which he elected against and preferred to leave the hospital.

He returned to the hospital two weeks later with decreased appetite, melena, hematochezia, abdominal pain, and weakness. He was found to be anemic with a hemoglobin of 6.4 g/dL (down from 7.8 g/dL). CT scan and angiographic images revealed worsening diffuse multifocal parenchymal perfusion abnormalities and innumerable punctate foci of contrast pooling in the spleen, compatible with high-grade splenic injury and the Seurat spleen angiographic sign (Figures , ).

Coil embolization of the splenic artery was performed with postembolization angiography showing no antegrade flow through the splenic artery, significantly decreased opacification of the previously noted intraparenchymal pseudoaneurysms, and opacification of the spleen via collaterals (Figure ).

CT scan one month", "Doctor: Hello, how are you feeling today?

Patient: I've been better, I've been having some pain in my abdomen and weakness.

Doctor: I see. Can you tell me about your medical problems before this?

Patient: I didn't have any medical problems before, but I was in a car accident three weeks ago.

Doctor: Okay. And when you presented to the outside hospital, what was your concern?

Patient: I was worried about intraabdominal hemorrhage.

Doctor: And what were your symptoms when you presented?

Patient: I had right upper quadrant abdominal pain, left-sided chest pain, nausea, and vomiting.

Doctor: I see. And did they do a CT scan?

Patient: Yes, they did a CT scan and found fluid in the lesser sac, suggestive of pancreatic hemorrhage.

Doctor: Okay. So they transferred you to the University of Kentucky Medical Center for further management?

Patient: Yes, that's right.

Doctor: And did they consult interventional radiology?



Patient: Yes, they did.

Doctor: And what did the celiac angiogram show?

Patient: It showed an arterio-portal fistula in the liver which was embolized, as well as a few tiny rounded foci of contrast enhancement in the spleen which was managed conservatively.

Doctor: I see. And did you have any complications after the procedure?

Patient: Yes, I developed an elevated white blood cell count and increased abdominal distension.

Doctor: And what did the repeat CT scan show?

Patient: It showed an increase in the size of the lesser sac hematoma and a pseudoaneurysm in the anterior spleen.

Doctor: I see. Did you discuss surgery with the doctors?

Patient: Yes, they did discuss surgery with me, but I elected against it and preferred to leave the hospital.

Doctor: Okay. And when did you return to the hospital?

Patient: I returned two weeks later with decreased appetite, melena, hematochezia, abdominal pain, and weakness.

Doctor: And what did they find when they examined you?

Patient: They found that I was anemic with a hemoglobin of 6.4 g/dL (down from 7.8 g/dL).

Doctor: I see. And what did the CT scan and angiographic images reveal?

Patient: They revealed worsening diffuse multifocal parenchymal perfusion abnormalities and innumerable punctate foci of contrast pooling in the spleen, compatible with high-grade splenic injury and the Seurat spleen angiographic sign.

Doctor: Okay. And what was done to treat the splenic injury?

Patient: Coil embolization of the splenic artery was performed.

Doctor: And how did the postembolization angiography look?

Patient: It showed no antegrade flow through the splenic artery, significantly decreased opacification of the previously noted intraparenchymal pseudoaneurysms, and opacification of the spleen via collaterals.

Doctor: I see. Well, we will need to keep a close eye on you and follow up with some tests."

"A 15-year-old girl presented with chronic complaints of nasal obstruction and hyposmia on the left side. The patient had nasal obstruction symptoms for 6 months; before which she was asymptomatic. She was taking self-administered medications without relief. She had no history of maxillo-facial surgery or trauma in the past. She had no relevant family history or congenital anomalies. Upon clinical examination of the nose, there was a bump along the floor of the left nasal cavity, and her intraoral dentition appeared normal.

A plain radiograph of the paranasal sinus and nasal cavity was performed which showed a radiopaque focus in the left nasal cavity (Figure ).

The CT scan of paranasal sinuses showed a tooth-like bony structure with a pulp cavity in the hard palate extending into the left inferior nasal cavity and a deviated nasal septum with convexity to the left (Figures -); a shape resembling a canine with a relatively smaller size.

Orthopantomogram showed a tooth-like radiopaque structure (white arrow) (Figure ). A three-dimensional computed tomography (3D CT) scan showed a tooth-like structure in the left nasal cavity (Figure ).

This intranasal tooth was supernumerary. Mild mucosal thickening was noted in the bilateral maxillary and sphenoid sinuses. No tooth-like structures were found on the right side. All other teeth appeared normal. The patient had complete resolution of nasal obstruction and hyposmia following endoscopic removal of the ectopic intranasal tooth.", "Doctor: Hello, how are you feeling today?

Patient: I'm not feeling well. I've been having nasal obstruction and hyposmia on the left side.

Doctor: How long have you had these complaints?

Patient: It's been bothering me for the last 6 months.

Doctor: Were you asymptomatic before that?

Patient: Yes, I was.

Doctor: Have you been taking any medications for it?

Patient: Yes, but they haven't provided any relief.

Doctor: Okay, let me take a closer look. Have you had any maxillo-facial surgery or trauma in the

past?

Patient: No, I haven't.

Doctor: Do you have any relevant family history or congenital anomalies?

Patient: No, not that I know of.

Doctor: Upon clinical examination of your nose, I found a bump along the floor of the left nasal cavity. Your intraoral dentition appeared normal. I recommend a radiograph of the paranasal sinus and nasal cavity.

Patient: Okay, what does that involve?

Doctor: It's a simple scan that will show us what's going on inside your nose.

Patient: Alright.

Doctor: The radiograph showed a radiopaque focus in the left nasal cavity, which we need to investigate further. I recommend a CT scan of the paranasal sinuses.

Patient: Why is that necessary?

Doctor: It will give us a more detailed picture of what's going on in your sinuses.

Patient: Okay, let's do it.

Doctor: The CT scan showed a tooth-like bony structure with a pulp cavity in the hard palate extending into the left inferior nasal cavity. There's also a deviated nasal septum with convexity to the left. You have a shape resembling a canine with a relatively smaller size.

Patient: What does that mean?

Doctor: You have an ectopic intranasal tooth that needs to be removed. We also found mild mucosal thickening in the bilateral maxillary and sphenoid sinuses. No tooth-like structures were found on the right side. All other teeth appeared normal.

Patient: How can the tooth be removed?

Doctor: We will perform endoscopic removal of the ectopic intranasal tooth.

Patient: Will that provide relief?

Doctor: Yes, it will. We expect complete resolution of your nasal obstruction and hyposmia following the procedure.

Patient: Okay, when should we schedule the procedure?

Doctor: As soon as possible. We need to remove the ectopic tooth to prevent further complications.

Patient's Family: Is there anything we can do to help?

Doctor: Thank you for your concern. Please make sure the patient follows all post-operative instructions and attends all follow-up appointments."

"A 56-year-old woman underwent laparoscopic bilateral salpingo-oophorectomy by the gynecological team. The patient has a history of total abdominal hysterectomy 20 years prior for endometriosis. Therefore, adhesions were obscuring the anatomy of the left ureter during her later surgery. In the early postoperative days, there was mild pain at the left iliac fossa and was managed with paracetamol and oral morphine. In the early period, there was no flank pain and no costovertebral angle tenderness. One week later, the patient presented to the emergency department with severe left iliac fossa pain associated with nausea and vomiting. Her investigations were within normal range, stable renal function, and normal inflammatory markers. Contrast CT showed extravasation of the contrast at the level of the left renal pelvis (Figure ) and ureteric dilatation down to the pelvic ureter (Figure ).

Considering the recent pelvic surgery, immediate diagnosis of left ureteric iatrogenic injury was concluded, and the patient was managed initially with urgent CT-guided nephrostomy insertion. The patient was in pain and an adequate nephrostogram was not performed during nephrostomy insertion. Therefore, three weeks posttraumatic injury, the patient underwent a proper antegrade nephrostogram. The contrast extravasated into the peritoneal cavity and there was no contrast passing into the distal left ureter (Figures , ). Therefore, a diagnosis of complete transection of ureteric injury was suspected. The nephrostomy was left in situ and the patient was planned for reconstructive surgery.

Eleven weeks posttraumatic injury, the patient was admitted for her planned surgery. Prior to the surgery, left retrograde study was performed and surprisingly the contrast went up to the left kidney with only annular stricture at the level of the injury (Figures , ). Therefore, a decision was taken for ureteroscopic dilatation of the stricture. The ureteroscopy showed a small annular stricture, less than

0.5 cm, that was passed easily over the safety guidewire and a ureteric stent, size 8 French," "Doctor: Good morning, how are you feeling today?

Patient: Hmm, not too good. I am still experiencing some pain.

Doctor: I see, well let's review your medical history. I understand you had a laparoscopic bilateral salpingo-oophorectomy. Can you tell me more about that?

Patient: Yes, I had that surgery because of endometriosis. I also had a total abdominal hysterectomy 20 years ago.

Doctor: Ah, I see. That history is important to note. During your recent surgery, there were some adhesions that made it difficult to see the left ureter.

Patient: Yes, I remember the doctors telling me that.

Doctor: In the days after surgery, you had some mild pain in the left iliac fossa, right?

Patient: Yes, but it was manageable with paracetamol and oral morphine.

Doctor: That's good. Did you experience any flank pain or costovertebral angle tenderness during that time?

Patient: No, I did not.

Doctor: Okay. Now, one week later, you went to the emergency department with severe left iliac fossa pain, nausea, and vomiting. Do you recall that?

Patient: Yes, I was really in a lot of pain.

Doctor: Your test results were within the normal range, including your renal function and inflammatory markers. However, the contrast CT showed extravasation of the contrast at the level of the left renal pelvis and ureteric dilatation down to the pelvic ureter.

Patient: Yes, I remember them telling me that.

Doctor: Based on your recent surgery, we concluded that you had a left ureteric iatrogenic injury. We initially managed it with urgent CT-guided nephrostomy insertion.

Patient: Okay.

Doctor: Unfortunately, during the nephrostomy insertion, you were in too much pain to complete an adequate nephrostogram.

Patient: Oh, I see.

Doctor: So, three weeks later, you underwent a proper antegrade nephrostogram, which revealed that there was no contrast passing into the distal left ureter. We suspected a complete transection of ureteric injury at that point.

Patient: Oh no.

Doctor: We left the nephrostomy in situ and planned for reconstructive surgery.

Patient: Okay.

Doctor: Eleven weeks after the traumatic injury, you were admitted for your planned surgery. We performed a left retrograde study and surprisingly, the contrast went up to the left kidney with only an annular stricture at the level of the injury.

Patient: Oh, that's good news!

Doctor: Yes, it was a pleasant surprise. We decided to perform a ureteroscopic dilatation of the stricture, which passed easily over the safety guidewire. We also placed a ureteric stent, size 8 French, to ensure proper function.

Patient: Okay, thank you for explaining all of that to me."

"A 76-year-old female with a past medical history of hypertension presented to the emergency department with persistent forehead swelling two months after recovering from COVID-19 infection. The patient was diagnosed with COVID-19 pneumonia in Egypt and completed a six-week course of dexamethasone. Per family, she also received multiple antibiotics during this time, the names and courses of which were unknown. She subsequently developed progressively tender frontal scalp swelling. Initial evaluation with otorhinolaryngology (ENT) in Egypt showed mucor-like organisms on pathology. She then came to the United States and was admitted for further evaluation. Her CT head showed evidence of multifocal sinusitis with breach of the inner and outer tables of the right frontal sinus with dural enhancement (Figure ). The CT scan also confirmed dehiscence of the inner table (Figure ). She was then empirically started on a course of Amphotericin for post-COVID mucormycosis. The patient underwent surgical debridement of significant underlying purulence with intraoperative cultures growing extended-spectrum beta-lactamase-producing *Escherichia coli* and

methicillin-resistant *Staphylococcus aureus*. Due to these culture results, the patient was initiated on vancomycin and meropenem with minimal improvement in edema. She underwent repeat surgical debridement two weeks later with cultures redemonstrating previously identified bacteria with rare *Pseudomonas aeruginosa* growth as well. The patient endorsed moderate improvement in frontal scalp tenderness following this debridement. She was thus discharged home on a six-week course of IV vancomycin through a peripherally inserted central catheter, PO levofloxacin, and PO posaconazole, with a plan to continue the latter until fungal cultures were finalized. Two weeks later, she presented to the outpatient clinic with new-onset generalized weakness. Initial workup revealed profound hypokalemia (potassium of 1.5 mEq/L; normal range 3.4-5.3 mEq/L) and acute kidney injury (creatinine of 3.03 mg/dL from baseline of 1.20 mg/dL). "Doctor: Good afternoon, how can I help you today?"

Patient: Hi doctor, I've been experiencing persistent forehead swelling for the past two months.

Doctor: Could you tell me a little bit about your past medical history, such as any medical conditions you have or medications you're taking?

Patient: Yes, I have hypertension and I recently recovered from a COVID-19 infection where I took dexamethasone.

Doctor: I see, and did you take any antibiotics during that time?

Patient: Yes, I did, but I'm not sure about the names or courses of them.

Doctor: Okay, thank you. Based on your symptoms, it's possible that you may have developed sinusitis. We'll need to do further evaluation to confirm.

Patient: Alright, what kind of evaluation will I need?

Doctor: We'll need to do a CT scan of your head to see what's going on. Depending on the results, we may need to start you on a course of antibiotics.

Patient: Okay, that sounds good. What are the possible side effects of the antibiotics?

Doctor: The most common side effects are nausea, diarrhea, and stomach pain. However, it's important to take the full course of antibiotics as prescribed to ensure that the infection is fully treated.

Patient: Understood. What happens if the antibiotics don't work?

Doctor: If the antibiotics don't work, we may need to consider surgery to remove the infected tissue. However, we'll cross that bridge if we come to it.

Patient: Alright, thank you for explaining everything to me.

Doctor: Of course, it's my pleasure. We'll get you set up for a CT scan and go from there."

"A 29-year-old male was brought to the emergency department following a car accident. It was reported that the wheel of a 5-ton water tanker rolled over his lower body as he was stepping into a car. Workup revealed a Glasgow Coma Scale (GCS) score of 15 with a pulse rate of 80 beats per minute and blood pressure of 90/60 mmHg. There was profuse bleeding due to a perineum injury. No fractures of the skull, cervical spine, and pelvis were detected in the X-rays. Urinary catheterization was performed without difficulty and there was no hematuria. No internal bleeding was seen during the abdominal ultrasound. The patient was immediately taken to the operating theatre for injury assessment after the replacement of fluid and blood.

#### Operative Findings and Procedure

While the patient was placed in the lithotomy position, the anterior displacement of the anus could be seen with a circular skin defect surrounding the region. The anus looked normal. There was a remaining 1 cm of normal perianal skin with no actual skin loss. Digital and proctoscopy examination showed an intact anorectum and its surrounding sphincters. Whereas exploring the wound revealed complete disruption of the posterior pelvic floor with lateral extensions into both gluteal regions and the right thigh. In addition, a hand could be passed behind the rectum and into the sacral promontory.

The case was associated with extensive venous bleeding with the absence of major arterial tears. It was managed by the insertion of multiple packs along with partial closure of the skin defect. A small incision was made to perform a defunctioning sigmoid colostomy. No intra-abdominal bleeding was reported. The packs were removed two days later without any bleeding complications. A total of 22 units of blood were required during the first 48 hours of admission. Figures , show the site of injury before and after treatment, respectively.



## Progress

Continuous follow-up examinations were done during the following", "Doctor: Hi there, how are you feeling today?

Patient: Not too good, still in a lot of pain.

Doctor: I understand. Can you tell me what happened to you?

Patient: I was in a car accident and the wheel of a water tanker rolled over my lower body.

Doctor: I see. According to your clinical note, your Glasgow Coma Scale score was 15, and your pulse rate was 80 beats per minute. Do you remember anything else?

Patient: My blood pressure was 90/60 mmHg, and I was bleeding a lot from a perineum injury.

Doctor: Yes, that's correct. We performed some tests, including X-rays, urinary catheterization, and abdominal ultrasound. Do you recall any difficulty with the catheterization or any hematuria?

Patient: No, there were no issues with the catheterization, and I didn't have any hematuria.

Doctor: Great. We took you to the operating theatre for injury assessment after replacing your fluid and blood. During the procedure, we found that you had a complete disruption of the posterior pelvic floor with lateral extensions into both gluteal regions and the right thigh. We also inserted multiple packs and made a small incision to perform a defunctioning sigmoid colostomy. Do you understand what that means?

Patient: Not really. Can you explain it to me?

Doctor: Of course. We had to insert multiple packs to stop the extensive venous bleeding caused by the injury. We also made a small incision to create an opening in your colon so that feces could be diverted away from the injured area while it heals.

Patient: Oh, I see. Is everything okay now?

Doctor: Yes, we removed the packs without any bleeding complications, and you required a total of 22 units of blood during the first 48 hours of admission. Now, we need to do some follow-up examinations to monitor your progress."

"A 44-year-old female patient had a car accident and she was thrown out from the car landing on a hard rock on her buttocks. In the district hospital, she was found to have a partial laceration of the

posterior perineum surrounding an intact anorectum. The bladder, urethra, and pelvis were not injured. A sigmoid colostomy was performed and then she was transferred to a tertiary hospital. She had a crescent-shaped wound surrounding the anus from the three to nine o'clock position. In addition, the anus was displaced forward towards the vagina. Digital and proctoscopy examinations showed an intact anorectum and surrounding sphincters.

## Progress

In this case, the patient's wound was subject to identical conservative management procedures as in the previously mentioned case. However, the patient was discharged from the hospital earlier as it was determined that she had adequate support from a daughter who has adequate experience in nursing. As the patient's wound was clean and in its proliferation stage of healing, the patient was instructed to perform daily irrigation using handheld bidets. She was scheduled for follow-up appointments every three weeks, which she attended punctually. Consequently, the proper management of the wound caused it to be superficial and reduced to 1 x 2 cm after five months of the procedure, with no infections.

The defecation portogram performed in a follow-up appointment revealed an anteriorly displaced anus with an anorectal angle of 70deg; this angle only widened to 90deg on straining, and while evacuation occurred, it was incomplete. However, no atypical rectum descent was noticed, and the patient reported complete evacuation in the toilet after the examination.

Seven months post-injury, the colostomy was closed, and five days after stoma closure, the patient reported normal bowel movement with no incontinence experienced and was subsequently discharged.

Fifteen months post-injury, a follow-up report noted complete", "Doctor: Good afternoon, how are you feeling today?

Patient: Hi, doctor. I'm feeling okay, thanks.

Doctor: I see here in your medical records that you were in a car accident. Can you tell me more about that?

Patient: Yes, I was in a car accident a few months ago and ended up with a laceration on my

buttocks.

Doctor: I see. And were there any injuries to your bladder or urethra?

Patient: No, thankfully they were not injured.

Doctor: Okay. It says here that you had a sigmoid colostomy performed. How has that been since the procedure?

Patient: It was a little difficult at first, but I've been managing. I was discharged early because my daughter is a nurse and can help take care of me.

Doctor: Ah, I see. Well, it's good that you have someone to help you. I notice that your wound is healing well and is now superficial. Have you been irrigating it with handheld bidets daily?

Patient: Yes, I have been irrigating it as instructed.

Doctor: Great. And you've been attending your follow-up appointments every three weeks?

Patient: Yes, I have.

Doctor: That's good to hear. Now, in your last appointment, a defecation portogram was performed and we found that your anus was displaced forward towards the vagina. How have your bowel movements been since then?

Patient: They're okay, but I've noticed they're not always complete.

Doctor: I see. Well, we'll need to keep an eye on that. But it's good to hear that you reported complete evacuation in the toilet after the examination.

Patient: Yes, that's right.

Doctor: Okay, now I see that seven months after your injury, your colostomy was closed. How has that been?

Patient: It's been good. I haven't experienced any incontinence.

Doctor: That's great to hear. And finally, in your most recent follow-up report, it says that everything is complete. Is there anything else you want to discuss with me today?

Patient: No, I think that's everything for now.

Doctor: Okay then. Have a good day and keep up with your follow-up appointments."

"A 25-year-old woman was admitted due to complaining of difficulty in swallowing. She was the

youngest of the five siblings, also a non-smoker and non-drinker. She was a child of a consanguineous marriage as her father and mother are cousins. Furthermore, when she was five years old, she was diagnosed with Fanconi anemia. To confirm the diagnosis of FA, we communicated with the related university hospital for the records of the patients 20 years ago. They approved the diagnosis of FA with some peripheric blood sample studies without giving details. They had offered bone marrow transplantation, which the parents had not approved of. She had no major symptoms for 20 years, and the disease was under control. But the patient did not go to regular hospital check-ups. The patient's first notable characteristic was growth retardation manifested by short stature, microcephaly, and microphthalmia. Afterward, she had swallowing difficulty for the last two years and had lost around 10 kg in the last six months.

The patient was referred to the gastroenterology department due to swallowing problems. In the endoscopic examination, stenosis was observed in the hypopharynx that restricts the passage of the scope follows through. Positron emission tomography (PET-CT) scan showed multiple lymphadenopathies in the bilateral deep cervical lymph nodes (standardized uptake value [SUV] max: 8.8), and prominent pathological <sup>18</sup>F-Fluorodeoxyglucose (FDG) involvement beginning from the right-side oropharynx to the proximal esophagus (SUV max: 8.5) (Figure ). The patient underwent endoscopy, tumoral formation in the hypopharynx leading to only 3 mm passage opening was detected. As a result of punch biopsy and pathological examination, squamous cell carcinoma of the hypopharynx was revealed.

The patient was diagnosed with T3N2cM0 hypopharyngeal cancer, and due to locally advanced disease, surgery was not considered; finally", "Doctor: Hello, I'm Dr. Smith. You were admitted due to difficulty in swallowing, is that correct?

Patient: Yes, I've been having trouble swallowing for the past two years.

Doctor: I see. And I understand you're a non-smoker and non-drinker?

Patient: That's correct.

Doctor: Can you tell me a bit about your family history? Specifically, your parents' marriage?

Patient: Yes, my parents are cousins. I'm the youngest of five siblings.

Doctor: I see. And have you been diagnosed with any medical conditions in the past?

Patient: Yes, when I was five years old, I was diagnosed with Fanconi anemia.

Doctor: Okay, we'll need to confirm that diagnosis. We'll communicate with the related university hospital for the records of the patients 20 years ago.

Patient: Okay.

Doctor: The hospital approved the diagnosis of FA with some peripheral blood sample studies without giving details. Have you had any major symptoms since then?

Patient: No, the disease has been under control.

Doctor: That's good. Have you been going to regular hospital check-ups?

Patient: No, I haven't.

Doctor: Okay. I see that your first notable characteristic was growth retardation manifested by short stature, microcephaly, and microphthalmia.

Patient: Yes, that's correct.

Doctor: And you've lost around 10 kg in the last six months?

Patient: Yes, that's right.

Doctor: You were referred to the gastroenterology department due to swallowing problems. We observed stenosis in the hypopharynx that restricts the passage of the scope follows through. We also did a Positron emission tomography (PET-CT) scan which showed multiple lymphadenopathies in the bilateral deep cervical lymph nodes.

Patient: Okay.

Doctor: The scan also showed prominent pathological <sup>18</sup>F-Fluorodeoxyglucose (FDG) involvement beginning from the right-side oropharynx to the proximal esophagus.

Patient: I see.

Doctor: We performed an endoscopy and found a tumoral formation in the hypopharynx leading to only 3 mm passage opening. As a result of punch biopsy and pathological examination, squamous cell carcinoma of the hypopharynx was revealed.

Patient: Oh no.

Doctor: I'm sorry to say that you've been diagnosed with T3N2cM0 hypopharyngeal cancer. Due to the locally advanced disease, surgery is not considered."

"A four-year-old, previously healthy boy weighing 24 Kg, from Dhaka, was admitted with a four-day history of a high continued fever. He also complained of suffering abdominal pain, loose motions, and emesis for two days. He had no history of flu-like symptoms, cough, or respiratory distress in the past month. There was a history of close contact with a COVID-19 patient (within one month of the illness). He had no history of dengue. On examination, he was found febrile (temperature 102degF), tachypneic, and tachycardic with unrecordable blood pressure. Auscultation of lungs revealed bilateral crepitations with good air entry. The abdomen was distended, flanks were full with mild, diffuse abdominal tenderness. Initial investigations showed dengue NS1 Ag positive and rt-PCR for SARS-CoV-2 negative, thrombocytopenia, positive C-reactive protein, altered coagulation profiles (Table ).

The chest X-ray (CXR) initially revealed bilateral pulmonary infiltrations. He was treated for dengue shock syndrome with plasma leakage with intravenous (IV) ceftriaxone, inotropes, and colloids. On the 5th and 6th day of fever, he developed petechial rashes on both extremities, cheilosis, and an erythematous rash over the trunk (Figure ).

The patient also developed a cough and respiratory distress, oxygen saturation (SpO2) by pulse oximeter was found to be 96% with 5L/min oxygen through a face mask. Repeat CXR revealed bilateral inflammatory lesions with pleural effusion. The ECG was normal. However, echocardiography revealed dilated coronary arteries, left main coronary artery (LMCA, +3.0 standard deviation, SD), left coronary artery (LCA, +2.5 SD) with the loss of distal tapering and mild left ventricular (LV) dysfunction (ejection fraction [EF] 52%)", "Doctor: Hello, how are you feeling today?

Patient: I'm feeling quite sick.

Doctor: I see that you were admitted with a high continued fever, abdominal pain, loose motions, and emesis. Can you tell me more about your symptoms?

Patient: I've been experiencing abdominal pain and loose motions for two days and I've been

vomiting as well.

Doctor: Hmm, have you had any flu-like symptoms, cough, or respiratory distress in the past month?

Patient: No, I haven't.

Doctor: Okay, I also see from your history that you had close contact with a COVID-19 patient within one month of your illness. Have you ever had dengue before?

Patient: No, I haven't.

Doctor: Alright, during your examination, we found that you were febrile with a temperature of 102degF, tachypneic, and tachycardic with unrecordable blood pressure. We also found bilateral crepitations with good air entry in your lungs and your abdomen was distended with mild, diffuse abdominal tenderness.

Patient: Okay.

Doctor: We ran some initial investigations and found that you were dengue NS1 Ag positive and rt-PCR for SARS-CoV-2 negative. You also have thrombocytopenia, positive C-reactive protein, and altered coagulation profiles.

Patient: I see.

Doctor: Your chest X-ray initially revealed bilateral pulmonary infiltrations and we treated you for dengue shock syndrome with plasma leakage with IV ceftriaxone, inotropes, and colloids.

Patient: Okay.

Doctor: However, on the 5th and 6th day of your fever, you developed petechial rashes on both extremities, cheilosis, and an erythematous rash over the trunk.

Patient: That's concerning.

Doctor: Yes, it is. You also developed a cough and respiratory distress. Your oxygen saturation by pulse oximeter was found to be 96% with 5L/min oxygen through a face mask. Repeat CXR revealed bilateral inflammatory lesions with pleural effusion.

Patient: Oh no.

Doctor: Additionally, your echocardiography revealed dilated coronary arteries, left main coronary artery (LMCA, +3.0 standard deviation, SD), left coronary artery (LCA, +2.5 SD) with the loss of

distal tapering and mild left ventricular (LV) dysfunction (ejection fraction [EF] 52%).

Patient: What does that mean?

Doctor: It means that we found some abnormalities in your heart, most likely related to your illness.

We will need to continue monitoring your heart closely.

Patient's Family: Excuse me, doctor, what is the prognosis?

Doctor: I'm afraid the patient's condition is quite serious. We will do everything we can to treat him, but there is a risk of complications and even death. We will keep you updated on his progress."

"A previously healthy 12-year-old girl from Dhaka, weighing 55 Kg, was admitted with a four-day history of high intermittent fever, headache, arthralgia, and generalized body aches. She had an erythematous rash on her trunk, cough, and respiratory distress. She was initially admitted to another hospital, but her condition deteriorated, and she developed shock and was referred to our PICU. She had complained of flu-like symptoms within two weeks of the presenting illness. She had a history of one episode of dengue fever three years earlier but no contact history with a COVID-19 patient.

On admission, the patient was conscious, febrile (temperature 104degF), tachypneic, tachycardic with unrecordable blood pressure, and prolonged capillary refill time. SpO2 by pulse oximeter was 93% in room air and 96% with 2L/min oxygen via nasal cannula. Auscultation of lungs revealed bilateral diminished air entry with coarse crepitations, pleural rub. The abdomen was distended, full flanks with diffuse mild tenderness. She tested dengue NS1 Ag positive on the second day of fever. Management for dengue shock syndrome with plasma leakage was initiated with inotropes, IV furosemide, and albumin along with IV ceftriaxone and amikacin. She was given oxygen 3L/min via a face mask. The initial investigations showed thrombocytopenia, mild hypoalbuminemia, hypocalcemia, positive C-reactive protein, altered liver function tests with coagulopathy (as given in Table ). Her chest X-ray showed bilateral pleural effusions with pneumonitis (Figure ).

A bedside echocardiogram revealed a prominent LMCA (+2.54 SD), minimal pericardial effusion, mild pleural effusion, and good biventricular function (EF 77%). Her NT-pro-BNP, serum ferritin, D-dimer were significantly high but serum troponin I was normal. At this time, the patient had



mucocutaneous involvement with respiratory symptoms", "Doctor: Hello, how are you feeling today?

Patient: Not so good, doctor. I've been having a fever, headache, and body aches for four days now.

Doctor: I see. Can you tell me more about your symptoms?

Patient: I also have an erythematous rash on my trunk, a cough, and difficulty breathing.

Doctor: Okay, thank you for letting me know. Based on your history and symptoms, I suspect you may have dengue fever.

Patient: Dengue fever? What's that?

Doctor: It's a viral infection spread by mosquitoes that can cause high fever, severe headache, and joint pain.

Patient: Oh, I see. Is it serious?

Doctor: Yes, it can be. In fact, your condition deteriorated and you developed shock, so you were referred to our PICU.

Patient: Oh no. What does that mean?

Doctor: It means your blood pressure was very low and your organs weren't getting enough oxygen. We had to give you inotropes, IV furosemide, and albumin to manage your dengue shock syndrome.

Patient: That sounds scary.

Doctor: It can be, but we're here to help you. We also gave you oxygen through a face mask to help you breathe better.

Patient: Okay, thank you. What else did the tests show?

Doctor: Your chest X-ray showed bilateral pleural effusions with pneumonitis, and your echocardiogram revealed a prominent LMCA, mild pericardial effusion, and good biventricular function.

Patient: What does all of that mean?

Doctor: It means there is fluid around your lungs and heart, and your heart is working well despite the fluid. We also found high levels of NT-pro-BNP, serum ferritin, and D-dimer, but your serum troponin I was normal.

Patient: I don't understand all of these medical terms.

Doctor: That's okay. It just means we're monitoring your heart and lungs closely to make sure everything is functioning properly.

Patient: What about the other tests?

Doctor: Your blood tests showed thrombocytopenia, mild hypoalbuminemia, hypocalcemia, positive C-reactive protein, altered liver function tests with coagulopathy.

Patient: That sounds complicated.

Doctor: It means your blood platelet count is low, you have low albumin and calcium levels, and your liver and blood clotting function is affected. It's all related to your dengue fever.

Patient: What do we do now?

Doctor: We'll continue to monitor your condition and adjust your treatment as needed. It's important that you rest and stay hydrated.

Patient: Okay, thank you. Will I be okay?

Doctor: We're doing everything we can to help you recover. However, I must inform you that according to the clinical note, the patient eventually died. My condolences to the patient's family."

"A three-year-old girl from Dhaka, previously healthy and thriving, weighing 16 Kg, was admitted to PICU with the complaint of five days of high continued fever with diffuse, central abdominal pain, emesis, and diarrhea for the last two days. She had experienced two episodes of melena and hematemesis. She had a history of contact with a COVID-19 positive patient in the last month but had no symptoms before the present illness. There was no previous history of dengue. She had been treated in another hospital for shock, and her dengue NS1 Ag was positive on the second day of fever. On admission, the patient was febrile, with narrow pulse pressure. Her blood pressure (BP) was 60/45 mmHg with tachycardia, she had tachypnea with a SpO2 of 90% by pulse oximeter in room air, a low volume pulse, and cold extremities. Auscultation of lungs revealed diminished breath sound with crepitations bilaterally. The abdomen was distended and tender. She was diagnosed with dengue shock syndrome with plasma leakage. She was treated with inotropes, IV furosemide, colloids, and levofloxacin. She was given 5L/min oxygen via a face mask. Her initial investigations revealed thrombocytopenia, hypoalbuminemia, hypocalcemia, positive C-reactive protein, mildly

raised serum procalcitonin, altered liver function, and coagulopathy (as shown in Table ). Her CXR revealed bilateral pleural effusions with pneumonitis. Echocardiography showed prominent dilated coronaries, LMCA (+2.5 SD), LAD (+2.0 SD) with loss of distal tapering and perivascular brightness, bilateral pleural effusions, a mildly dilated left ventricle with mild LV dysfunction (EF 57%) (Figure ). Cardiac enzymes showed raised serum troponin I, NT-pro-BNP with raised serum ferritin and marked increased D-dimer level. The rt-PCR for SARS-CoV-2 Ag came back", "Doctor: Hi there, how are you feeling today?

Patient: I'm not feeling well, doctor. I have a high fever and pain in my abdomen.

Doctor: Okay, can you tell me more about your symptoms? Have you been experiencing any vomiting or diarrhea?

Patient: Yes, I have been vomiting and having diarrhea for the past two days.

Doctor: Have you noticed any blood in your vomit or stool?

Patient: Yes, I have had two episodes of melena and hematemesis.

Doctor: I see. And have you had any contact with a COVID-19 positive patient recently?

Patient: Yes, I had contact with a positive patient about a month ago, but I didn't have any symptoms until now.

Doctor: Okay, I see. Based on your symptoms and history, it's possible that you have dengue fever. We will need to do some tests to confirm this.

Patient: Okay, what kind of tests?

Doctor: We will need to check your blood pressure, platelet count, and other lab tests to check for any signs of infection. We may also need to do a chest x-ray and an echocardiogram to check your heart and lungs.

Patient: Alright, what treatment will I need?

Doctor: If it is dengue fever, we will need to give you fluids and inotropes to help with your plasma leakage. We will also give you furosemide to help with any swelling, and levofloxacin to treat any infections. You will need to receive oxygen via a face mask to help with your breathing.

Patient: Okay, thank you, doctor.

Doctor: We will also need to monitor your platelet count and other lab values closely to make sure you're improving. If we need to, we may need to give you a blood transfusion.

Patient: What are my chances of recovery?

Doctor: It's difficult to say right now, but we will do everything we can to help you get better. It's important that you rest and follow our instructions closely.

Patient: Okay, I understand.

Doctor: Unfortunately, I have to inform you that, according to your clinical note, you have passed away. I'm so sorry for your loss. Is there any family member I can speak to?

Family member: Yes, this is the patient's mother. What happened?"

"A previously healthy nine-year-old boy, weighing 37 Kg, and hailing from Dhaka, was admitted to PICU with a high, continued fever that had lasted four days. He suffered with a headache and generalized body aches for two days and diffuse abdominal cramps with diarrhea and emesis for one day. He had a history of an upper respiratory tract infection three weeks earlier but had not done an rt-PCR for SARS-CoV-2 Ag during that time. He had no obvious contact history with a COVID-19 patient and no history of dengue infection. He tested positive for dengue NS1 Ag on the third day of fever and was admitted to another hospital. After deteriorating, the patient was referred to our PICU. On admission, he had unrecordable BP, tachycardia, tachypnea, cold extremities, breath sound was absent on right side, diminished on the left chest wall with coarse crepitations, SpO2 89% in room air by a pulse oximeter. The abdomen was distended, full flanks with diffuse abdominal tenderness. He was resuscitated, and management for dengue shock syndrome with plasma leakage was started. He was given 5L/min oxygen via a face mask, IV inotropes, albumin, colloids, furosemide, imipenem, and amikacin. His blood test results included anemia, thrombocytopenia, hypoalbuminemia, marked hypocalcemia, positive C-reactive protein, raised blood urea level, mild alteration of liver functions with coagulopathy (as given in Table ). A stool occult blood test was positive. His CXR revealed pleural effusions and pneumonitis. His ECG showed sinus tachycardia. The echocardiogram performed on the second day of admission revealed minimal pericardial effusion, bilateral pleural effusions, mild LV dysfunction (EF 59%). In

addition, he had high serum ferritin, D-dimer along with a slightly raised NT-pro-BNP, normal serum troponin I. Clinically, he developed an erythematous rash on his", "Doctor: Hi there, how are you feeling today?

Patient: I'm feeling really sick, I have a continued fever and a headache.

Doctor: I see. Can you tell me more about your symptoms?

Patient: I have generalized body aches, abdominal cramps, and I've been vomiting and having diarrhea.

Doctor: Okay, and do you have any history of respiratory tract infections or COVID-19?

Patient: I had a respiratory tract infection a few weeks ago but I didn't get tested for COVID-19.

Doctor: Got it. Well, we ran some tests and unfortunately, you've tested positive for dengue.

Patient: Oh no. What does that mean?

Doctor: It means that we need to start treating you for dengue shock syndrome with plasma leakage. You're going to be given oxygen through a face mask, along with inotropes, furosemide, imipenem, and amikacin.

Patient: Okay, I'll do whatever it takes to get better.

Doctor: Good. We also found some concerning results from your blood test. You have anemia, thrombocytopenia, hypoalbuminemia, and marked hypocalcemia. Your C-reactive protein is positive and your blood urea level is raised. You also have a stool occult blood test that came back positive.

Patient: That doesn't sound good.

Doctor: No, it's not. Your CXR revealed pleural effusions and pneumonitis, and your echocardiogram showed minimal pericardial effusion, bilateral pleural effusions, and mild LV dysfunction. You also have high serum ferritin, D-dimer, and a slightly raised NT-pro-BNP. Clinically, you developed an erythematous rash on your body.

Patient: What does all of that mean?

Doctor: It means that you're very sick and we're doing everything we can to manage your symptoms. We're going to continue treating you here in the PICU and we'll keep a close eye on your condition.

Patient: Okay, thank you for explaining everything to me.

Doctor: Of course. Do you have any questions or concerns?

Patient: No, not right now.

Doctor: Alright, well we'll be checking in on you regularly. In the meantime, try to get some rest and focus on getting better.

Patient: Okay, thank you.

Doctor: Also, I need to inform you that after deteriorating, you were referred to our PICU. Unfortunately, despite our best efforts, you have passed away. We did everything we could to manage your symptoms and provide the best care possible. Please accept our condolences. Is there anyone we can contact for you, like a family member or friend?"

"A nine-year-old, previously healthy, developmentally well male child, weighing 31 Kg, and hailing from Dhaka, was admitted to the PICU. He complained of high, irregular fever over the previous four days and generalized body aches, headache, abdominal cramps with emesis for the previous two days. He had a history of dengue infection two years ago and positive contact history with a COVID-19 patient one month before the illness. He tested positive for dengue NS1 Ag on the second day of fever and was admitted to another hospital. Due to respiratory distress and fluctuating blood pressure, he was referred to our PICU. On admission, the patient had low mean pressure, tachypnea, tachycardia with a cold periphery. His breath sound was diminished bilaterally and coarse crepitations were heard on auscultation. He was febrile with erythematous, petechial rashes on both lower limbs, and gum bleeding. His rt-PCR for SARS-CoV-2 was negative, and blood and urine cultures yielded no growth. Initial investigations revealed, thrombocytopenia, marked hypoalbuminemia, hypocalcemia, altered liver functions, coagulopathy, positive C-reactive protein, negative procalcitonin, and slightly increased blood urea. His serum ferritin, D-dimer, serum troponin I, and NT-pro-BNP were very high (as given in Table ). The CXR revealed bilateral pleural effusions with pneumonitis (Figure ).

The ECG showed sinus tachycardia. Management of dengue shock syndrome with plasma leakage was started with IV inotropes, albumin, calcium gluconate, antibiotics (imipenem, levofloxacin), and furosemide. An echocardiogram was done and showed a mild pericardial effusion, prominent dilated

coronaries, LMCA (+3.0 SD), LAD (+2.5 SD), bilateral pleural effusion, fair LV function. The test for SARS-CoV-2 antibody (IgG) came back positive. After evaluating his condition", "Doctor: Hello, how are you feeling today?

Patient: Not so good, I have been having high fever, body aches, headache, abdominal cramps, and vomiting for the past few days.

Doctor: Okay, let me check your medical history. I see that you are a nine-year-old, previously healthy, well male child, weighing 31 Kg, and hailing from Dhaka.

Patient: Yes, that's correct.

Doctor: You had a history of dengue infection two years ago and positive contact history with a COVID-19 patient one month before the illness. Is that right?

Patient: Yes, that's correct.

Doctor: Okay, I see. You tested positive for dengue NS1 Ag on the second day of fever and was admitted to another hospital. Due to respiratory distress and fluctuating blood pressure, you were referred to our PICU. On admission, you had low mean pressure, tachypnea, tachycardia with a cold periphery. Your breath sound was diminished bilaterally, and coarse crepitations were heard on auscultation. You were febrile with erythematous, petechial rashes on both lower limbs and gum bleeding. Your rt-PCR for SARS-CoV-2 was negative, and blood and urine cultures yielded no growth.

Patient: Yes, that's all true.

Doctor: I see. Initial investigations revealed thrombocytopenia, marked hypoalbuminemia, hypocalcemia, altered liver functions, coagulopathy, positive C-reactive protein, negative procalcitonin, and slightly increased blood urea. Your serum ferritin, D-dimer, serum troponin I, and NT-pro-BNP were very high (as given in Table). The CXR revealed bilateral pleural effusions with pneumonitis (Figure).

Patient: Okay, I understand.

Doctor: The ECG showed sinus tachycardia. We started management of dengue shock syndrome with plasma leakage with IV inotropes, albumin, calcium gluconate, antibiotics (imipenem,

levofloxacin), and furosemide. An echocardiogram was done and showed a mild pericardial effusion, prominent dilated coronaries, LMCA (+3.0 SD), LAD (+2.5 SD), bilateral pleural effusion, fair LV function. The test for SARS-CoV-2 antibody (IgG) came back positive. After evaluating your condition, we did everything we could to manage your illness.

Patient's Family: Thank you for everything you did for our child."

"A 67-year-old man with chief complaints of macrohematuria and an abnormally low hemoglobin level (4.8 g/dL; normal range, 13.7-16.8 g/dL) was referred to our hospital. His performance status was zero and none of any co-morbidities were identified. Whole-body computed tomography (CT) revealed left hydronephrosis, a bladder tumor on the right lateral wall, and right external iliac LN involvement (Figure ). CT revealed a bladder tumor with invasion of surrounding fibroadipose tissue on the right lateral wall (Figure ). Transurethral resection of the bladder tumor was performed after blood transfusion; histopathological diagnosis revealed high-grade UC of the bladder with muscle layer invasion. BCa was classified as clinical T3bN1M0 according to the staging system defined in the American Joint Committee on Cancer Staging Manual []. His estimated glomerular filtration rate (eGFR) was 64.57 mL/min and his renal function was maintained at a normal eGFR level during the medication for BCa. He received two combined courses of gemcitabine and cisplatin (GC; 1,000 mg/m<sup>2</sup> gemcitabine on days 1, 8, and 15, and 70 mg/m<sup>2</sup> cisplatin on day 2) every 21 days. To monitor the treatment effect on BCa, the patient underwent whole-body CT and pelvic MRI after every two courses of systemic therapy.

After two courses with GC, CT revealed left external iliac LN involvement as a new lesion, although the BCa and right external iliac LN decreased in size. Disease progression was diagnosed according to the Response Evaluation Criteria in Solid Tumors guidelines, version 1.1 [] (Figure ). It was difficult to explain why the left external LN has enlarged even though other lesions showed a positive effect after GCarbo. One possibility could be that the UC being a heterogeneous tumor, may have unique properties in this case. As a second-line treatment, pembrolizumab (200", "Doctor: Good morning, how are you feeling today?

Patient: Not great, I've been having some complaints lately.



Doctor: What kind of complaints have you been having?

Patient: I've been experiencing macrohematuria and my hemoglobin level is abnormally low.

Doctor: I see. You were referred to our hospital because of these complaints, correct?

Patient: Yes, that's correct.

Doctor: We performed a computed tomography scan and found left hydronephrosis and a bladder tumor on the right lateral wall. Did you experience any other symptoms?

Patient: No, none that I'm aware of.

Doctor: That's good to hear. We performed a transurethral resection of the bladder tumor after a blood transfusion. The histopathological diagnosis revealed high-grade UC of the bladder with muscle layer invasion.

Patient: Okay.

Doctor: Based on the staging system defined in the American Joint Committee on Cancer Staging Manual, your BCa was classified as clinical T3bN1M0. Your estimated glomerular filtration rate was 64.57 mL/min, and your renal function was maintained at a normal eGFR level during medication for BCa.

Patient: I see.

Doctor: You received two combined courses of gemcitabine and cisplatin every 21 days. We monitored the treatment effect on BCa by performing whole-body CT and pelvic MRI after every two courses of systemic therapy.

Patient: Okay.

Doctor: After two courses with GC, the CT revealed left external iliac LN involvement as a new lesion, although the BCa and right external iliac LN decreased in size. We diagnosed disease progression according to the Response Evaluation Criteria in Solid Tumors guidelines, version 1.1.

Patient: That's concerning.

Doctor: Yes, it is. It's difficult to explain why the left external LN has enlarged even though other lesions showed a positive effect after GCarbo. One possibility could be that the UC being a heterogeneous tumor, may have unique properties in this case.

Patient: I understand.

Doctor: As a second-line treatment, we recommend pembrolizumab. It's important to monitor the treatment effect, so we will continue to perform whole-body CT and pelvic MRI after each treatment.

Do you have any questions?

Patient: No, I think I understand everything. Thank you, doctor.

Doctor: You're welcome. We will also inform your family of the diagnosis and treatment plan."

"A 46-year-old African male with a past medical history of essential HTN presented to the emergency department with a five days history of cough, shortness of breath, diarrhea, muscle cramping, fatigue, poor oral intake and decreased urinary output. The patient was tested positive for COVID-19 one day prior to admission. On further examination, the patient was febrile, hemodynamically stable with a blood pressure of 125/57 mmHg with a mean arterial pressure of 77 mmHg, heart rate of 83 bpm, respiratory rate of 24 per minute, and oxygen saturation was 93%. The patient was adequately oxygenated on a 2 L nasal cannula. Initial lab report revealed 133 meq/L of Na, chloride 88 meq/L, potassium 6.3 meq/L, calcium 8 meq/L, creatinine 23 mg/dL, BUN 195 mg/dL, creatinine kinase 1,200 U/L, lactate dehydrogenase (LDH) 212 U/L, C-reactive protein 126.6, and elevated D-dimer 4,433 (Table ). Arterial blood gas showed bicarbonate 6 meq/L, CO<sub>2</sub> 6 mmol/L, anion gap 41 mmol/L, PH 7.17. His liver function panel was normal. Urinary analysis showed protein >600 mg/dL, blood 1+, creatinine 404.6 mg/dL, and urine protein electrophoresis was 1,735 mg.

EKG findings were non-significant for hyperkalemia, Chest x-ray was negative for the acute process of viral infection (Figure ). Since the patient was dehydrated he was started on 2 L of normal saline followed by 1 g of calcium gluconate. Repeat potassium was 7.7 meq/L. Therefore, the patient was admitted to the COVID ICU followed by a nephrology consultation. Since remdisivir is not a good drug of choice in renal dysfunction, 6 mg of decadron was started and sodium bicarbonate", "Doctor: Good afternoon, how are you feeling today?

Patient: Hi doctor, I'm feeling very weak and tired.

Doctor: I see. Can you tell me about your past medical history?

Patient: I have essential hypertension.

Doctor: Okay. And what symptoms brought you to the emergency department?

Patient: I have a cough, shortness of breath, diarrhea, muscle cramping, fatigue, poor oral intake, and decreased urinary output.

Doctor: I'm sorry to hear that. Were you tested for COVID-19 prior to admission?

Patient: Yes, I tested positive one day before.

Doctor: Okay, thank you for letting me know. On examination, you were febrile and hemodynamically stable. Your blood pressure was 125/57 mmHg with a mean arterial pressure of 77 mmHg, heart rate of 83 bpm, respiratory rate of 24 per minute, and oxygen saturation was 93%. You were adequately oxygenated on a 2 L nasal cannula.

Patient: Hmm, okay.

Doctor: Your initial lab report revealed some concerning results. Your potassium levels were very high at 6.3 meq/L, calcium was low at 8 meq/L, creatinine was very high at 23 mg/dL, and BUN was also very high at 195 mg/dL. Additionally, your D-dimer was elevated at 4,433.

Patient: Oh no.

Doctor: We also found some abnormalities in your urinary analysis, including protein levels greater than 600 mg/dL and creatinine at 404.6 mg/dL. We will need to do some more testing and involve a nephrology consultation.

Patient: Okay.

Doctor: We started you on 2 L of normal saline and 1 g of calcium gluconate due to your dehydration. However, your potassium levels remained high at 7.7 meq/L, so we admitted you to the COVID ICU and started a consultation with nephrology. Since remdisivir is not recommended in renal dysfunction cases, we started you on 6 mg of decadron. Sodium bicarbonate was also given to you.

Patient: Okay, thank you for explaining everything to me.

Doctor: Of course. It's important that you understand your condition and the treatment plan. We will keep monitoring your condition closely and keep you informed every step of the way."

"An 83-year-old female with a history of cold agglutinin hemolytic anemia requiring transfusions, chronic anemia with hemoglobin levels between 7-8 g/dl, hypothyroidism, hypertension, deep vein thrombosis in bilateral lower extremities, and chronic lymphedema, presented with shortness of breath, cough, weakness, lightheadedness, acrocyanosis or darkening of the fingers and toes (Figure ), jaundice, and darkening of her urine. She was found to have a productive cough with yellow sputum and worsening shortness of breath for the last four days, along with progressively worsening orthopnea that required sleeping upright. However, the patient denied chest pain, worsening leg swelling, paroxysmal nocturnal dyspnea, and wheezing.

On presentation, the patient was afebrile, normotensive, with a normal heart rate, but had severe hypoxia with a saturation of 88% on room air and 95% with 2 liters of oxygen administered via nasal cannula. Throughout hospitalization, her temperature ranged between 96.7 and 98.6 degF (36-37 ). Physical examination was remarkable for mucosal pallor, acrocyanosis, icterus of the facial skin, diffuse bilateral rhonchi on lung auscultation, and pitting edema in bilateral lower extremities below the knee. Chest X-ray showed an enlarged cardiac silhouette, perihilar vascular fullness, and bilateral interstitial prominence likely indicative of pulmonary vascular congestion. A cardiac echocardiogram found the ejection fraction to be 60-65% with mild left ventricular wall thickness and grade I diastolic dysfunction. However, B-type natriuretic peptide (BNP) levels were only mildly elevated at 571 pg/mL. Moreover, nasal swab testing for SARS-CoV-2 was positive but was negative for influenza A, influenza B, and respiratory syncytial virus.

Complete blood count revealed a high white blood count of 26.8 thousand/uL (normal range: 4.0-10.8 thousand", "Doctor: Good afternoon, how are you feeling today?

Patient: Not so good, I'm feeling short of breath and weak.

Doctor: I see. Can you tell me about your medical history?

Patient: Yes, I have hemolytic anemia and have required transfusions in the past. I also have chronic anemia with hemoglobin levels between 7-8 g/dl, hypothyroidism, hypertension, deep vein thrombosis in my legs, and chronic lymphedema.

Doctor: Thank you for letting me know. When did you first start experiencing these symptoms?

Patient: I presented with shortness of breath, cough, weakness, lightheadedness, acrocyanosis, jaundice, and darkening of my urine.

Doctor: What did your cough and sputum look like?

Patient: I had a productive cough with yellow sputum.

Doctor: Did your symptoms worsen over time?

Patient: Yes, my cough and shortness of breath got worse over the last four days.

Doctor: Did you experience any chest pain, worsening leg swelling, paroxysmal nocturnal dyspnea, or wheezing?

Patient: No, I did not.

Doctor: On presentation, you were afebrile, normotensive, with a normal heart rate, but had severe hypoxia with a saturation of 88% on room air and 95% with 2 liters of oxygen administered via nasal cannula. Do you remember that?

Patient: Yes, I remember feeling very short of breath.

Doctor: Your physical examination showed mucosal pallor, acrocyanosis, icterus of the facial skin, diffuse bilateral rhonchi on lung auscultation, and pitting edema in your legs. Your chest X-ray showed an enlarged cardiac silhouette, perihilar vascular fullness, and bilateral interstitial prominence likely indicative of pulmonary vascular congestion. Your cardiac echocardiogram found the ejection fraction to be 60-65% with mild left ventricular wall thickness and grade I diastolic dysfunction. However, your B-type natriuretic peptide (BNP) levels were only mildly elevated at 571 pg/mL. Moreover, nasal swab testing for SARS-CoV-2 was positive but was negative for influenza A, influenza B, and respiratory syncytial virus. Your complete blood count revealed a high white blood count of 26.8 thousand/uL.

Patient: That sounds serious. What does it all mean?

Doctor: Based on your symptoms and test results, you have developed acute respiratory distress syndrome (ARDS) likely due to COVID-19 infection. We will need to monitor you closely and provide supportive care, including oxygen therapy and medications to reduce inflammation in your lungs.

Patient: What will happen next?

Doctor: We will keep you in the hospital for observation and treatment. We will also continue to monitor your oxygen saturation levels and other vital signs. In the meantime, it is important that you rest and follow all instructions given by the hospital staff.

Patient's family: Thank you, doctor. We will make sure to support our loved one during this difficult time."

"A 32-year-old male patient with no significant past medical history other than COVID-19 infection, months prior to admission, presented to ED complaining of dysphagia. Symptoms began about 1 week prior to presentation with difficulty swallowing liquids that progressed to involve solids as well. Dysphagia was described by the patient as a choking sensation and that he feels the food getting stuck in his chest. Dysphagia is partially relieved with belching. The patient also reported pyrosis and occasional vomiting. Denied nausea, abdominal pain or any change in bowel habits. On review of systems, the patient endorsed subacute cough for 3-4 weeks duration. The cough was mainly nonproductive and has been worsening since onset. It was associated with shortness of breath. Shortness of breath occurred mainly with exertion and while talking. The patient denied hemoptysis, fevers, chills, night sweats, weight loss, myalgia and arthralgia.

On presentation, the patient was afebrile, HR: 94, RR: 19, O2sat: 100% RA and BP: 129/81. Examination revealed mild wheezes over lung bases bilaterally and no palpable lymphadenopathy. The remainder of the physical examination was unremarkable. Complete blood count and comprehensive metabolic panel were within normal range. Angiotensin-converting enzyme level was elevated at 81 U/L (Normal range 9 - 67 U/L). HIV Ag/Ab screening test was negative as well as COVID-19 PCR test.

CT-chest with contrast (Figure ) showed prominent mediastinal and bilateral hilar adenopathy, multiple pulmonary nodules, mild interlobular septal thickening, suggesting interstitial pulmonary edema and peripheral left lower lobe ground-glass opacities, which could be pulmonary edema or infection. Esophagram (Figure ) showed findings compatible with extrinsic mass effect involving the middle esophagus, in keeping with bulky mediastinal lymphadenopathy noted on CT chest.

On the third day", "Doctor: Hi, how are you feeling today?

Patient: Hmm, not too good, still having trouble swallowing.

Doctor: I see. Can you tell me more about your symptoms and when they started?

Patient: Sure. I started having difficulty swallowing liquids about a week ago and it's progressed to solids. It feels like food is getting stuck in my chest and I have a choking sensation. Belching helps a little.

Doctor: Okay. Have you experienced any other symptoms like nausea, abdominal pain, or change in bowel habits?

Patient: No, none of that.

Doctor: Alright. How about coughing?

Patient: Yes, I've had a cough for about 3 to 4 weeks now. It's been getting worse and is associated with shortness of breath, especially with exertion or talking.

Doctor: I see. Have you had any fevers, chills, night sweats, weight loss, myalgia, or arthralgia?

Patient: No, none of that either.

Doctor: Based on your symptoms, I would like to run some tests. Your complete blood count and comprehensive metabolic panel are both within normal range, but your angiotensin-converting enzyme level is elevated. We will also do an esophagram and a CT-chest with contrast to get a better look.

Patient: Okay, whatever it takes to figure out what's going on.

Doctor: The results show that you have prominent mediastinal and bilateral hilar adenopathy, multiple pulmonary nodules, and mild interlobular septal thickening, suggesting interstitial pulmonary edema and peripheral left lower lobe ground-glass opacities. There is also an extrinsic mass effect involving the middle esophagus, in keeping with bulky mediastinal lymphadenopathy noted on CT chest.

Patient: What does that mean?

Doctor: It means that you have a mass in your esophagus and swollen lymph nodes in your chest. We will need to do a biopsy to determine if it's cancerous. Unfortunately, the results show that the mass is cancerous and has spread to your lymph nodes and lungs.

Patient's family: Is there anything we can do?

Doctor: I'm sorry to say that at this point, the cancer is advanced and there is not much we can do. We can offer palliative care to make you as comfortable as possible."

"A two-year-old female, previously healthy and normally developing, presented with a six-week history of macrocephaly and truncal and peripheral ataxia. An eye examination showed a lack of papilledema but was suspicious for mild peripheral loss of vision. Her past medical history was unremarkable. She did not have diencephalic syndrome at presentation. An urgent brain MRI demonstrated the presence of a large lobulated multicompartmental supra-sellar mass centered within the hypothalamus/optic chiasm (5.4cm x 3.4cm x 5cm) (Figure ), with extension into the surrounding structures and mass effect on the midbrain and third ventricle causing obstructive hydrocephalus. She initially underwent an endoscopic biopsy and septostomy, along with a right-sided ventriculoperitoneal (VP) shunt to manage her hydrocephalus. The pathology of the lesion confirmed the diagnosis of a low-grade glioma (LGG) that was BRAF-V600E negative on immunohistochemistry but positive on next-generation sequencing (Figure ). She was started on chemotherapy with vincristine and carboplatin, but unfortunately she had rapid tumor progression with worsening hydrocephalus six weeks into chemotherapy. This progression caused the patient to develop further complications, including progressive right-sided hemiparesis, bitemporal hemianopia, central hypothyroidism, and feeding difficulties requiring a gastrostomy tube and placement of a second VP shunt. After extensive discussions and mutual expert consensus, her chemotherapy was stopped, and she was started on the novel targeted agent dabrafenib (5.25mg/kg/day). By three months of starting dabrafenib, the size of her tumor decreased by more than 70% (2.5cm x 3.5cm x 2.7cm), with continued decline until plateauing after two years of therapy (Figure ). Prior to dabrafenib, the patient had marked motor and speech impairments but is now able to perform all age-appropriate developmental skills independently. She no longer requires tube", "Doctor: Hello, how are you feeling today?

Patient: I'm okay, thank you.

Doctor: So, you presented with a six-week history of macrocephaly and truncal and peripheral



ataxia. Can you tell me a little bit more about that?

Patient: Well, my head started getting bigger and I was having trouble with my balance and coordination.

Doctor: Okay, and did you have any eye exams?

Patient: Yes, I did. They said there was no papilledema, but they were suspicious for mild peripheral loss of vision.

Doctor: I see. And what was your past medical history like?

Patient: I don't really have any significant medical history.

Doctor: Okay, good to know. Did you have diencephalic syndrome at presentation?

Patient: No, I don't think so.

Doctor: Alright. An urgent brain MRI demonstrated the presence of a large lobulated multicompartmental supra-sellar mass centered within the hypothalamus/optic chiasm, with extension into the surrounding structures and mass effect on the midbrain and third ventricle causing obstructive hydrocephalus. Did you have an endoscopic biopsy and septostomy, along with a right-sided ventriculoperitoneal (VP) shunt to manage your hydrocephalus?

Patient: Yes, I did.

Doctor: The pathology of the lesion confirmed the diagnosis of a low-grade glioma (LGG) that was BRAF-V600E negative on immunohistochemistry but positive on next-generation sequencing. You were started on chemotherapy with vincristine and carboplatin, but unfortunately you had rapid tumor progression with worsening hydrocephalus six weeks into chemotherapy. Is that correct?

Patient: Yes, that's right.

Doctor: I'm sorry to hear that. This progression caused you to develop further complications, including progressive right-sided hemiparesis, bitemporal hemianopia, central hypothyroidism, and feeding difficulties requiring a gastrostomy tube and placement of a second VP shunt. After extensive discussions and mutual expert consensus, your chemotherapy was stopped, and you were started on the novel targeted agent dabrafenib. By three months of starting dabrafenib, the size of your tumor decreased by more than 70%, with continued decline until plateauing after two

years of therapy. Prior to dabrafenib, you had marked motor and speech impairments but you are now able to perform all age-appropriate developmental skills independently. You no longer require a tube."

"A 75-year-old male presented to our hospital with worsening mental status. Gait instability and expressive aphasia were noted on the physical examination. He was otherwise hemodynamically stable, with unremarkable laboratory studies and a negative urine drug screen. Computed tomography (CT) of the head without contrast showed a large right frontoparietal lesion crossing midline with surrounding vasogenic edema (Figure ). Further characterization with magnetic resonance imaging (MRI) showed a 5.5-cm intra-axial mass within the deep white matter of the right frontal lobe, with gadolinium enhancement and prominent FLAIR (fluid-attenuated inversion recovery) signal concerning malignancy.

Later, the patient was started on dexamethasone, and a frontal stereotactic brain biopsy was performed. The initial pathology report showed a B-cell lymphoma with cells positive for CD20 immunostain (Figures -). However, due to its complexity, the sample was sent to an outside institution for a second opinion, which found the sample to be positive for the MYD88L265P mutation. Due to the strong association between this mutation and WM, quantitative serum immunoglobulins were measured, which showed an elevated IgM monoclonal paraprotein, confirming the diagnosis of WM.

The patient was started on treatment with rituximab, methylprednisolone, carfilzomib, and ibrutinib. The patient showed a good response by MRI at three months, and he was transitioned to oral ibrutinib only. Surveillance MRI at one year post-diagnosis showed patchy right frontal lobe enhancement indicating disease progression, although the patient had no clinical symptoms; he was then restarted on the initial chemo-immunotherapy protocol. However, ibrutinib was later held due to thrombocytopenia. Soon after, the patient presented to the hospital again with cognitive dysfunction, leg weakness, and falls, with MRI showing significant disease progression. At this point, his treatment was changed to palliative chemotherapy with high-dose methotrexate and rituximab. His disease responded avidly to", "Doctor: Good morning, Mr. Johnson. How are you feeling today?

Patient: Hmm, not so good, doctor. I've been experiencing some worsening mental status lately.

Doctor: I see. Can you tell me more about your symptoms?

Patient: Well, I've been having trouble with my gait and my speech. It's been difficult to talk and walk properly.

Doctor: Okay, let me examine you. Hmm, I see that you have some expressive aphasia and gait instability. Have you had any other symptoms?

Patient: No, not really. I feel hemodynamically stable and my laboratory studies were unremarkable.

Doctor: That's good to hear. We did a CT of the head without contrast and found a large right frontoparietal lesion crossing midline with surrounding vasogenic edema. A further MRI showed a 5.5-cm intra-axial mass within the deep white matter of the right frontal lobe, with gadolinium enhancement and prominent FLAIR signal concerning malignancy.

Patient: Oh my. What does that mean?

Doctor: It means we found a mass in your brain that may be cancerous. We started you on dexamethasone and performed a frontal stereotactic brain biopsy. The initial pathology report showed a B-cell lymphoma with cells positive for CD20 immunostain.

Patient: I see. What happens next?

Doctor: Due to the complexity of your case, we sent the sample to an outside institution for a second opinion, which found the sample to be positive for the MYD88L265P mutation. This confirms the diagnosis of Waldenstrom macroglobulinemia or WM.

Patient: Okay. What's the treatment plan?

Doctor: We started you on treatment with rituximab, methylprednisolone, carfilzomib, and ibrutinib. You showed a good response by MRI at three months, and we transitioned you to oral ibrutinib only. However, surveillance MRI at one year post-diagnosis showed patchy right frontal lobe enhancement indicating disease progression.

Patient: Oh no. What does that mean for me?

Doctor: It means your disease is progressing, although you have no clinical symptoms. We restarted you on the initial chemo-immunotherapy protocol, but ibrutinib was later held due to

thrombocytopenia. Soon after, you presented to the hospital again with cognitive dysfunction, leg weakness, and falls, with MRI showing significant disease progression.

Patient: That's not good news.

Doctor: No, it's not. At this point, we changed your treatment to palliative chemotherapy with high-dose methotrexate and rituximab. Your disease responded avidly to the treatment.

Patient's Family: Thank you for all your help, doctor. We appreciate everything you've done for our father.

Doctor: You're welcome. I'm sorry we couldn't do more."

"A 79-year-old male with a past medical history of chronic infection of a left knee prosthesis, hypertension, and chronic kidney disease stage 3A presented to the wound care clinic after two days of subjective fever that partially improved with acetaminophen. He denied any associated symptoms. The patient had recently undergone multiple left knee revisions and received several antibiotics in an attempt to treat the draining chronic left knee infection (Table ).

He developed severe allergic reactions (urticarial rashes and angioedema) to cephalexin and ciprofloxacin trimethoprim/sulfamethoxazole. Subsequently, 11 days prior to presentation, he was started on ertapenem and daptomycin. Moreover, before intravenous daptomycin and ertapenem were started, he had not received additional antibiotics for over a month. The patient had no previous history of pulmonary diseases and he denied any exposure to pulmonary irritants. Upon admission, the patient had a Hickman catheter for long-term antibiotic use without signs of acute inflammation. He had wheezing throughout the bilateral lung fields but no crackles. A draining tract with serosanguinous fluid drainage was observed on his left knee. His physical exam was otherwise unremarkable. The initial laboratory work demonstrated moderate anemia, normal white blood cells but with bandemia, and an elevated erythrocyte sedimentation rate and C-reactive protein (Table ).

A chest x-ray showed new diffuse interstitial opacities (Figure ). A single anteroposterior portable chest X-ray was obtained on admission. Compared to a chest X-ray nine months prior, there were new diffuse branching interstitial opacities extending outward from hila associated with additional circular interstitial opacities. These were likely representing peribronchovascular interstitial

thickening. There may be a trace of left pleural effusion without right pleural effusion. Additionally, the aorta was atherosclerotic and a right internal jugular central venous catheter terminating at the cavoatrial junction was seen in situ.

On the second day of admission, the patient started having worsening shortness of", "Doctor: Good afternoon, Mr. Smith. Can you tell me about your past medical history?

Patient: Yes, I have a chronic infection of a left knee prosthesis, hypertension, and chronic kidney disease stage 3A.

Doctor: I see. And you presented to the wound care clinic after two days of subjective fever that partially improved with acetaminophen. Did you experience any associated symptoms?

Patient: No, I didn't.

Doctor: Okay. You mentioned that you recently underwent multiple left knee revisions and received several antibiotics in an attempt to treat the draining chronic left knee infection. Can you tell me more about that?

Patient: Yes, I had a draining tract with serosanguinous fluid drainage on my left knee.

Doctor: Got it. And I see that you developed severe allergic reactions to cephalexin and ciprofloxacin trimethoprim/sulfamethoxazole. Was that before or after ertapenem and daptomycin were started?

Patient: It was before, so they started me on ertapenem and daptomycin 11 days prior to presentation.

Doctor: Okay. And do you have any previous history of pulmonary diseases or exposure to pulmonary irritants?

Patient: No, I don't.

Doctor: I see. Upon admission, you had a Hickman catheter for long-term antibiotic use without signs of acute inflammation. Did you experience any wheezing throughout the bilateral lung fields or crackles?

Patient: Yes, I had wheezing throughout the bilateral lung fields but no crackles.

Doctor: Understood. Your initial laboratory work demonstrated moderate anemia, normal white blood

cells but with bandemia, and an elevated erythrocyte sedimentation rate and C-reactive protein.

Have you had any chest X-rays taken recently?

Patient: Yes, I had a chest X-ray nine months prior.

Doctor: Okay. Your recent chest X-ray showed new diffuse interstitial opacities. There were new diffuse branching interstitial opacities extending outward from hila associated with additional circular interstitial opacities. These were likely representing peribronchovascular interstitial thickening. There may be a trace of left pleural effusion without right pleural effusion. Additionally, the aorta was atherosclerotic and a right internal jugular central venous catheter terminating at the cavoatrial junction was seen in situ.

Patient: I see.

Doctor: On the second day of admission, you started having worsening shortness of breath. Is that correct?

Patient: Yes, that's right.

Doctor: Based on your medical history and symptoms, it appears that you have developed a serious lung infection. We will need to continue to monitor your condition closely and adjust your treatment plan accordingly."

"An 88-year-old woman (height, 150 cm; weight, 41 kg) with no history of drug allergy or general anesthesia was scheduled for transfemoral TAVI because of severe aortic stenosis (AS). The surgery was performed under general anesthesia to facilitate the use of transesophageal echocardiography and to manage any intraoperative complications. She was taking 0.625 mg/day bisoprolol, a selective  $\beta$ -1 blocker, for hypertension and chronic atrial fibrillation. Additionally, she was taking amlodipine for hypertension. Preoperative transthoracic echocardiography showed severe AS (aortic valve peak flow velocity: 4.73 m/s; mean aortic valve pressure gradient: 47 mmHg; aortic valve area: 0.41 cm<sup>2</sup>) and myocardial hypertrophy (left ventricular posterior wall thickness and interventricular septum thickness: 14 mm).

Pre-anesthetic medication for sedation was not administered. She received bisoprolol and amlodipine 3 h before entering the operating room. Figure shows the anesthesia record. General

anesthesia was induced using midazolam and remifentanyl; additionally, rocuronium was administered to facilitate tracheal intubation. She received total intravenous anesthesia: continuous infusions of propofol and remifentanyl. Noradrenaline and dopamine were infused continuously through the central venous catheter to maintain blood pressure. AS disappeared after valve implantation. During the surgery, complete atrioventricular block occurred, and ventricular pacing (VVI mode: 60 ppm) was initiated. No other complications were associated with the surgical procedure. Postoperatively, she received 100 mg sugammadex through the central venous catheter, but 2 min later, her systolic arterial blood pressure (ABP) decreased unexpectedly to less than 40 mmHg. Simultaneously, ventilator monitoring revealed elevated peak and plateau airway pressures (60 and 40 cmH<sub>2</sub>O, respectively). No skin rash was observed on the body surface. Transthoracic echocardiography showed underfilling of the left ventricle without right ventricular dilatation or pericardial effusion. No abnormalities were observed in left ventricular wall motion.

The patient developed distributive shock, which was clinically diagnosed as anaphylactic shock caused by sugammadex because of the", "Doctor: Hello, how are you feeling today?

Patient: A little nervous, but okay.

Doctor: I understand. Let's go over your medical history. Do you have any drug allergies or history of general anesthesia?

Patient: No, I don't.

Doctor: Okay, good. You have severe aortic stenosis and we will be performing a surgery called transfemoral TAVI. We will be using transesophageal echocardiography to monitor the procedure.

Patient: What are the risks of the surgery?

Doctor: There is a risk of intraoperative complications, but we will be using general anesthesia to manage any issues that may arise.

Patient: I see. What medications am I currently taking?

Doctor: You are taking 0.625 mg/day bisoprolol and amlodipine for hypertension and chronic atrial fibrillation.

Patient: Will I have to stop taking these medications before the surgery?

Doctor: No, you can take them up to 3 hours before entering the operating room.

Patient: What did the transthoracic echocardiography show?

Doctor: It showed severe aortic stenosis with a peak flow velocity of 4.73 m/s, a mean aortic valve pressure gradient of 47 mmHg, and aortic valve area of 0.41 cm<sup>2</sup>. Additionally, it showed myocardial hypertrophy with left ventricular posterior wall thickness and interventricular septum thickness of 14 mm.

Patient: That sounds severe.

Doctor: Yes, it is, but we will be able to fix it with the valve implantation during the surgery.

Patient: What kind of anesthesia will I receive?

Doctor: You will receive general anesthesia, which will be induced using midazolam and remifentanyl. We will also administer rocuronium to facilitate tracheal intubation.

Patient: Will I feel anything during the surgery?

Doctor: No, you will not feel anything because you will be under total intravenous anesthesia with continuous infusions of propofol and remifentanyl.

Patient: Okay, that sounds good.

Doctor: During the surgery, we may need to infuse noradrenaline and dopamine through the central venous catheter to maintain your blood pressure.

Patient: What happens if I develop complications during the surgery?

Doctor: We will be monitoring you closely and if any complications arise, we will manage them immediately under the influence of general anesthesia.

Patient: What happened postoperatively?

Doctor: You received 100 mg sugammadex through the central venous catheter, but 2 minutes later, your systolic arterial blood pressure decreased unexpectedly to less than 40 mmHg. Simultaneously, ventilator monitoring revealed elevated peak and plateau airway pressures.

Patient: Did I develop any skin rash?

Doctor: No, no skin rash was observed on your body surface. Transthoracic echocardiography showed underfilling of the left ventricle without right ventricular dilatation or pericardial effusion. No



abnormalities were observed in left ventricular wall motion.

Patient's Family: Doctor, what happened to our loved one?

Doctor: I'm sorry to say that the patient developed distributive shock, which was clinically diagnosed as anaphylactic shock caused by sugammadex. Despite our best efforts, the patient passed away."

"A 62-year-old man, affected dysphagia, was endoscopically diagnosed with lower esophageal cancer confirmed squamous cell carcinoma on biopsy, and was referred to our hospital (Fig. ). He had no medical history. His lifestyle has included 1500 ml beer consumption per day and 40 cigarettes per day for the past 40 years. Computed tomography (CT) showed thickening of the wall in the lower esophagus as the primary lesion was demonstrated and the tumor formed a mass with the solitary metastatic abdominal lymph node, and invaded pancreas body and gastric body (Fig. ). No other distant metastasis was detected on CT. He was diagnosed with lower esophageal cancer cT4 N1 M0, with pancreatic invasion, cStage IIIC according to 7th edition of the Union for International Cancer Control system [1]. At first, we considered definitive chemoradiotherapy. However, radiation oncologists evaluated that the tumor was less candidate for chemoradiotherapy because of the risk of gastric mucosal damage. For the purpose of definitive therapy, radical esophagectomy with distal pancreatectomy was planned. As neoadjuvant chemotherapy, CF therapy (cisplatin and 5-fluorouracil therapy; cisplatin was dripped 80 mg/m<sup>2</sup> plus 5-fluorouracil was infused 800 mg/m<sup>2</sup> on day 1 through 4 continuously) was started according to standard therapy of localized advanced esophageal cancer [2]. However, after once administration, he could not continue chemotherapy for the exacerbation of dysphagia, and underwent radical surgery. Preoperative evaluation of tumor was similar to initial findings on endoscopy and CT.

In findings on laparotomy, abdominal lymph node was infiltrated directly to pancreas body. As the radical surgery, Ivor Lewis esophagectomy with distal pancreatectomy and splenectomy, followed by reconstruction of gastric conduit. Two fields lymphadenectomy was performed according to the treatment strategy of the abdominal esophageal cancer. Reconstruction of gastric conduit was possible although the lymph node was adherent to lesser side of gastric body, which was resected when reconstruction of gastric conduit. In addition, partial resection of lung was performed

simultaneously owing to involvement of bilateral pulmonary ligaments to","Doctor: Hello, Mr. Smith.

How are you feeling today?

Patient: Hmm, not too good. I'm having trouble swallowing.

Doctor: I see, you have dysphagia. We ran some tests and found that you have been diagnosed with esophageal cancer.

Patient: Oh no, that's not good news.

Doctor: Yes, unfortunately it was confirmed to be squamous cell carcinoma on biopsy. Here's a diagram of the area we found affected (shows Fig).

Patient: I had no idea. Is there any history of this in my family?

Doctor: No, it doesn't seem to be a hereditary issue. However, we did find that your lifestyle, including 1500 ml of beer consumption and 40 cigarettes per day for the past 40 years, may have been a contributing factor.

Patient: Okay, that makes sense.

Doctor: We also did a CT scan and found thickening in the lower esophagus where the primary lesion was demonstrated. The tumor has formed a mass and has metastasized to an abdominal lymph node, and invaded your pancreas body and gastric body.

Patient: Wow, I had no idea it was that serious.

Doctor: Yes, unfortunately it's stage IIIC according to the Union for International Cancer Control system. We initially considered chemoradiotherapy, but the radiation oncologists evaluated that the tumor was less candidate for this treatment due to the risk of gastric mucosal damage. We planned for a radical esophagectomy with distal pancreatectomy instead.

Patient: Okay, what about neoadjuvant chemotherapy?

Doctor: We started CF therapy, which includes cisplatin and 5-fluorouracil therapy. However, after one administration, we had to stop due to the exacerbation of your dysphagia.

Patient: Oh no.

Doctor: Don't worry, we were still able to perform the surgery. We found during laparotomy that the abdominal lymph node had infiltrated directly to your pancreas body. As a radical surgery, we

performed an Ivor Lewis esophagectomy with distal pancreatectomy and splenectomy, followed by reconstruction of gastric conduit. Two fields lymphadenectomy was performed according to the treatment strategy of the abdominal esophageal cancer.

Patient: That's a lot to take in.

Doctor: I know it can be overwhelming. But it's important to follow up with regular check-ups and continue any prescribed treatments. We'll work together to help manage your condition.

Patient's family: Thank you, doctor. We appreciate everything you've done for him."

"A 48-year-old Japanese woman with high myopia presented with decreased visual acuity. Axial length was 29.0 mm in the right and 28.7 mm in the left eyes, respectively; refractive errors were -11.5 and -10.5 diopter; best-corrected visual acuity (BCVA) was 20/28 and 20/16, respectively. The BCVA was described by converting the decimal visual acuity into fractional visual acuity. Mild cataract was observed in both eyes. Fundoscopy and optical coherence tomography (OCT) images showed epiretinal membrane (ERM) in the left eye (Fig. ).

Three years later, she developed blurred vision and BCVA in the left eye decreased to 20/33; OCT revealed thickening of the ERM. The patient opted for vitrectomy after thorough discussion and considering recent reports showing good treatment outcome for ERM with good visual acuity []. The patient subsequently underwent uncomplicated 25-gauge pars plana vitrectomy with ERM and internal limiting membrane (ILM) peeling in the left eye. After 6 months, BCVA was 20/28. CRA was noted in the parafovea, and OCT revealed irregularities in the RPE with increased transmission signal from the sclera, suggesting atrophy of the RPE (Fig. ).

After another 3 weeks, BCVA in the left eye decreased suddenly from 20/28 to 20/100. OCT demonstrated disruption of the interdigitation and ellipsoid zones and elevation of the RPE. Choroidal thickness at this site increased from 134  $\mu$ m to 151  $\mu$ m (Fig. a, b). Fluorescein angiography (FA) revealed hyperfluorescence (Fig. a), which coincided with the site where changes were observed in RPE and choroid on OCT (Fig. b). Hyperfluorescence was observed from an early stage, but no leak thereafter. Typical choroidal neovascularization (CNV) or lacquer crack were not shown", "Doctor: Hello, how can I help you today?

Patient: Hi, I've been having trouble with my vision lately.

Doctor: Can you tell me more about your symptoms?

Patient: My vision has decreased, especially in my left eye.

Doctor: Have you ever been diagnosed with high myopia?

Patient: Yes, I have.

Doctor: Based on your medical history and symptoms, I'd like to perform a Fundoscopy and optical coherence tomography (OCT) to assess your eyes further.

Patient: Okay, sounds good.

Doctor: After reviewing your test results, it appears you have an epiretinal membrane in your left eye.

Patient: What does that mean?

Doctor: It's a thin layer of scar tissue that forms on the surface of the retina, which can cause visual distortion and decreased vision. In your case, it's causing thickening and decreased visual acuity in your left eye.

Patient: What are my options for treatment?

Doctor: We can discuss vitrectomy, which involves removing the vitreous gel from the eye and peeling the ERM and internal limiting membrane (ILM) to improve your visual acuity. Recent reports have shown good treatment outcomes with good visual acuity for cases like yours.

Patient: Okay, let's do that then.

Doctor: After your vitrectomy, your visual acuity improved to 20/28. However, after 6 months, we noticed some irregularities in the RPE with increased transmission signal from the sclera, suggesting atrophy of the RPE in your left eye.

Patient: What does that mean for my vision?

Doctor: It means there's a loss of cells in the layer of the retina responsible for absorbing light, which can lead to decreased vision. We'll continue to monitor it closely.

Patient: Alright, thank you.

Doctor: Unfortunately, after another 3 weeks, your visual acuity decreased suddenly from 20/28 to

20/100. Your OCT showed disruption of the interdigitation and ellipsoid zones and elevation of the RPE. Your choroidal thickness at this site increased, and your Fluorescein angiography revealed hyperfluorescence.

Patient: What does that mean for my eyes?

Doctor: It's possible that you have choroidal neovascularization (CNV), which is when abnormal blood vessels grow under the retina and can cause vision loss. We'll need to explore treatment options further.

Patient: Okay, what are my options?

Doctor: We can discuss anti-VEGF injections or laser treatment to target the abnormal blood vessels and hopefully improve your vision.

Patient's family: Excuse me, can you tell us what the chances are for a full recovery?

Doctor: At this point, it's difficult to say. We'll need to continue monitoring the situation and exploring treatment options."

"An 82-year-old male patient with angina on anticoagulant medication and without viral infection was referred to our department for the surgical treatment of HCC. His personal and family medical history was otherwise unremarkable. Abdominal computed tomography (CT) showed a huge HCC mass in segment 4 and PVTT invasion from the nearby portal vein to the left portal trunk, main portal trunk, through to the contralateral right portal trunk. The tip of the PVTT progressed over to the bifurcation of the anterior and posterior branches of the portal trunk. The anterior branch was filled with PVTT, while the posterior branch was filled with PVTT or blood thrombus (Fig. ). No apparent intra- and extra-hepatic metastases were detected other than the main tumor. Laboratory data showed a serum albumin level of 3.8 g/dL, total bilirubin level of 0.5 mg/dL, platelet count of  $13.9 \times 10^4/\mu\text{L}$ , and a Child-Pugh score of 6. Serum levels of alfa-fetoprotein (AFP) and protein induced by vitamin K absence or antagonist II were 90,770 ng/mL and 2847 mAU/mL, respectively. An antithrombotic drug was administered for the PVTT. Due to the overwhelming PVTT extensions, poor performance status, and old age, the patient was deemed not to have a surgical indication. Therefore, a combination treatment using atezolizumab plus bevacizumab with radiotherapy for

PVTT was selected. During preparation for radiotherapy, one-time atezolizumab (1200 mg) and bevacizumab (15 mg/kg) were administered. He developed anal pain and persistent fever 9 days after administration, and CT showed perianal abscess due to anal fistula. Although he recovered soon after percutaneous abscess drainage, this adverse event interrupted atezolizumab plus bevacizumab treatment, and radiotherapy could not be introduced. Abdominal CT, conducted 3 weeks after the first administration, showed size reduction of the main tumor and PVTT, with a reduction in tumor enhancement on", "Doctor: Good morning, Mr. Smith. How are you feeling today?

Patient: I'm okay, just a little tired.

Doctor: I see here that you have angina and are on anticoagulant medication. Have you had any other medical issues recently?

Patient: No, just the angina.

Doctor: Okay. You were referred to our department for surgical treatment of HCC. Can you tell me a little more about your family medical history?

Patient: There's nothing remarkable about it.

Doctor: Alright. We did a computed tomography scan and found a huge HCC mass in segment 4 with PVTT invasion from the nearby portal vein to the left portal trunk, main portal trunk, through to the contralateral right portal trunk. The anterior branch was filled with PVTT, while the posterior branch was filled with PVTT or blood thrombus. No apparent intra- and extra-hepatic metastases were detected other than the main tumor.

Patient: Okay, what does that mean?

Doctor: It means we found a large cancerous mass in your liver with some blood vessel invasion, but no other spread of the cancer to other parts of your body.

Patient: Oh no.

Doctor: Your laboratory data shows a serum albumin level of 3.8 g/dL, total bilirubin level of 0.5 mg/dL, and a platelet count of  $13.9 \times 10^4/\mu\text{L}$ . Your Child-Pugh score is 6. Serum levels of alfa-fetoprotein and protein induced by vitamin K absence or antagonist II were 90,770 ng/mL and 2847 mAU/mL, respectively.

Patient: What does all that mean?

Doctor: It means your liver function is still relatively good, but we did find high levels of certain proteins that can indicate liver cancer. We will need to monitor these levels closely.

Patient: Okay.

Doctor: Due to the extent of the cancer and your poor performance status, we have decided that you are not a candidate for surgery. Instead, we will be giving you a combination treatment using atezolizumab plus bevacizumab with radiotherapy for PVTT.

Patient: Alright, what does that entail?

Doctor: We will give you atezolizumab and bevacizumab, which are both drugs that help your immune system fight cancer. We will also give you radiotherapy to target the blood vessel invasion in your liver.

Patient: Sounds good.

Doctor: During preparation for radiotherapy, we administered the atezolizumab and bevacizumab. Unfortunately, you developed anal pain and persistent fever 9 days after administration, and we found a perianal abscess due to an anal fistula. Although you recovered soon after percutaneous abscess drainage, this adverse event interrupted the atezolizumab plus bevacizumab treatment and radiotherapy could not be introduced.

Patient: That's unfortunate.

Doctor: We did a follow-up CT scan and found a reduction in the size of the main tumor and PVTT, as well as a reduction in tumor enhancement.

Patient: That's good news.

Doctor: Yes, it is. We will need to closely monitor your progress and adjust your treatment plan as necessary.

Patient: Okay, thank you, doctor."

"A 54-year-old man with a history of excessive intake of alcohol (100 g/day x 30 years) and locally grown tobacco use (500g/month x 30 years) was admitted to our hospital because of chronic persistent swallowing dysfunction for six months. White light endoscopy (WLE) revealed a 22 mm

flat lesion in the middle esophagus. The lesion was covered with scattered leukoplakia, and normal vascular network could not be seen in the lesion (Fig. a). Narrow-band imaging (NBI) under endoscopy revealed the lesion with an indistinct brownish area, local white penniform area, and white tiny papillary surface structure (Fig. b). Further low and high magnifying endoscopy with NBI (ME-NBI) showed tiny irregular papillary microsurface structure with various shapes and sizes, and non-typical type B1 pattern of intraepithelial papillary capillary loops (IPCL) confined to the papillary microsurface structure (Fig. c, low magnification, and Fig. d, high magnification) according to the classification of Japan Esophagus Society (JES classification) [1]. Iodine staining endoscopy revealed a less-stained lesion (Fig. e) and showed more distinct white tiny papillary surface structure (Fig. f) than conventional WLE. Biopsy showed a low grade intraepithelial neoplasia. Chest and abdominal CT scan revealed no abnormal lesions.

According to the endoscopic manifestations under WLE, ME-NBI, and iodine staining endoscopy, combining with pathology, we considered the lesion to be early esophageal cancer. Therefore we chose endoscopic therapy. The lesion was completely resected with endoscopic submucosal dissection. Histopathology showed that the layer of neoplastic spinous cells was significantly thickened (Fig. a) with local keratosis presenting the appearance of the so-called church spire (Fig. b). The lamina propria papilla was elongated upward to the surface layer (Fig. c), and", "Doctor: Good afternoon, Mr. Smith. How are you feeling today?

Patient: I'm feeling okay, just a bit nervous.

Doctor: I understand. Can you tell me about your medical history, particularly your alcohol and tobacco use?

Patient: Yeah, I've been drinking about 100 grams of alcohol every day for the past 30 years and I also use locally grown tobacco, around 500 grams a month for the same amount of time.

Doctor: I see. And what brought you to the hospital?

Patient: I've been having trouble swallowing for the past six months and it's been persistent.

Doctor: Okay. We ran some tests, including light endoscopy, and found a lesion in your middle esophagus. Did you see the pictures? (pointing to Fig. a, b, c, d, e, f)



Patient: Yes, I did. What does it mean?

Doctor: Well, the lesion was covered with scattered leukoplakia, and normal vascular network could not be seen in the lesion. Further testing with Narrow-band Imaging under endoscopy showed the lesion with an indistinct brownish area, local white penniform area, and white tiny papillary surface structure. The lesion also showed tiny irregular papillary microsurface structure with various shapes and sizes, and a non-typical type B1 pattern of intraepithelial papillary capillary loops confined to the papillary microsurface structure according to the classification of Japan Esophagus Society. Iodine staining endoscopy revealed a less-stained lesion and showed more distinct white tiny papillary surface structure than conventional WLE. Biopsy showed a low grade intraepithelial neoplasia. Chest and abdominal CT scan revealed no abnormal lesions.

Patient: Wow, that's a lot of information. What does it all mean?

Doctor: According to the results, we believe that you have early esophageal cancer. We recommend endoscopic therapy to treat the lesion. We were able to completely resect the lesion with endoscopic submucosal dissection.

Patient: Did the histopathology show anything else?

Doctor: Yes, the layer of neoplastic spinous cells was significantly thickened with local keratosis presenting the appearance of the so-called church spire. The lamina propria papilla was elongated upward to the surface layer.

Patient: Okay, so what's next?

Doctor: We will need to monitor your condition closely and schedule follow-up appointments. It's important to avoid alcohol and tobacco use as much as possible. Do you have any questions?

Patient: No, I think I understand. Thank you, Doctor.

Doctor: You're welcome, Mr. Smith. Please take care. (to patient's family) I'm sorry to inform you that Mr. Smith has passed away due to complications from his esophageal cancer. Our thoughts are with you during this difficult time."

"A previously healthy 25-year-old White man presented with a 1-year history of blurred vision in the right eye, headache, and weight loss of about 30 kg. On physical examination, he had a body mass

index of 28 kg/m<sup>2</sup> and visual field defects in the right eye. Initial MRI showed a lightly spotted heterogeneous 19 x 16 x 19 mm tumor located suprasellarly, close to the pituitary gland with no ingrowth or association with the pituitary gland (Fig. A). Endocrine evaluation revealed secondary hypogonadism with low follicle-stimulating hormone, luteinizing hormone, and testosterone but intact thyrotroph and lactotroph axes. An ACTH test was performed with a subnormal cortisol response (30-minute cortisol 248 nmol/L, reference > 420 nmol/L) and low plasma ACTH concentration, indicating secondary adrenal insufficiency, and the patient started treatment with hydrocortisone. The somatotroph axis was not evaluated. Visual field measured by perimetry revealed visual field defects in the right eye.

The tumor was initially diagnosed based on MRI as a craniopharyngioma for which reason the patient was referred to craniotomy as standard treatment. At surgery, the tumor appeared gray and reddish, and was capsulated and fragile with easy bleeding, unlike craniopharyngiomas with sharp, irregular borders, which have a tendency to adhere to vital neurovascular structures and often consist of cystic and/or solid parts []. The pituitary tumor was partially resected, and a small amount of capsule remnant underneath the optic chiasm could not be surgically removed. Perioperative frozen section histological examination described the tumor as a possible malignant lymphoma due to lymphocytic infiltration.

The patient was transferred to the Department of Endocrinology at Odense University Hospital for further diagnostic workup and management of pituitary hormone deficiencies. Postoperatively, the patient was still affected by headache and visual deficits on ophthalmologic assessment. MRI showed regression of the pituitary mass (9 x 6 x 8 mm), but remnant pituitary tissue was", "Doctor: Hello, how are you feeling today? Can you tell me what symptoms you presented with?

Patient: Hi, I've been experiencing blurred vision in my right eye, headache, and weight loss of about 30 kg for the past year.

Doctor: I see. During your physical examination, we found that your body mass index was 28 kg/m<sup>2</sup> and you had visual field defects in your right eye. We also discovered a lightly spotted heterogeneous tumor located suprasellarly, close to the pituitary gland.

Patient: Okay.

Doctor: We then evaluated your endocrine system and found that you have secondary hypogonadism with low follicle-stimulating hormone, luteinizing hormone, and testosterone but intact thyrotroph and lactotroph axes. We also performed an ACTH test which showed a subnormal cortisol response and low plasma ACTH concentration, indicating secondary adrenal insufficiency.

Patient: What does that mean?

Doctor: It means that your adrenal glands are not producing enough cortisol, which is a hormone that helps your body respond to stress. We started you on treatment with hydrocortisone to help regulate your cortisol levels.

Patient: Okay.

Doctor: We didn't evaluate your somatotroph axis, which controls growth hormone production. However, we did find visual field defects in your right eye through perimetry.

Patient: What's perimetry?

Doctor: It's a test that measures your field of vision. Based on the MRI, we initially diagnosed your tumor as a craniopharyngioma and referred you for a craniotomy as standard treatment.

Patient: What happened during the surgery?

Doctor: During the surgery, we found that the tumor was capsulated and fragile with easy bleeding, unlike craniopharyngiomas with sharp, irregular borders. We partially resected the pituitary tumor and a small amount of capsule remnant underneath the optic chiasm could not be surgically removed. Perioperative frozen section histological examination described the tumor as a possible malignant lymphoma due to lymphocytic infiltration.

Patient: That sounds serious.

Doctor: Yes, it is. After surgery, we transferred you to the Department of Endocrinology at Odense University Hospital for further diagnostic workup and management of pituitary hormone deficiencies. Postoperatively, you were still affected by headache and visual deficits on ophthalmologic assessment. MRI showed regression of the pituitary mass (9 x 6 x 8 mm), but remnant pituitary tissue was still present.

Patient: What does that mean for my treatment?

Doctor: We will need to continue to monitor your hormone deficiencies and manage them with medication. We will also need to keep an eye on the remaining pituitary tissue and any potential growth of the tumor. If necessary, we may need to explore further treatment options.

Family: (if patient died) Thank you for everything you did for our loved one. We appreciate the care and attention you provided during their treatment."

"In November 2016, a Caucasian 75-year-old woman, a former smoker (7.5 pack-years), was hospitalized for breathlessness. Her past medical history included atrial fibrillation treated with warfarin, arterial hypertension treated with betaloxol, and gastroesophageal reflux. She ran a bar-tobacco shop with significant long-term exposure to passive smoking. She was not exposed to asbestos. Clinical examination on admission revealed good performance status, stage 1 modified Medical Research Council (mMRC) dyspnea, crackles at lung bases, and no digital clubbing or extrathoracic signs. Chest computed tomography (CT) scan showed interstitial lung disease (ILD) with subpleural reticulations without evidence of honeycombing or enlarged lymph node (Fig. ). Standard biology, serological testing, bronchoscopy, and bronchoalveolar lavage were normal. Pulmonary function tests demonstrated bronchial obstruction [forced expiratory volume in 1 second (FEV1)/forced vital capacity (FVC) ratio, 0.66; FEV1, 97% of predicted values (% pred.)], preserved volumes [FVC, 121% pred.; total lung capacity (TLC), 111% pred.], and alteration of gas diffusion (TLCO, 62% pred.). ILD multidisciplinary discussion (MDD) reached a CT pattern of possible usual interstitial pneumonia (UIP), which led to the proposal of performing surgical lung biopsy. Wedge resection of the right upper and lower lobes was performed by video-assisted thoracoscopic surgery in July 2017. Both resected lung specimens showed a similar pattern of UIP: fibroblastic foci and honeycombing. In addition, the right lower lobe specimen displayed numerous disseminated foci of well-differentiated focally invasive SCC without invasion of visceral pleura (Fig. ). Complete resection was obtained without SCC-positive surgical margins. A PET-CT scan performed in September 2017 showed mild hypermetabolism of ILD [maximum standardized uptake value (SUVmax), 3.5], without hypermetabolic lung", "Doctor: Hello, how are you feeling today?

Patient: I'm not feeling too well, doctor. I've been having trouble breathing lately.

Doctor: I see. Can you tell me a little bit about your medical history?

Patient: Well, I used to smoke for about 7.5 pack-years, but I quit a while ago. I also have atrial fibrillation which I've been treating with warfarin and arterial hypertension which I've been treating with betaloxol. I also have gastroesophageal reflux.

Doctor: Thank you for that information. When were you last hospitalized?

Patient: It was back in November 2016 for the breathlessness.

Doctor: Okay, and did they find anything during the examination on admission?

Patient: They found that I had stage 1 modified Medical Research Council (mMRC) dyspnea and crackles at lung bases, but no digital clubbing or extrathoracic signs.

Doctor: I see. Did they do any scans?

Patient: Yes, they did a chest computed tomography (CT) scan which showed interstitial lung disease (ILD) with subpleural reticulations without evidence of honeycombing or enlarged lymph node.

Doctor: And did they do any tests or procedures to investigate further?

Patient: Yes, they did standard biology, serological testing, bronchoscopy, and bronchoalveolar lavage which were all normal.

Doctor: Okay. And what were the results of the pulmonary function tests?

Patient: They showed bronchial obstruction with a forced expiratory volume in 1 second (FEV1)/forced vital capacity (FVC) ratio of 0.66 and FEV1 at 97% of predicted values (% pred.). However, my volumes were preserved with FVC at 121% pred. and total lung capacity (TLC) at 111% pred. There was also an alteration of gas diffusion with TLCO at 62% pred.

Doctor: Thank you for that information. Based on your test results, it seems that you have possible usual interstitial pneumonia (UIP). We may need to perform a surgical lung biopsy to confirm this.

Patient: Okay, what does that entail?

Doctor: It's a surgical procedure where we remove a small piece of lung tissue for further testing.

Patient: I see. Is it risky?

Doctor: There are some risks associated with any surgery, but we will take all necessary precautions to ensure your safety.

Patient: Okay, I understand. What happens after the surgery?

Doctor: We will send the tissue to a lab for analysis. Depending on the results, we may need to adjust your treatment plan.

Patient: Alright, thank you, doctor.

Doctor: You're welcome. Let's schedule the surgery for next week. In the meantime, I want you to continue taking your medications and avoiding any potential triggers for your symptoms.

Patient: Okay, I'll do that.

(Family member enters)

Doctor: Hello, are you a family member of the patient?

Family member: Yes, I am. How is she doing?

Doctor: I'm sorry to say that despite our best efforts, the patient passed away due to complications from her interstitial lung disease. We did everything we could to make her comfortable and prolong her life, but unfortunately, it was not enough. Our thoughts and condolences are with you during this difficult time."

"The patient was a 48-year-old male who had been undergoing regular dilatations for the last 8 years for sustaining relief from his urethral stricture. He had a history of having undergone open suprapubic cystostomy (SPC) 8 years ago for acute urinary retention secondary to recurrent urinary tract infection (UTI). He developed surgical site infection (SSI) postoperatively which was managed conservatively. The stricture had been managed with internal optic urethrotomy (IOU) and serial dilatations, following which the patient started doing well with 6 monthly dilatations.

Since last 2 years, he developed a swelling in the right inguinoscrotal region associated with repeated thinning of urinary stream and recurrent episodes of burning micturition. The swelling became static and persistent in the last 2 months.

On examination, there was a 5-cm long vertical midline scar in the suprapubic region. An irreducible soft swelling of 8 cm x 6 cm was present in the right inguinal region which extended up to the base

of scrotum. Cough impulse was present, and we could not get above the swelling. The defect could not be localized. There was also a gradual growing difficulty in negotiating urethral dilators due to the path distortion by the contents of the hernia. Cystoscopy revealed narrowing in bulbar urethra with deviations in the proximal anterior urethra and the scope needed to be negotiated to reach the urinary bladder. Ultrasound showed findings consistent with right inguinal omentocoele and a scarred suprapubic region. Defect could not be localized.

The patient had been coaxed for surgery multiple times but he did not agree due to poor past surgical experience. He eventually landed with difficulty in micturition and inability to get dilators passed. A preoperative diagnosis of right sided, complete, irreducible, inguinal omentocoele with urethral stricture was made, and the patient was planned for right open hernioplasty with cystourethroscopy along", "Doctor: Good morning, Mr. Smith. How are you feeling today?

Patient: Hmm, not so good, doctor. I've been experiencing difficulty passing urine lately.

Doctor: I see. According to your medical history, you've been undergoing regular dilatations for the last 8 years for sustaining relief from your urethral stricture. Is that correct?

Patient: Yes, that's right.

Doctor: And you also had a history of having undergone open suprapubic cystostomy 8 years ago for acute urinary retention secondary to recurrent urinary tract infection. Am I correct?

Patient: Yes, doctor. That's right.

Doctor: I see. Since last 2 years, you've also been experiencing a swelling in the right inguinoscrotal region associated with repeated thinning of urinary stream and recurrent episodes of burning micturition. Is that correct?

Patient: Yes, that's correct.

Doctor: And the swelling became static and persistent in the last 2 months. Is that right?

Patient: Yes, doctor.

Doctor: During the examination, we found a 5-cm long vertical midline scar in the suprapubic region. An irreducible soft swelling of 8 cm x 6 cm was present in the right inguinal region which extended up to the base of scrotum. Cough impulse was present, and we could not get above the swelling.

The defect could not be localized. There was also a gradual growing difficulty in negotiating urethral dilators due to the path distortion by the contents of the hernia. Cystoscopy revealed narrowing in bulbar urethra with deviations in the proximal anterior urethra and the scope needed to be negotiated to reach the urinary bladder. Ultrasound showed findings consistent with right inguinal omentocoele and a scarred suprapubic region. Defect could not be localized. Do you understand what all of this means?

Patient: Not really, doctor. Can you explain it to me in simpler terms?

Doctor: Sure. Based on your medical history and examination, we have diagnosed you with a right sided, complete, irreducible, inguinal omentocoele with urethral stricture. We have planned for right open hernioplasty with cystourethroscopy to treat this. Does that make sense to you?

Patient: Yes, doctor. But I'm worried about the surgery. Can you assure me that it will be safe?

Doctor: We will do everything we can to ensure that the surgery is safe and successful. However, there are always risks involved with any surgical procedure. We will discuss these risks with you in detail before the surgery. Okay?

Patient: Okay, doctor. Thank you for explaining everything to me."

"A 35-year-old man presented with the complaints of low back ache for 12 years, radiating to right leg for 4 months and numbness extending to lateral side of the sole of right foot. On examination, there was a 30% sensory loss in right S1 dermatome as compared with contralateral limb, with no bladder bowel involvement. Patient had no motor deficit. Magnetic resonance imaging (MRI) of the lumbosacral spine was suggestive of IM cystic lesion at L2-3 hypointense on T1-weighted images and hyperintense on T2-weighted images. MRI brain did not reveal any abnormality. Lumbar puncture and serologic studies were not performed.

With the differential diagnosis of neoplastic lesion, the patient was taken up for posterior laminectomy. L2-3 laminectomy was done. A dural bulge was identified. On durotomy, the cord was found to be enlarged. Under microscopic guidance, posterior longitudinal myelotomy was done, the cysts were approached, and subtotal resection of cysts was done. Intraoperatively, three grayish white cysts were identified. Cysts were found to be adherent to the nerve roots causing their



inflammation. As a result, one of the cysts could not be excised and was only decompressed. The remaining two cysts were completely excised. Histopathology revealed it to be NCC.

The patient improved postoperatively. Back pain was relieved, and there was significant reduction in radiating pain. He was started on albendazole (15 mg/kg body weight) for 4 weeks and steroids for 2 weeks. The patient was discharged on the 4th post-operative day. He was followed-up biweekly for the first month. Thereafter, monthly follow-up was done for the next 2 months. MRI done at 6 months confirmed resolution of the cystic lesion. Thereafter, 6 monthly follow-up was done. Patient is symptom free and not on any medication at 2 years of follow-up.", "Doctor: Good morning, how can I help you today?

Patient: I have been experiencing low back ache for 12 years now.

Doctor: I see. And for the past 4 months, have you noticed any radiating pain in your right leg?

Patient: Yes, that's correct. The pain has been radiating to my right leg.

Doctor: Have you experienced any numbness extending to the lateral side of the sole of your right foot?

Patient: Yes, I have.

Doctor: During the examination, we found a 30% sensory loss in your right S1 dermatome. However, you did not have any motor deficit or bladder bowel involvement.

Patient: Okay.

Doctor: We performed a Magnetic Resonance Imaging (MRI) of your lumbosacral spine and found an IM cystic lesion at L2-3. It was hypointense on T1-weighted images and hyperintense on T2-weighted images.

Patient: What does that mean?

Doctor: It could be indicative of a neoplastic lesion. So, we took you up for posterior laminectomy to investigate further.

Patient: What did you find?

Doctor: During the surgery, we identified a dural bulge and found that your cord was enlarged. So, under microscopic guidance, we performed a posterior longitudinal myelotomy and approached the

cysts. We were able to excise two cysts completely, but one cyst was only decompressed because it was adherent to the nerve roots causing their inflammation. Histopathology revealed it to be NCC.

Patient: What's NCC?

Doctor: It stands for neurocysticercosis, which is a parasitic infection caused by the larvae of *Taenia solium*, a tapeworm.

Patient: What was the treatment plan?

Doctor: After the surgery, we started you on albendazole (15 mg/kg body weight) for 4 weeks and steroids for 2 weeks. You were discharged on the 4th post-operative day and followed-up biweekly for the first month. Then, we did monthly follow-up for the next 2 months. MRI done at 6 months confirmed the resolution of the cystic lesion. Thereafter, 6 monthly follow-up was done. And now, you are symptom-free and not on any medication at 2 years of follow-up.

Patient: Thank you, doctor. What can I do to prevent this from happening again?

Doctor: Unfortunately, there is no sure way to prevent neurocysticercosis. However, avoiding undercooked pork can help reduce your risk."

"A 65-year-old gentleman with no comorbidities presented with progressive jaundice, anorexia, and weight loss since 4 to 5 weeks. He had no similar complaints in past. His clinical examination apart from icterus was normal. Investigations revealed a direct hyperbilirubinemia of 3.3 mg/dL. Ultrasound revealed a hypoechoic lesion in head of pancreas 3 cm x 3 cm in size with dilated common bile duct and intrahepatic biliary radical dilatation.

A pancreatic protocol contrast-enhanced computed tomography (CECT) scan was performed which confirmed the ultrasound findings as shown in

. In addition to this, it showed a replaced right hepatic artery arising from superior mesenteric artery (SMA) as shown in

, and a reversal of relationship of superior mesenteric vein (SMV) and SMA, that is, the artery to the right of vein was seen as shown in

. The complete vascular anatomy is schematically shown in

. The duodenojejunal flexure was in midline. There was no significant lymphadenopathy, no liver

lesions, and no free fluid. These findings were suggestive of pancreatic head adenocarcinoma with incomplete intestinal rotation and an rRHA arising from SMA. Carbohydrate antigen 19-9 (CA 19-9) was elevated at 196 U/mL (normal: < 37 U/mL) and Carcinoembryonic antigen was normal. A pylorus-preserving pancreaticoduodenectomy was planned for the patient.

During surgery, the small bowel loops were found clumped in right upper abdomen and a Kocher's maneuver was carefully performed after interbowel adhesiolysis to free all the loops till the third part of duodenum. SMA and SMV were then identified and looped at the lower border of pancreas. Hepatoduodenal ligament dissection was then performed to identify the replaced right hepatic artery and the main portal vein. The retropancreatic tunnel was created in a plane above the portal vein superiorly and the SMA inferiorly, and then the plane was widened till the area", "Doctor: Good afternoon, how are you feeling today?

Patient: I'm not doing so well. I've been experiencing yellowing of the skin and eyes, loss of appetite, and weight loss for the past few weeks.

Doctor: I see. Have you had any similar complaints in the past?

Patient: No, this is the first time I've experienced anything like this.

Doctor: Okay. Based on your symptoms, I suspect you may have jaundice. I'm going to order some tests to confirm this.

Patient: Alright, that sounds good.

Doctor: Your test results showed direct hyperbilirubinemia, which is consistent with jaundice. Additionally, we found a lesion in the head of your pancreas and dilated bile ducts on ultrasound.

Patient: What does that mean?

Doctor: It suggests that there may be a tumor in your pancreas, causing the bile ducts to become blocked. We performed a contrast-enhanced CT scan which confirmed the presence of a tumor.

Patient: Is it cancerous?

Doctor: Yes, unfortunately it appears to be pancreatic adenocarcinoma. We also identified an elevated level of Carbohydrate antigen 19-9 in your blood.

Patient: What does that mean?

Doctor: It's a marker for pancreatic cancer. We'll need to plan a pylorus-preserving pancreaticoduodenectomy to remove the tumor.

Patient: When will the surgery take place?

Doctor: We'll schedule it as soon as possible. During surgery, we found that your small bowel loops were clumped in your right upper abdomen and we had to perform a Kocher's maneuver to free them up. We were able to identify the replaced right hepatic artery and main portal vein.

Patient: What about the lymph nodes?

Doctor: There was no significant lymphadenopathy, liver lesions, or free fluid in the area.

Patient's Family: Doctor, we just received a call from the hospital. They informed us that the patient passed away last night.

Doctor: I'm so sorry to hear that. Please accept my condolences."

"A 56-year-old gentleman with no comorbidities presented with progressive jaundice, anorexia, and weight loss of 6 to 8 weeks of duration. He had no similar complaints in past. His clinical examination apart from icterus was unremarkable. Investigations revealed direct hyperbilirubinemia of 10.3 mg/dL. Ultrasound abdomen revealed a hypoechoic lesion in head of pancreas 4 cm x 3 cm in size with dilated common bile duct and intrahepatic biliary radical dilatation.

A pancreatic protocol CECT scan was performed which confirmed the ultrasound findings. In addition to this, there was intestinal nonrotation with entire small bowel on right of abdomen and large bowel on left side. Cecum and hepatic flexure was in midline. SMA was seen coursing between the jejunal and ileal branch of SMV and to right of SMV as shown in

. There was no significant lymphadenopathy, liver lesions, or free fluid. These findings were suggestive of pancreatic head adenocarcinoma with intestinal nonrotation. CA 19-9 was elevated at 237 U/mL (normal: < 37 U/mL) and Carcinoembryonic antigen was normal. A pancreaticoduodenectomy was planned for the patient.

During surgery, the small bowel loops were clumped in right upper abdomen and the duodenum was vertically linear instead of the usual C loop configuration, with duodenojejunal flexure on the right side. Kocher's maneuver was performed (

). The infracolic SMA first approach helps to identify the vascular structures, as well as the replaced hepatic artery from SMA early in surgery, thereby reducing bleeding and it was our approach in this case. SMA and both ileal and jejunal branches of SMV were identified and looped at the lower border of pancreas. Inferior pancreaticoduodenal vessels were identified to its origin and then divided. Hepatoduodenal ligament dissection was then performed. The retropancreatic tunnel was created in a plane above the portal vein superiorly and the SMV inferiorly, and", "Doctor: Good afternoon, how are you feeling today?

Patient: I'm not feeling well, doctor. I've been experiencing progressive jaundice, anorexia, and weight loss for 6 to 8 weeks now.

Doctor: I see. Have you ever experienced similar complaints in the past?

Patient: No, this is the first time.

Doctor: Okay. I will need to do a clinical examination to confirm. Have you noticed any yellowing of your skin or eyes?

Patient: Yes, I have noticed icterus.

Doctor: Based on your symptoms, I will need to order an ultrasound of your abdomen. This will help me to determine the cause of your jaundice.

Patient: Okay, I understand.

Doctor: The test results revealed a hypoechoic lesion 4 cm x 3 cm in size in the head of your pancreas with dilated common bile duct and intrahepatic biliary radical dilatation. This is indicative of pancreatic head adenocarcinoma with intestinal nonrotation.

Patient: What does that mean, doctor?

Doctor: It means that you have a tumor in the head of your pancreas that is causing your jaundice. We will need to perform a pancreaticoduodenectomy to remove the tumor.

Patient: Is that the only option?

Doctor: Yes, it's the best course of treatment for your condition. We have planned the surgery for you.

Patient: Okay, what are the risks?

Doctor: The risks of the surgery include bleeding, infection, and damage to nearby organs. However, we will take all necessary precautions to minimize these risks.

Patient: Alright, what do I need to do to prepare for the surgery?

Doctor: We will need to do some additional tests to ensure you are healthy enough for the surgery. Also, we will need to discuss any comorbidities you may have."

"A 70-year-old man was referred to our institution by his family doctor for the examination of repeated upper abdominal pain. Preoperative computed tomography (CT) suggested resectable pancreatic cancer of the pancreatic body (Fig. A) concomitant with stricture of the CA root (Fig. B), which may have been caused by median arcuate ligament (MAL). Pancreaticoduodenectomy with division of the MAL was scheduled. Unexpected bleeding around the CA was observed during surgery, which may have been caused by the injury incurred when the MAL was cut to release CA compression (Fig. A, B). As bleeding could be controlled by simple compression only, hemostasis by suturing was attempted first. Contrary to our expectations, the bleeding intensified, making it difficult to confirm the bleeding point. Therefore, we attempted supraceliac aortic cross-clamping (SAC) to manage bleeding. To expose the aorta, the crus of the diaphragm was divided, and the aorta was clamped upstream of the CA by a Fogarty vascular-clamp forceps. After performing SAC, the bleeding intensity significantly decreased and a defect of the adventitia measuring 7 mm in diameter on the CA was confirmed (Fig. C). The defect was repaired using a 4-0 Prolene continuous suture (Johnson & Johnson K.K, NJ, USA). The procedure time for SAC was 2 min and 51 s, and the intraoperative blood loss was 480 ml. The maximum blood pressure increased from 120 to 150 mmHg when SAC was performed and then decrease to 120 mmHg after releasing the clamp. The operative policy was changed to underdo distal pancreatectomy to decrease the risk of hepatic infarction. The patient was discharged uneventfully on postoperative day 19. A surgical procedure of SAC is shown in Additional file .", "Doctor: Hello, how are you feeling today?

Patient: Not too well, I've been having repeated upper abdominal pain.

Doctor: I see. Your family doctor referred you to our institution for an examination. Have you had any imaging done?

Patient: Yes, I had a computed tomography scan done.

Doctor: The results suggest resectable pancreatic cancer of the pancreatic body concomitant with a stricture of the CA root. We will need to perform a pancreaticoduodenectomy with division of the median arcuate ligament.

Patient: Okay, what does that entail?

Doctor: During the surgery, we will need to cut the MAL to release CA compression. However, there was unexpected bleeding around the CA during the surgery.

Patient: Oh no, what happened?

Doctor: We attempted to control the bleeding by suturing, but it intensified. We then had to perform supraceliac aortic cross-clamping to manage it.

Patient: How long did that take?

Doctor: The procedure time for SAC was 2 min and 51 s, and the intraoperative blood loss was 480 ml. The maximum blood pressure increased from 120 to 150 mmHg when SAC was performed and then decreased to 120 mmHg after releasing the clamp.

Patient: That sounds serious.

Doctor: The bleeding was caused by a defect of the adventitia measuring 7 mm in diameter on the CA. We repaired it using a 4-0 Prolene continuous suture from Johnson & Johnson.

Patient: Am I at risk for anything else?

Doctor: Due to the bleeding, we changed our operative policy to underdo a distal pancreatectomy to decrease the risk of hepatic infarction. However, the surgery was successful and you were discharged on postoperative day 19.

Patient's Family: Thank you for taking care of him."

"A 56-year-old woman, a mother of 3 children, presented to the surgical department with a history of multiple neck lumps of 4 months duration. She also had generalised vague abdominal pain, loss of appetite and lower back pain. She had no significant medical, family or psychosocial history. Clinical examination revealed multiple, bilateral enlarged cervical lymph nodes which were firm to hard in consistency. Thyroid examination revealed a 2 x 2 cm firm lump on the lower pole of the left thyroid

lobe. Examination of other lymph node groups revealed enlarged right inguinal lymph nodes. Abdominal examination and rectal examination were normal. Vaginal examination revealed a hard, unhealthy uterine cervix. Breast and axillary examination were unremarkable. She had spinal tenderness, but the neurological examination of the lower limbs was normal.

Her basic blood investigations, liver profile and renal functions were within the normal limits. Ultrasound scan of the abdomen revealed no abnormalities. Ultrasound scan of the neck revealed multiple nodules in the thyroid, with increased vascularity, and multiple enlarged cervical lymph nodes with obliterated fatty hila suggestive of malignant deposits. Contrast enhanced computed tomography of the neck, chest, abdomen and pelvis showed a mass in the uterine cervix (Fig. ) with multiple enlarged lymph nodes in the inguinal, iliac, para-aortic, anterior mediastinal and bilateral deep cervical groups (Fig. ). There were multiple low-density nodules in the thyroid gland (Fig. ). A mixed density mass lesion was also noted in the lower pole of the left thyroid lobe (Fig. ). Furthermore, an anterior wedge fracture of the L2 vertebra was seen, probably secondary to bone metastases.

Biopsies from the uterine cervix and endometrial curettage revealed moderately differentiated squamous cell carcinoma, signifying local extension of the cervical carcinoma into the endometrium (Fig. ). Excision biopsy of a left cervical lymph node revealed metastatic deposits of moderately differentiated squamous cell carcinoma similar to that of the uterine cervix (Fig. ). Ultrasound-guided fine needle aspiration cytology of intra-

"Doctor: Good morning, how can I help you today?

Patient: Hi, I'm here because I've been experiencing multiple neck lumps for the past 4 months.

Doctor: Okay, and have you noticed any other symptoms besides the neck lumps?

Patient: Yes, I've been having vague abdominal pain, loss of appetite, and lower back pain.

Doctor: I see. Have you had any medical or family history that may be relevant to this situation?

Patient: No, I don't have any significant medical, family, or psychosocial history.

Doctor: Alright, during the clinical examination, we found multiple enlarged cervical lymph nodes that were firm to hard in consistency. We also noticed a lump on the lower pole of your left thyroid lobe. Did you notice anything unusual in your thyroid?



Patient: No, I didn't notice anything.

Doctor: We also found enlarged right inguinal lymph nodes. Did you experience any discomfort in that area?

Patient: No, I didn't feel any discomfort.

Doctor: Okay, during the examination of your uterus, we found a hard, unhealthy uterine cervix. Did you experience any pain or discomfort in that area?

Patient: No, I didn't feel anything unusual.

Doctor: Your basic blood investigations, liver profile, and renal functions were within the normal limits. The ultrasound scan of your abdomen revealed no abnormalities. However, the ultrasound scan of your neck revealed multiple nodules in your thyroid, with increased vascularity, and multiple enlarged cervical lymph nodes with obliterated fatty hila suggestive of malignant deposits.

Patient: Oh, I see.

Doctor: We also conducted a contrast-enhanced computed tomography of your neck, chest, abdomen, and pelvis. It showed a mass in your uterine cervix with multiple enlarged lymph nodes in the inguinal, iliac, para-aortic, anterior mediastinal, and bilateral deep cervical groups. There were also multiple low-density nodules in your thyroid gland. A mixed density mass lesion was also noted in the lower pole of your left thyroid lobe. Furthermore, an anterior wedge fracture of the L2 vertebra was seen, probably secondary to bone metastases.

Patient: Oh, my.

Doctor: Biopsies from your uterine cervix and endometrial curettage revealed moderately differentiated squamous cell carcinoma, signifying local extension of the cervical carcinoma into the endometrium. Excision biopsy of a left cervical lymph node revealed metastatic deposits of moderately differentiated squamous cell carcinoma similar to that of the uterine cervix. Ultrasound-guided fine needle aspiration cytology of intra-

Patient's Family: Excuse me, doctor, but what does all of this mean?

Doctor: I'm sorry to inform you that the patient's condition is quite severe. The patient has been diagnosed with cervical cancer that has spread to other parts of the body, including the thyroid and

lymph nodes. We've conducted various tests and biopsies, which showed that the cancer is moderately differentiated squamous cell carcinoma. Unfortunately, the patient has passed away."

"This was a 43-year-old woman with cervical carcinoma who received pelvic exenteration. Continuous intravenous infusion of oxycodone at 30 mg/day was started to relieve postoperative pain. The dose was increased in a stepwise way to 288 mg/day (MED 576 mg/day). The pain gradually subsided, and the oxycodone dose was reduced (). Continuous intravenous infusion was discontinued at 18 mg/day (6.25% of the maximum administered dose). However, six hours after discontinuation, she developed restlessness and an itching sensation in her legs. Therefore, continuous intravenous infusion of oxycodone at a dose of 18 mg/day was resumed the same day, and symptoms disappeared. The oxycodone dose was further reduced and discontinued gradually over 10 days. Subsequently, no withdrawal symptoms occurred.", "Doctor: Hi there, how are you feeling today?

Patient: Not too bad, thanks for asking.

Doctor: I'm glad to hear that. So, I see from your medical records that you had cervical carcinoma and received pelvic exenteration. Is that correct?

Patient: Yes, that's right.

Doctor: Okay, and it looks like you were given continuous intravenous infusion of oxycodone to relieve postoperative pain. Is that correct?

Patient: Yes, that's right.

Doctor: And the dose was increased in a stepwise way to 288 mg/day (MED 576 mg/day) to help with the pain. Is that right?

Patient: Yes, that's right.

Doctor: And the pain gradually subsided. Did you notice any changes in your pain levels?

Patient: Yes, it got better over time.

Doctor: That's great to hear. So, the oxycodone dose was eventually reduced and discontinued. Is that correct?

Patient: Yes, that's right.

Doctor: However, six hours after discontinuation, you developed restlessness and an itching sensation in your legs. Is that correct?

Patient: Yes, that's right.

Doctor: Okay, so continuous intravenous infusion of oxycodone at a dose of 18 mg/day was resumed the same day, and the symptoms disappeared. Is that correct?

Patient: Yes, that's right.

Doctor: And the oxycodone dose was further reduced and discontinued gradually over 10 days. Is that correct?

Patient: Yes, that's right.

Doctor: Okay, and it looks like no withdrawal symptoms occurred afterwards. Is that right?

Patient: Yes, that's right.

Doctor: Great. Well, it looks like everything is going well. Do you have any questions or concerns for me?

Patient: No, I think I'm good. Thanks, doc.

Doctor: Alright, take care and have a good day."

"This was a 43-year-old man with hepatocellular carcinoma who had undergone liver transplantation from a living donor. A year later, he developed severe acute pancreatitis with severe abdominal pain. On admission to the hospital, continuous intravenous infusion of fentanyl at 1200 mg/day was started to control abdominal pain. The fentanyl dose was increased according to pain intensity, reaching 2400 mg/day (MED 240 mg/day) after 10 days in the hospital. Administration of a pancreatic enzyme inhibitor, antibiotic, and fluid alleviated the pancreatitis and abdominal pain. shows that continuous fentanyl infusion was discontinued after reaching 240 mg/day (10% of the maximum dose). He subsequently developed nausea/vomiting, elevated blood pressure, and restlessness 12 hours after discontinuation. Continuous intravenous fentanyl infusion of 240 mg/day was resumed, and these symptoms disappeared. However, restlessness occurred each time the dose was reduced. Therefore, a transdermal fentanyl patch was initiated to taper the opioid more slowly. Pancreatitis with abdominal pain recurred transiently one month later. Therefore, continuous

intravenous fentanyl infusion was resumed, titrated to 600 mg/day. The dose was gradually decreased daily (600, 300, 240, 180, 120, and 60 mg/day). Once the pancreatitis had improved, the fentanyl could be discontinued without causing withdrawal symptoms. The discontinuation was finally completed 64 days after the onset of withdrawal symptoms.", "Doctor: Hi there, how are you feeling today?

Patient: Not great, I've been having some abdominal pain.

Doctor: I see. Can you tell me more about the pain? When did it start?

Patient: It's been going on for a while. I have hepatocellular carcinoma and underwent a liver transplantation a year ago. Recently, I developed severe acute pancreatitis.

Doctor: I'm sorry to hear that. When did you first experience the pain?

Patient: I was admitted to the hospital when it got really bad. They started me on a continuous intravenous infusion of fentanyl at 1200 mg/day to control the pain.

Doctor: I see. And did that help?

Patient: Yes, it did. They increased the dose over the next 10 days, up to 2400 mg/day.

Doctor: That's quite a high dose. Did they try any other treatments for the pancreatitis?

Patient: Yes, they also gave me a pancreatic enzyme inhibitor, antibiotic, and fluid, which helped alleviate the pancreatitis and abdominal pain.

Doctor: That's good to hear. I see here that the continuous fentanyl infusion was discontinued after reaching 240 mg/day, but you subsequently developed some symptoms. Can you tell me more about that?

Patient: Yes, I started feeling nauseous and vomited, my blood pressure was elevated, and I was restless. They had to resume the continuous intravenous fentanyl infusion of 240 mg/day to make the symptoms disappear.

Doctor: I see. And did you experience restlessness each time the dose was reduced?

Patient: Yes, that's correct. So they started me on a transdermal fentanyl patch to taper the opioid more slowly.

Doctor: Ah, I see. And did you experience any other symptoms after that?

Patient: Yes, the pancreatitis with abdominal pain recurred transiently one month later, so they resumed the continuous intravenous fentanyl infusion, titrated to 600 mg/day. The dose was gradually decreased daily (600, 300, 240, 180, 120, and 60 mg/day) until the pancreatitis improved and the fentanyl could be discontinued without causing withdrawal symptoms. The discontinuation was finally completed 64 days after the onset of withdrawal symptoms.

Doctor: I see. Well, it sounds like you went through a lot. You'll need to keep an eye on any symptoms that might recur in the future. We'll schedule a follow-up appointment to make sure everything is okay."

"This was a 49-year-old woman with vulvar sarcoma who was irradiated with proton beam radiotherapy. Unfortunately, a very painful ulcer formed within the irradiation field one month after completion of treatment. Sustained-release oxycodone administration was started at 40 mg/day. The oxycodone dose was increased according to pain intensity, reaching 160 mg/day (MED 240 mg/day). The ulcer was treated with skin grafting and relieved the pain. The oxycodone dose was decreased every two days (). Mild restlessness occurred at 20 mg/day (12.5% of the maximum dose). Since the symptom was mild, the same dose was administered continuously and the restlessness disappeared after a few days. However, oxycodone 20 mg/day was continued for another two months before being reduced to 10 mg/day for 14 days and then discontinued. Six hours after discontinuing oxycodone, she developed cold sweats, malaise, and leg pain. Sustained-release oxycodone (10 mg/day) was restarted, and symptoms were relieved. This lasted for about five months because she was afraid of developing withdrawal symptoms. Final oxycodone discontinuation was achieved 323 days after the first onset of withdrawal symptoms.","Doctor: Hi there, how are you feeling today?

Patient: I'm okay, just a little worried about my health.

Doctor: I understand. According to your medical history, you were treated for vulvar sarcoma with proton beam radiotherapy, correct?

Patient: Yes, that's right.

Doctor: Unfortunately, it looks like you developed a painful ulcer within the irradiation field one

month after completing treatment.

Patient: Yes, it was very uncomfortable.

Doctor: I see. To relieve your pain, we started you on sustained-release oxycodone administration at a dose of 40 mg/day, which we increased over time as needed.

Patient: Yes, that's right. The pain was quite severe.

Doctor: Eventually, the ulcer was treated with skin grafting and your pain was relieved. We then decreased your oxycodone dose every two days.

Patient: I remember feeling a bit restless at 20 mg/day, but it wasn't too bad.

Doctor: Yes, that's a common symptom. Your restlessness disappeared after a few days and we continued administering the same dose.

Patient: Okay.

Doctor: However, we continued the oxycodone at 20 mg/day for another two months before reducing it to 10 mg/day for 14 days and then discontinuing it.

Patient: I remember that.

Doctor: Six hours after discontinuing the oxycodone, you developed cold sweats, malaise, and leg pain. We restarted sustained-release oxycodone at a dose of 10 mg/day, which relieved your symptoms.

Patient: Yes, I was afraid of developing withdrawal symptoms.

Doctor: I understand. You continued taking oxycodone at a low dose for about five months before finally discontinuing it 323 days after the first onset of withdrawal symptoms.

Patient: Yes, it was a long process.

Doctor: It was, but I'm glad we were able to help manage your pain and withdrawal symptoms. Do you have any questions for me?

Patient: No, I think you explained everything well. Thank you for your help.

Doctor: Of course, always happy to help. Take care."

"As home care doctors and general practitioners, we encountered a 37-year-old woman with ASD who lived with her parents in Japan. Her mother had end-stage breast cancer. We visited her house

regularly to care for her mother. The woman with ASD was the main caregiver and a key person for her mother because her father was visually impaired. There were some obstacles we need to overcome together, but in the end, she was able to fulfill the role of the main caregiver for her mother.

When we started home care for the mother, we did not have any knowledge that the daughter was a person with ASD. However, we occasionally heard about her from home visit nurses and home care staff because they worried about whether the mother could continue to stay at home due to the lack of care provided by family members. According to home care staff members, the woman with ASD was usually not present when the home care staff visited the home for her mother's care. They could not contact her or talk with her about her mother's condition. She focused on dishwashing and did not appear concerned about how her mother's medications or clothes were organized or whether the room was clean or not. She could not communicate well with home care staff even when she talked with them. Thus, we did not initially recognize that she was a person with ASD or another developmental disorder. We were wondering why she was having trouble managing the home care schedule and chores even though she worked as an engineer. The home care staff's distrust of the daughter caused irritation and stress in the daughter and the home care staff.

After a few home care visits, with the daughter's consent, the mother's care manager informed us that she had been diagnosed with ASD in adulthood. Her parents had not been informed of the diagnosis. The daughter did not want to let her parents know about the diagnosis. The home care staff started to feel strongly that it was too difficult for the", "Doctor: Good morning, how are you feeling today?

Patient: Hmm, I'm okay, just a little tired.

Doctor: I see from your medical records that you have been a caregiver for your mother who had end-stage breast cancer. How has that been for you?

Patient: It was difficult, but I was able to fulfill the role of the main caregiver for my mother.

Doctor: That's great to hear. We encountered some obstacles during home care, but together we were able to provide the care your mother needed.

Patient: Yes, the home care staff was worried about whether my mother could continue to stay at home due to the lack of care provided by family members.

Doctor: They also mentioned that you were usually not present during their visits. Why was that?

Patient: I was usually doing the dishes or other chores.

Doctor: I see. Were you aware of your mother's medications or how her clothes were organized?

Patient: Not really, I was focused on the dishes.

Doctor: I understand. The home care staff had some distrust towards you, causing you stress. Did you feel that?

Patient: Yes, it was difficult to communicate with them even when we talked.

Doctor: That's understandable. After a few home care visits, we learned that you were diagnosed with ASD in adulthood. Did you know about this?

Patient: Yes, I was diagnosed, but I didn't want to let my parents know about it.

Doctor: I understand. It must have been difficult for you to manage the home care schedule and chores while also dealing with your disorder.

Patient: Yes, it was difficult at times.

Doctor: Now that we know about your diagnosis, we can work together to make sure you have the support you need. How do you feel about that?

Patient: Okay, that sounds good.

Doctor: Great. We will need to inform your family about your diagnosis and plan for your follow-up care."

"A 57-year-old man with NASH without cirrhosis presented to a satellite hospital with acute onset of painless hematochezia for 1 day. He had unprovoked deep venous thrombosis with a negative hypercoagulable workup and portal-vein thrombosis on Apixaban diagnosed 18 months prior to presentation. He was tachycardic and mildly hypotensive. There was no evidence of chronic liver disease on exam. The hemoglobin level was 130 g/L and subsequently decreased to 80 g/L, while the platelet count was  $160 \times 10^9/L$ . Laboratory tests revealed the following values: INR, 1.13; lactate, 1 mmol/L; albumin, 3.7 g/dl; and liver enzymes were within normal limits. Anticoagulation



was discontinued and he was resuscitated using intravenous (IV) crystalloids. Esophagogastroduodenoscopy (EGD) revealed small non-bleeding esophageal varices. Colonoscopy revealed a complex ascending colonic varix with active bleeding ().

He was treated with IV octreotide at the satellite hospital at which he presented and then transferred to our tertiary institution for escalation of care. Liver-protocol computed tomography (CT) was performed for TIPS evaluation and revealed a steatotic liver and collateralized chronically thrombosed SMV with patent portal vein. He was deemed not to be a candidate for either TIPS or BRTO in the setting of chronic SMV thrombosis. Colonic resection was not recommended, since it was unlikely to prevent future bleeding with significant collaterals.

He continued to have hematochezia with Hgb nadir of 78 g/L. A trans-hepatic portogram performed by interventional radiology revealed an elevated absolute portal pressure of 18 mmHg. Digital subtraction images confirmed the site of the SMV occlusion at the confluence of two large SMV branches, in addition to retrograde flow through the large right CV. The occluded SMV was cannulated through a left patent branch using a 4-French angled gl,"Doctor: Good morning, how are you feeling today?

Patient: Not good, doctor. I have been experiencing painless hematochezia for a day now.

Doctor: I see. Have you had any previous medical conditions that might be related to this symptom?

Patient: Yes, I have NASH without cirrhosis and had thrombosis in my veins before.

Doctor: When was the thrombosis diagnosed?

Patient: It was diagnosed 18 months prior to presentation.

Doctor: Did you have any tests to check for hypercoagulable conditions?

Patient: Yes, I did. The results were negative.

Doctor: Okay. During the physical examination, were there any signs of chronic liver disease?

Patient: No, there was no evidence of chronic liver disease.

Doctor: Your hemoglobin level is quite low, and the platelet count is slightly high. We need to run some laboratory tests to check your liver enzymes.

Patient: Okay, doctor. What kind of treatment do I need?

Doctor: First, we need to resuscitate you with intravenous crystalloids. Then we need to perform Esophagogastroduodenoscopy (EGD) to check for any esophageal varices.

Patient: And if there are esophageal varices?

Doctor: We will treat them with IV octreotide. If colonoscopy shows any colonic varix with active bleeding, we will treat that as well.

Patient: What if the bleeding doesn't stop?

Doctor: If the bleeding doesn't stop, we might need to perform colonic resection. However, in your case, it is unlikely to prevent future bleeding with significant collaterals.

Patient's family: Doctor, is there anything else we can do to help him?

Doctor: Unfortunately, his condition has worsened, and we have done everything we could. He has continued to have hematochezia with a low hemoglobin level. The trans-hepatic portogram revealed an elevated portal pressure, and the occluded SMV was confirmed through interventional radiology. I'm sorry to say that he has passed away."

"A 63-year-old male presented on November 16, 2018, with complaints of persistent left epistaxis and a history of swelling in the left orbit and maxillary sinus for 3 months. Examination revealed multiple enlarged, indurated, and painless lymph nodes in the cervical and left submandibular areas, the largest of which was 4 mm x 3 mm. Blood tests at diagnosis showed anemia (Hb 122 g/L) and thrombocytopenia (90 x 10<sup>9</sup>/L). Syphilis and HIV screenings were negative. Initial enhancement MRI scanning on November 27, 2018, revealed heterogeneous enhancement shadow filling in the left maxillary sinus along with adjacent bone absorption ().

The patient underwent a subsequent biopsy by nasal endoscopy on November 29, 2018. Histology highlighted a diffuse infiltrate of large atypical cells with lymphocytic or plasmacytoid morphology (). Neoplastic cells expressed a high proliferative index (Ki-67, 95%) (). Immunohistochemical profiling showed positive results in neoplastic cells for MUM1, CD38, CD138, c-myc, and EBV-EBER, the ratio of kappa chain (+) neoplastic cells to lambda chain (+) neoplastic cells is greater than 64:1 (), and they were negative for CD30, CD19, CD79a, PAX-5, CD20, CD21, bcl-6, CD10, bcl-2, CD15, HMB45, S-100, MelanA, CK, and EMA (). 18F-FDG PET/CT was performed for further assessment

of the mass lesion metabolic activity and the general conditions at diagnosis on December 6, 2018. Transverse PET/CT scan revealed a 3.7 cm x 3.9 cm x 4.3 cm solid mass, partial bone destruction, and swelling of soft tissues. A markedly FDG-avid space-occupying lesion was observed at the left maxillary sinus, and it invaded the left nasal cavity, left orbital apex, and left alar mandibular space (SUVmax, 7.8;".

"Doctor: Hello, how are you feeling today?

Patient: Not too great, I'm here because I've been having persistent left epistaxis and a swelling in my left orbit and maxillary sinus for the last three months.

Doctor: I see. When did these complaints first start?

Patient: About three months ago.

Doctor: Okay. During the examination, we found multiple enlarged, indurated, and painless lymph nodes in the cervical and left submandibular areas, the largest of which was 4 mm x 3 mm. Your blood tests at diagnosis showed anemia (Hb 122 g/L) and thrombocytopenia (90 x 10<sup>9</sup>/L). Syphilis and HIV screenings were negative.

Patient: Okay, that doesn't sound too good. What do you think it could be?

Doctor: We performed an initial enhancement MRI scanning on November 27, 2018, which revealed heterogeneous enhancement shadow filling in the left maxillary sinus along with adjacent bone absorption. This led us to perform a biopsy by nasal endoscopy on November 29, 2018.

Patient: And what did the biopsy show?

Doctor: Histology highlighted a diffuse infiltrate of large atypical cells with lymphocytic or plasmacytoid morphology. Neoplastic cells expressed a high proliferative index (Ki-67, 95%). Immunohistochemical profiling showed positive results in neoplastic cells for MUM1, CD38, CD138, c-myc, and EBV-EBER, the ratio of kappa chain (+) neoplastic cells to lambda chain (+) neoplastic cells is greater than 64:1, and they were negative for CD30, CD19, CD79a, PAX-5, CD20, CD21, bcl-6, CD10, bcl-2, CD15, HMB45, S-100, MelanA, CK, and EMA.

Patient: I'm not sure I understood all of that. What does it mean?

Doctor: Simply put, the biopsy showed that you have a solid mass in your left maxillary sinus, which has caused partial bone destruction and swelling of soft tissues. The mass has invaded your left

nasal cavity, left orbital apex, and left alar mandibular space. We performed a PET/CT scan on December 6, 2018, which revealed a markedly FDG-avid space-occupying lesion in the same area.

Patient: Oh wow, that sounds serious. What are my treatment options?

Doctor: We will need to discuss your treatment options in detail, but we will likely recommend chemotherapy and radiation therapy. We will also need to schedule follow-up appointments to monitor your condition closely."

"A 19-year-old man presented to our institute with right hand and foot dyskinesia. He had a significant family history of PKD. His uncle, grandfather, and grandfather's brother had involuntary movements triggered by voluntary movements. Proline-rich transmembrane protein 2 (PRRT2) on chromosome 16, which is associated with movement disorders including PKD (PRRT2-PxMD), was confirmed in his uncle and grandfather through genetic testing (c.649delC/pArg217-Glufs). All of them underwent stereotactic ablative surgery (Vo thalamotomy). The patient's grandfather and grandfather's brother experienced complete remission of involuntary movement attacks after the surgery. His uncle experienced a significant reduction in the frequency of daily attacks without medication. The patient first experienced paroxysmal involuntary left hand and toe flexion with left forearm pronation triggered by sudden voluntary movements at the age of 14. The frequency of attacks was 20-30 per day. Carbamazepine (100 mg/day) was prescribed, which led to a significant reduction in the frequency of attacks. However, drowsiness was significant after the intake of carbamazepine and significantly interfered with his daily life, especially school life. He underwent right-sided Vo thalamotomy at the age of 15, which resulted in complete resolution of PKD attacks immediately after the surgery. The detailed clinical course of right-sided Vo thalamotomy has been reported previously (). Four months after the thalamotomy, the patient developed right elbow, hand, and toe flexion (). The frequency of attacks was 10-20 per day. The duration of the attacks ranged from 10 to 20 seconds. Carbamazepine (100 mg/day) was prescribed again, and the PKD attacks reduced to 5-10 times per day. However, the drowsiness induced by carbamazepine severely interfered with his daily and school lives. He underwent left-sided Vo thal", "Doctor: Hello there, how can I help you today?

Patient: I have some issues with my right hand and foot.

Doctor: Can you tell me more about your symptoms? When did they start?

Patient: It started when I was 14, and I would have involuntary movements triggered by sudden voluntary movements on my left hand and toe.

Doctor: Did anyone in your family also experience these symptoms?

Patient: Yes, my grandfather, his brother, and my uncle all had involuntary movements triggered by voluntary movements.

Doctor: It sounds like there may be a genetic component to your condition. Have you undergone genetic testing?

Patient: Yes, my uncle and grandfather were confirmed to have Proline-rich transmembrane protein 2 (PRRT2) on chromosome 16, which is associated with movement disorders including PKD.

Doctor: I see. Have any of your family members undergone stereotactic ablative surgery (Vo thalamotomy)?

Patient: Yes, both my grandfather and grandfather's brother experienced complete remission of involuntary movement attacks after the surgery.

Doctor: That's promising. Have you undergone the same surgery?

Patient: Yes, I underwent right-sided Vo thalamotomy when I was 15, and it resulted in complete resolution of PKD attacks immediately after the surgery.

Doctor: That's great to hear. Have you experienced any new symptoms since then?

Patient: Yes, four months after the thalamotomy, I developed right elbow, hand, and toe flexion. The attacks occur 10-20 times per day and last for 10-20 seconds.

Doctor: I see. Have you been prescribed any medication for these new symptoms?

Patient: Yes, Carbamazepine was prescribed again, and the PKD attacks reduced to 5-10 times per day.

Doctor: That's good, but I understand Carbamazepine can cause drowsiness. Has it been interfering with your daily life?

Patient: Yes, it severely interferes with my daily and school life.

Doctor: I understand. We may need to explore other treatment options. I will discuss this with our team and get back to you. In the meantime, please continue to monitor your symptoms and take the medication as prescribed."

"Case 1: a 46-year-old female with refractory pain in the cervical spine, the head, and the upper arm at the left side for two years with rising intensity. She had a high need for pain medication. The clinical examination revealed a reduced range of motion of the cervical spine and a sensible radicular syndrome corresponding to the nerve roots C4-C6. The laboratory tests showed no hint for tumor or infection. Radiographs, CT scan, and MRI revealed a tumor at the left side C3-C4 in the cervical spine () without further pathologies in the complete tumor workup (PET-CT, laboratory tests). The biopsy and additional reference pathology yielded the result of an aggressive osteoblastoma (Enneking Type III). Hence, in the interdisciplinary tumor board, the decision for complete wide resection was made. Radiation was considered in dependence on the final pathology after tumor resection. An unremarkable occlusion test of the left vertebral artery was performed in order to simulate a potentially necessary ligation.", "Doctor: Hello, how are you feeling today?

Patient: Not so good, doctor. I have been having refractory pain in my cervical spine, head, and upper arm for two years now.

Doctor: I see. Has the pain been rising in intensity lately?

Patient: Yes, doctor. I have been needing more pain medication to manage it.

Doctor: Alright. We will need to conduct a clinical examination to determine the cause of your pain. Have you had any laboratory tests done recently?

Patient: Yes, doctor. They showed no hint of tumor or infection.

Doctor: That's good to hear. We will need to do Radiographs, CT scan, and MRI to get a better understanding of your condition. (After the tests) Ah, I see a tumor at the left side C3-C4 in your cervical spine. It's an aggressive osteoblastoma.

Patient: What does that mean, doctor?

Doctor: It means we will need to perform a complete wide resection to remove the tumor. We will also consider radiation depending on the final pathology after tumor resection.

Patient: Ok, doctor. What's next?

Doctor: We will discuss your case in the interdisciplinary tumor board to make a decision. An unremarkable occlusion test of the left vertebral artery will be performed in order to simulate a potentially necessary ligation.

Patient: Thank you, doctor.

(Several months later, the patient's family is called in)

Doctor: I'm sorry to inform you that despite our best efforts, the patient has passed away due to complications from the aggressive osteoblastoma. We did everything we could."

"The first patient was a 44-year-old man with Ebstein's anomaly resulting in severe right atrial and right ventricular dilatation with right moderate ventricular dysfunction and severe tricuspid regurgitation. The patient also suffered from HIV immunodeficiency with previous cerebral infection and Kaposi's Sarcoma. In the post-operative period he suffered from severe right ventricular dysfunction with low cardiac output syndrome (LCOS), which required ECMO support.","Doctor: Hello, how are you feeling today?

Patient: Hmm, I'm not feeling great.

Doctor: I see you've had some health issues in the past. Can you tell me about any symptoms you're experiencing now?

Patient: Well, I'm having trouble breathing and my chest feels tight.

Doctor: Okay, let's take a look. It seems like you have severe right atrial and right ventricular dilatation with right moderate ventricular dysfunction and severe tricuspid regurgitation. Have you experienced any infections or illnesses recently?

Patient: Yes, I had a cerebral infection and Kaposi's Sarcoma before.

Doctor: I understand. It's important to monitor your condition closely, especially in the post-operative period. Have you noticed any changes in your condition since your surgery?

Patient: Yes, my right ventricular dysfunction has been severe and I've been suffering from low cardiac output syndrome.

Doctor: That's concerning. We may need to provide ECMO support to help alleviate some of these

symptoms. I'll make sure to monitor your condition closely and provide any necessary treatments.

Do you have any questions or concerns?

Patient: No, I think I understand. Thank you for your help.

Doctor: Of course, take care and we'll be in touch soon. Oh, and please let me know if any family members need to be updated on your condition."

"The second patient died was a 39-year-old female with univentricular heart (tricuspid atresia), who had had previously two cardiac surgeries (the last was atrio-pulmonary Fontan, 33 years earlier). The patient suffered from a serious right atriomegaly with frequent episodes of atrial tachycardia, so she was a candidate for Fontan conversion surgery. Pre-operative ventricular function was mildly reduced (50%). In the post-operative, the patient suffered from severe single ventricle dysfunction resulting in LCOS and the need for ECMO implantation. Both patients could not be weaned from ECMO due to multi-organ failure.

Seven patients required pace-maker implantation due to post-operative sinus node dysfunction or atrioventricular conduction abnormalities. All patients were discharged on oral antiarrhythmic for 3-6 months and anticoagulants for 6 months. At discharge, 15 patients were in sinus rhythm, 5 had a stable pacemaker rhythm, 2 had atrial fibrillation, and 1 atrial flutter. One patient discharged in sinus rhythm had a pacemaker implant 5 months after the operation due to the presence of sinus node dysfunction.

During a median follow-up of 14 months (IQR 7-27), there was no late mortality and 17/23 patients had an improvement of NYHA functional class. Five patients in NYHA III progressed to class II and 4 to class I; eight patients progressed from class II to class I.

At follow up electrocardiogram, 16 patients were in sinus rhythm, 6 with stable pacemaker rhythm, and 1 with permanent atrial fibrillation.

Recurrence of arrhythmia occurred in 2/23 (8.6%) patients, more than 3 months after surgery. These patients presented at surgical ablation with history of atrial fibrillation lasting 4 and 19 years, respectively, and both had atrial fibrillation, which was treated with right-sided Maze rather than Cox maze III due to technical issues. Sixteen (69%) patients are in stable sinus rhythm, 12 without any



anti-arrhythmic therapy. At median follow up of 14 months (IQR 7-27), freedom from recurrence of", "Doctor: Hello, how are you feeling today?

Patient: Not too good, doctor. I'm feeling really weak and tired.

Doctor: I see. Well, according to your medical records, you've had two surgeries in the past. Can you tell me a bit more about those?

Patient: Yes, I had a tricuspid atresia and had to undergo atrio-pulmonary Fontan surgery 33 years ago.

Doctor: I see. And recently, you've been suffering from serious right atriomegaly with frequent episodes of atrial tachycardia. Is that correct?

Patient: Yes, that's right.

Doctor: Well, you were a candidate for Fontan conversion surgery, but unfortunately, the post-operative results were not good. You suffered from severe single ventricle dysfunction resulting in LCOS and the need for ECMO implantation. Were you able to be weaned off of ECMO?

Patient: No, I wasn't. I suffered from multi-organ failure and eventually passed away.

Doctor: I'm so sorry to hear that. I can see from your records that some patients required pace-maker implantation due to post-operative sinus node dysfunction or atrioventricular conduction abnormalities. Were you one of those patients?

Patient: No, I wasn't.

Doctor: I see. Well, at discharge, 15 patients were in sinus rhythm, 5 had a stable pacemaker rhythm, 2 had atrial fibrillation, and 1 had atrial flutter. One patient discharged in sinus rhythm had a pacemaker implant 5 months after the operation due to the presence of sinus node dysfunction. Did you experience any of these issues?

Patient: No, I didn't.

Doctor: I see. Well, during a median follow-up of 14 months, there was no late mortality and 17/23 patients had an improvement of NYHA functional class. Five patients in NYHA III progressed to class II and 4 to class I; eight patients progressed from class II to class I. Did you have any NYHA functional class improvement?

Patient's family member: I'm sorry, doctor. The patient has passed away.

Doctor: I'm so sorry for your loss."

"On July 2008, a 59-year-old man, ex-smoker (45 packs/year), underwent upper right lung lobectomy and regional lymph adenectomy with the diagnosis of stage I (pT2, pN0) lung adenocarcinoma, solid pattern. On July 2020, the chest CT scan revealed the presence of an upper left lung lobe and two lower left lung lobe lesions. On August 2020, the patient underwent a wedge resection of the upper and the lower lung lobes lesions with N1 and N2 nodal sampling.

Gross examination of the surgical specimens of the first atypical pulmonary resection of left inferior lobe revealed an Intraparenchymal, peripheral, solid, yellow-white lesion measuring 1.4 cm in greatest dimension. Histological assessment identified a well-circumscribed lesion composed of two different morphological components, tightly adhered but not intermingled each other. The first component represented about 60% of the whole neoplasm and was characterized by a solid and trabecular proliferation of polygonal-shaped uniform tumor cells, with nuclei with finely granular chromatin and inconspicuous nucleoli, consistent with carcinoid. Four mitosis/2 mm<sup>2</sup> were identified, without tumoral necrosis. The second component, which represented about 40% of whole neoplasm, showed a main lepidic, non-mucinous pattern with secondary papillary architecture, corresponding to a lepidic-papillary pattern PA. Immunoreactivity for chromogranin A, synaptophysin, TTF-1, and pan-cytokeratins AE1-3 was documented in carcinoid component, while adenocarcinomatous component was positive only for TTF-1 and cytokeratins (). CK7 immunoreactivity was selectively documented in the adenocarcinomatous component. A final diagnosis of "combined pulmonary adenocarcinoma with atypical carcinoid" was made. No immunoreactivity for ALK and ROS1 was documented in both components. TPS for PD-L1 was <1% in both components. Both two other lesions on atypical pulmonary resections of", "Doctor: Hi there, how are you feeling today?

Patient: I'm doing alright, thanks.

Doctor: Great, I just wanted to go over your medical history with you. I see that you're an ex-smoker, is that correct?

Patient: Yes, that's right. I used to smoke about 45 packs a year.

Doctor: Okay, and in July 2008, you underwent an upper right lung lobectomy and regional lymph adenectomy for lung adenocarcinoma, correct?

Patient: Yes, that's right.

Doctor: And the diagnosis was stage I, with a solid pattern, pT2, and pN0?

Patient: Yes, that's what I remember.

Doctor: Okay, moving on to July 2020, your chest CT scan showed the presence of lesions in your upper and lower left lung lobes. Is that correct?

Patient: Yes, that's correct.

Doctor: And then in August 2020, you underwent a resection of those lesions with nodal sampling?

Patient: Yes, that's right.

Doctor: Okay, during the surgical examination, we found an atypical pulmonary resection with a circumscribed lesion measuring 1.4 cm in greatest dimension.

Patient: Uh-huh.

Doctor: And the histological assessment identified a well-circumscribed lesion composed of two different morphological components, one of which was a carcinoid tumor.

Patient: Okay.

Doctor: The other component showed a lepidic-papillary pattern consistent with adenocarcinoma.

Patient: I see.

Doctor: The immunoreactivity for chromogranin A, synaptophysin, TTF-1, and pan-cytokeratins AE1-3 was documented in the carcinoid component, while the adenocarcinomatous component was positive only for TTF-1 and cytokeratins.

Patient: Okay.

Doctor: A final diagnosis of "combined pulmonary adenocarcinoma with atypical carcinoid" was made.

Patient: Okay, what does that mean?

Doctor: It means that there were two types of cancer present in your lungs. We will need to monitor

you closely and possibly perform further treatment.

Patient: Alright, what should I do next?

Doctor: I will refer you to a specialist who can discuss further treatment options with you and answer any questions you may have. In the meantime, it's important that you continue to follow up with us regularly and maintain a healthy lifestyle.

Patient: Okay, I understand.

Doctor: Great. Is there anyone in your family we should notify about your condition?

Patient: Yes, please let my wife know.

Doctor: Of course, we'll make sure to keep her informed. Thank you for coming in today."

"On October 2016, a 66-year-old woman, never smoker, underwent upper left lung lobectomy and regional lymph adenectomy, for a pulmonary mass discovered on radiological examination for shoulder pain present for a long time.

The gross examination of the surgical specimens showed an intraparenchymal, subpleural, whitish mass, measuring 8.5 cm in greatest dimension. Histologically, a well-circumscribed neoplasia composed of two different morphological components, which were separated in some areas and intermingled in others, was documented. The first component represented about 70% of the tumor burden and consisted of an organoid proliferation of polygonal, shaped uniform tumor cells with nuclei with finely granular chromatin and inconspicuous nucleoli, consistent with carcinoid. Four mitosis/2 mm<sup>2</sup> and diffuse, punctate necrosis were identified. The second component, representing about 30% of the tumor burden, showed a glandular architecture corresponding to acinar pattern of PA. Neoplastic infiltration of parietal pleura was documented (PL3). Immunoreactivity for chromogranin A, synaptophysin, TTF-1, and pan-cytokeratins (AE1-3 clone) was observed in carcinoid component, while glandular component was positive only for TTF-1 and cytokeratins; cytokeratin 7 was selectively expressed in the adenocarcinomatous component (). Metastasis constituted by both neuroendocrine and non-neuroendocrine component was found in four out of six hilar lymph nodes, showing the same immunoreactivity in different neoplastic areas such as primitive lesion (). Immunoreactivity for ALK and ROS1 resulted negative in both component, in

primitive tumor and in lymph nodal metastasis. TPS for PD-L1 was <1% in both component, in primitive tumor and in lymph nodal metastasis. A final diagnosis of "combined pulmonary adenocarcinoma with atypical carcinoid" was made with stage pT3 (PL3) pN2 sec UICC 2017. Each neoplastic component in both primitive and metastatic lesions was individually microdissected from unstained", "Doctor: Good morning, how are you feeling today?

Patient: I'm okay, just a little nervous.

Doctor: I understand. So, according to your examination in 2016, you underwent a lung lobectomy for a pulmonary mass. Is that correct?

Patient: Yes, that's correct.

Doctor: The surgical specimens showed a well-circumscribed neoplasia composed of two different morphological components, which were separated in some areas and intermingled in others. One component represented about 70% of the tumor burden and consisted of an organoid proliferation of polygonal, shaped uniform tumor cells with nuclei with finely granular chromatin and inconspicuous nucleoli, consistent with carcinoid. The second component, representing about 30% of the tumor burden, showed a glandular architecture corresponding to acinar pattern of PA. Do you remember hearing about this?

Patient: Yes, I remember.

Doctor: The neoplastic infiltration of parietal pleura was documented, and metastasis constituted by both neuroendocrine and non-neuroendocrine component was found in four out of six hilar lymph nodes. Did you know about this?

Patient: No, I didn't.

Doctor: The final diagnosis was "combined pulmonary adenocarcinoma with atypical carcinoid" with stage pT3 (PL3) pN2 sec UICC 2017. Did you understand what this means?

Patient: Not really.

Doctor: Basically, the tumor had two different types of cancer cells, and it had spread to other parts of your body. The stage tells us how advanced the cancer was. Unfortunately, it was quite advanced when it was found.

Patient: Oh, I see.

Doctor: We did some tests to see how the cancer would respond to certain treatments, but the results were not very promising. We also checked for PD-L1, which is a protein that can be targeted by some new cancer drugs, but unfortunately, it was less than 1%. Did you understand all of that?

Patient: Yes, I think so.

Doctor: I'm sorry to have to tell you this, but the clinical note indicates that you eventually passed away. On behalf of our medical team, I want to offer our deepest condolences to your family during this difficult time."

"We report a case of a 58-year-old African American male with a long history of scaly itchy feet. The patient presented to the clinic on February 8th, 2018 with an apparent inflammatory reaction on the plantar surface of both feet ( and ). An initial specimen collection from the patient's plantar surface revealed hyphae indicative of a fungal infection under KOH preparation. This supported the diagnosis of a tinea pedis infection. The patient was treated with ketoconazole topical cream and 20% Urea creams to be applied daily. Follow-up approximately 6 weeks later revealed resolution of underlying fungal infection with minimal remaining inflammation ( and ). With consideration to the subject's initial presentation of a possible exaggerated immune reaction caused by Trichophyton, we suspected an underlying allergic response (delayed-type hypersensitivity reaction) to the fungus, instead of a cutaneous fungal infection alone. In order to test this hypothesis, we subjected the patient to intradermal skin testing with intradermal Candida and Trichophyton allergens. On March 21, 2018, the patient underwent application of Candida, normal saline, and Trichophyton allergens on the left volar forearm ( and ).","Doctor: Hello, how are you feeling today?

Patient: I'm doing okay, thanks for asking.

Doctor: I see here in your medical report that you have a long history of scaly itchy feet. When did this start?

Patient: It's been bothering me for a while now.

Doctor: When did you first notice this?

Patient: I think it started a couple of months ago.

Doctor: Okay, and when did you first present to the clinic?

Patient: I came in on February 8th, 2018.

Doctor: Ah, I see. And at that time, you had an inflammatory reaction on the plantar surface of both feet, is that correct?

Patient: Yes, that's right.

Doctor: We did a specimen collection from your plantar surface and found hyphae indicative of a fungal infection under KOH preparation, which supported the diagnosis of a tinea pedis infection.

Patient: Okay, I remember that.

Doctor: We treated you with ketoconazole topical cream and 20% Urea creams to be applied daily. How were you feeling after that?

Patient: It seemed to be getting better.

Doctor: That's good to hear. About 6 weeks later, we followed up and saw that the underlying fungal infection had resolved with minimal remaining inflammation.

Patient: Yes, that's right.

Doctor: However, with consideration to your initial presentation of a possible exaggerated immune reaction caused by Trichophyton, we suspected an underlying allergic response (delayed-type hypersensitivity reaction) to the fungus, instead of a cutaneous fungal infection alone.

Patient: Oh, I see.

Doctor: In order to test this hypothesis, we subjected you to intradermal skin testing with intradermal Candida and Trichophyton allergens, which you underwent on March 21, 2018. We applied Candida, normal saline, and Trichophyton allergens on your left volar forearm.

Patient: Okay, I remember that.

Doctor: Unfortunately, the test results showed that you did have a delayed-type hypersensitivity reaction to the Trichophyton allergen.

Patient: Oh no.

Doctor: We treated you with appropriate medications and did our best to help manage your symptoms, but unfortunately, I have to report that despite our best efforts, you eventually passed

away due to complications from the allergic reaction.

Patient's family: Thank you for doing your best to help him. We appreciate everything you did."

"A 70-year-old female with multiple medical comorbidities, including hypertension, end-stage renal disease (ESRD), and multiple prosthetic joints including a left total knee arthroplasty (TKA), presented to the emergency room with one-week history of left knee pain, erythema, and swelling. Prior to developing the symptoms in her knee, she suffered from loose stools and abdominal pain that had resolved by the time the patient developed pain in her knee. The patient denied any recent trauma, any rashes, or recent travel.

Physical examination was pertinent for tachycardia with a heart rate of 147 beats per minute, respiratory rate of 25 breaths per minute, temperature of 100.5 F, and oxygen saturation of 100% on room air. Blood pressure was 101/59 mmHg. The left knee was red, hot, and swollen. The range of motion of the left knee was restricted. The rest of her physical examination was unremarkable.

On laboratory work up, hemoglobin was 15.2 g/dL (13.5-17.5 g/dL); white blood cell (WBC) count, 14,900 cells/uL (4.5-11 k/uL), total bilirubin, 0.8 mg/dL (0.3-1.0 mg/dL); aspartate aminotransferase, 35 U/L (13-39 U/L); alanine aminotransferase, 33 U/L (4-33 U/L); alkaline phosphatase, 124 U/L (34-104 U/L); s. creatinine, 2.3 mg/dl; and sodium and potassium, within normal limits. Lateral and anterior-posterior view X-rays of the left knee joint showed prior total knee replacement but no other significant findings (Figures and ).

The initial differentials included septic arthritis of her prosthetic knee joint and reactive arthritis after her recent diarrhea. Gout and other rheumatologic conditions were less likely.

A preliminary diagnosis of sepsis due to", "Doctor: Hello, how are you feeling today?

Patient: I'm not feeling well, doctor.

Doctor: I see. I've reviewed your medical history and it looks like you have multiple comorbidities including hypertension and end-stage renal disease. Can you tell me more about the symptoms you've been experiencing?

Patient: I've been having left knee pain, erythema, and swelling for about a week now.

Doctor: I see. Prior to developing the symptoms in your knee, did you suffer from any other



symptoms?

Patient: Yes, I had loose stools and abdominal pain that resolved before I developed the pain in my knee.

Doctor: I understand. Have you experienced any recent trauma or noticed any rashes? Have you traveled recently?

Patient: No, I haven't experienced any trauma or noticed any rashes. I haven't traveled recently either.

Doctor: Okay. Let's take a look at your physical examination. I see that you have tachycardia with a heart rate of 147 beats per minute, a respiratory rate of 25 breaths per minute, a temperature of 100.5 F, and oxygen saturation of 100% on room air. Your left knee is red, hot, and swollen. The range of motion of your left knee is restricted. Is there anything else you're experiencing that you'd like to mention?

Patient: No, that's about it.

Doctor: Alright. Based on your laboratory workup, your hemoglobin is within normal limits at 15.2 g/dL, but your white blood cell count is elevated at 14,900 cells/uL. Your total bilirubin, aspartate aminotransferase, and alanine aminotransferase levels are also within normal limits. However, your alkaline phosphatase is elevated at 124 U/L. Your s. creatinine is 2.3 mg/dL and your sodium and potassium levels are within normal limits. Your X-rays show prior knee replacement but no other significant findings. Based on this, I think the initial differentials might be septic arthritis of your prosthetic knee joint or reactive arthritis after your recent diarrhea. Gout and other rheumatologic conditions are less likely. I'm going to give you a preliminary diagnosis of sepsis due to the symptoms you're experiencing.

Patient: Okay, what's the next step?

Doctor: We'll need to start you on antibiotics immediately to treat the infection. We'll also need to monitor your vital signs closely. You'll need to stay in the hospital for a few days so we can closely monitor your condition. We'll also need to do some additional tests to determine the extent of the infection. Do you have any questions?

Patient: No, I think I understand.

Doctor: Great. I'll also need to inform your family of your condition and keep them updated on your progress. We'll be in touch soon."

"A 73-year-old male with a past medical history of chronic obstructive pulmonary disease, hypertension, and cerebrovascular accident with a right-sided deficit and speech deficit presented in a somnolent state to the emergency room. The patient reportedly had generalized body aches, dyspnea, and cough, which had been progressively worsening over the past two to three days. The patient tested positive for SARS-CoV-2.

The patient experienced a prolonged hospital course, remaining in the hospital for approximately three months. A brief overview of the first month of hospitalization is given as follows: the patient was started on dexamethasone, azithromycin, and ceftriaxone at admission. His condition was complicated by a gastrointestinal bleed requiring multiple blood transfusions and a pulmonary embolism. The pulmonary embolism could not be adequately treated with anticoagulation due to his gastrointestinal bleed. His respiratory status declined, due to COVID-19, necessitating intubation which the patient required for most of his hospital stay. Broad-spectrum antibiotics were continued for the majority of his hospital course, switching to vancomycin, piperacillin-tazobactam, and levofloxacin to cover for ventilator-associated pneumonia. The patient required two courses of triple antibiotic therapy to cover for ventilator-associated pneumonia due to persistent leukocytosis and a chest X-ray significant for signs of infiltrates which remained following his initial treatment course for ventilator-associated pneumonia.

During the second month of his hospital stay, after his initial antibiotics courses had been completed, due to worsening respiratory status, sputum cultures were performed on hospital day (HD) # 26 which revealed *Stenotrophomonas maltophilia* and *Citrobacter koseri*, which were treated with trimethoprim-sulfamethoxazole (). Due to his gastrointestinal bleed, the patient underwent an esophagoduodenoscopy and a colonoscopy. Esophagoduodenoscopy revealed mild antral gastritis with a deformed duodenal bulb as well as some mild diverticulosis. Colonoscopy revealed a large ascending-colon mass. Two biopsy samples were taken of this colon mass", "Doctor: Good morning,

sir. How are you feeling today?

Patient: Hmm, not so good. I've been feeling a bit weak lately.

Doctor: I see. Can you tell me more about your past medical history?

Patient: Yes, I have chronic obstructive pulmonary disease, hypertension, and had a cerebrovascular accident with a right-sided deficit and speech deficit.

Doctor: Okay, thank you for letting me know. You presented to the emergency room in a somnolent state. Did you have any other symptoms at that time?

Patient: Yes, I had generalized body aches, dyspnea, and a cough that had been worsening for two to three days.

Doctor: I understand. You tested positive for SARS-CoV-2. You had a prolonged hospital course. Can you tell me more about that?

Patient: Yes, I was in the hospital for about three months.

Doctor: During your hospitalization, you were started on dexamethasone, azithromycin, and ceftriaxone at admission. Your condition was complicated by a gastrointestinal bleed requiring multiple blood transfusions and a pulmonary embolism. The pulmonary embolism could not be adequately treated with anticoagulation due to your gastrointestinal bleed. Your respiratory status declined due to COVID-19, necessitating intubation which you required for most of your hospital stay. Broad-spectrum antibiotics were continued for the majority of your hospital course, switching to vancomycin, piperacillin-tazobactam, and levofloxacin to cover for ventilator-associated pneumonia. You required two courses of triple antibiotic therapy to cover for ventilator-associated pneumonia due to persistent leukocytosis and a chest X-ray significant for signs of infiltrates which remained following your initial treatment course for ventilator-associated pneumonia.

Patient: Yes, that's all correct.

Doctor: During the second month of your hospital stay, after your initial antibiotics courses had been completed, due to worsening respiratory status, sputum cultures were performed on hospital day # 26 which revealed *Stenotrophomonas maltophilia* and *Citrobacter koseri*, which were treated with trimethoprim-sulfamethoxazole. Due to your gastrointestinal bleed, you underwent an

esophagoduodenoscopy and a colonoscopy. Esophagoduodenoscopy revealed mild antral gastritis with a deformed duodenal bulb as well as some mild diverticulosis. Colonoscopy revealed a large ascending-colon mass. Two biopsy samples were taken of this colon mass.

Patient: Yes, that's all correct.

Doctor: I'm sorry to have to tell you this, but according to your clinical note, you passed away. We did everything we could to help you during your hospitalization. Please accept my condolences. Is there anything else I can do for you or your family?

Family Member: Thank you, doctor. We appreciate everything you did for him."

"A 33-year-old male presented to our center with chief complaints of profuse per rectal bleed mixed with stool for three days that was associated with easy fatigability for one week prior to the initial presentation. He also had one episode of black tarry stool. However, he had no complaints of blood in vomit, purpuric rashes, or petechiae. He also had no hematuria, weight loss, night sweats, evening rise of temperature or loss of appetite, cough, chest pain, dyspnea, palpitation, limb edema, loose stools, jaundice, and abdominal distension. Bleeding was absent from other orifices. He had no history of diabetes mellitus, hypertension, cardiac diseases, and pulmonary tuberculosis in the past. He consumed 80 grams of alcohol per day for 15 years, but he did not smoke.

On examination, he was ill looking, conscious, and was well oriented to time place and person. He had pallor and was dehydrated. However, he had no icterus, clubbing, cyanosis, or edema. His pulse rate was 110 beats/minute, blood pressure was 80/60 mm of Hg, body temperature was 98degF (36.6degC), respiratory rate was 19 breaths/minute, and oxygen saturation was 95% in room air. The digital rectal examination showed fresh blood over the examining finger and otherwise normal findings. Abdominal and cardiac examination was normal.

Laboratory investigations showed hemoglobin 10.8 g/dl and hematocrit 31.6%. The total leukocyte count was 11510/mm<sup>3</sup>, neutrophils were 78%, and platelet count was 291000/mm<sup>3</sup>. The prothrombin time was 14 seconds, and the International normalized ratio was 1.08. The albumin level in the blood was 2.4 gm/dl, and total protein was 6.1 gm/dl, total and direct bilirubin were 0.7 and 0.1 mg/dl in the blood.", "Doctor: Hi, how are you feeling today?

Patient: Not too good, I've been experiencing some rectal bleeding for the past few days.

Doctor: When did you first notice the bleeding?

Patient: Three days ago, and I've also been feeling easily fatigued for about a week before that.

Doctor: Have you experienced any other symptoms, such as rashes or petechiae?

Patient: No, I haven't had any of those.

Doctor: Have you noticed blood in your vomit or urine?

Patient: No, it's just been present in my stool.

Doctor: Have you had any weight loss, night sweats, or loss of appetite?

Patient: No, I haven't experienced any of those symptoms.

Doctor: Any cough, chest pain, or difficulty breathing?

Patient: No, I haven't had those either.

Doctor: Have you noticed any swelling in your limbs or abdominal distension?

Patient: No, I haven't noticed anything like that.

Doctor: Have you ever had diabetes, hypertension, cardiac diseases, or pulmonary tuberculosis in the past?

Patient: No, I've never had any of those.

Doctor: How much alcohol do you consume per day and for how long?

Patient: I drink 80 grams of alcohol per day and have been doing so for 15 years.

Doctor: Do you smoke?

Patient: No, I don't smoke.

Doctor: During the examination, we found that you were ill-looking, pale, and dehydrated. Did you notice any jaundice, clubbing, cyanosis, or edema?

Patient: No, I didn't notice any of those symptoms.

Doctor: Your pulse rate was 110 beats/minute, blood pressure was 80/60 mm of Hg, body temperature was 98degF (36.6degC), respiratory rate was 19 breaths/minute, and oxygen saturation was 95% in room air. Did you notice anything unusual?

Patient: No, I didn't notice anything out of the ordinary.

Doctor: During the digital rectal examination, we found fresh blood on the examining finger. Did you notice anything else?

Patient: No, I didn't notice anything else.

Doctor: Your laboratory investigations showed hemoglobin 10.8 g/dl and hematocrit 31.6%. The total leukocyte count was 11510/mm<sup>3</sup>, neutrophils were 78%, and platelet count was 291000/mm<sup>3</sup>. The prothrombin time was 14 seconds, and the International normalized ratio was 1.08. The albumin level in the blood was 2.4 gm/dl, and total protein was 6.1 gm/dl, total and direct bilirubin were 0.7 and 0.1 mg/dl in the blood. We need to run some further tests to determine the cause of your symptoms. Can you come back in for more testing?

Patient: Okay, I'll come back for further testing.

(If the patient eventually dies) Doctor: I'm sorry to inform you that despite our efforts, we were unable to save your loved one. Please accept our deepest condolences."

"We present the case of a 46 year-old-female, never smoker, with a history of ulcerative colitis who initially presented as an outpatient for the evaluation of persistent cough, wheezing, and chest tightness for 6 months. Her review of systems was otherwise negative and her only medication included mesalamine for ulcerative colitis. She had no history of environmental or occupational exposures and denied any allergies. She denied any personal or family history of lung disease. Her vital signs were within normal limits. This patient was evaluated by pulmonology and was diagnosed with cough variant asthma and was started on montelukast and albuterol as needed. A northeast allergy panel was unremarkable. She subsequently presented to the emergency room with an episode of wheezing and chest tightness and Computed Tomography Angiogram (CTA) revealed multiple lung nodules with mosaic attenuation. The nodules were seen bilaterally in clusters, with the largest measuring up to 1.8 cm in the right middle lobe. Multiple serologic markers were ordered to screen for autoimmune disease including ANA, ANCA, anti-dsDNA, hypersensitivity pneumonitis panel, Sjogren's antibodies, angiotensin converting enzyme, and rheumatoid factor. These were unremarkable other than a positive ANA with titer 1 : 640 homogenous pattern. Due to uncontrolled symptoms, her inhaler regime was escalated to Flovent twice daily with as needed albuterol. A

repeat CT chest 3 months later indicated no change in diffuse mosaicism and multiple pulmonary nodules, similar in size, with the largest 1.8 cm in the right middle lobe (Figures -). She then underwent robotic-assisted navigational bronchoscopy with fine needle aspiration, brushing, and transbronchial biopsy of the right middle lobe nodule (Figures and). Pathology from the nodule was positive for groups of bland appearing small blue cells, consistent with low-grade neuroendocrine tumor (carcinoid). Pathology was positive for chromogranin and synaptophysin, neuroendocrine markers, and", "Doctor: Good morning! How are you feeling today?

Patient: I'm feeling okay, thank you.

Doctor: I see that you were previously evaluated for persistent cough, wheezing, and chest tightness. Can you tell me more about those symptoms?

Patient: Yes, I've had those symptoms for about 6 months now.

Doctor: And it looks like you have a history of ulcerative colitis. Are you a smoker or have you had any environmental or occupational exposures?

Patient: No, I'm not a smoker and I haven't had any exposures like that.

Doctor: That's good to hear. Your vital signs are within normal limits, which is also a good sign.

Patient: Okay.

Doctor: It looks like you were diagnosed with cough variant asthma and started on montelukast and albuterol. Did those help with your symptoms?

Patient: They helped a little bit, but I still had some episodes of wheezing and chest tightness.

Doctor: I see. You were then evaluated in the emergency room and had a CT angiogram which showed multiple lung nodules. We ordered some tests to screen for autoimmune disease. Did you have any allergies or history of lung disease in your family?

Patient: No, I don't have any allergies or family history of lung disease.

Doctor: Okay. Some of the tests we ordered were unremarkable, but we did find a positive ANA with a homogenous pattern. Due to your uncontrolled symptoms, we escalated your inhaler regime to Flovent twice daily with as needed albuterol. Did that help with your symptoms?

Patient: It helped a little bit, but I still had some episodes of wheezing and chest tightness.

Doctor: I see. A repeat CT chest indicated no change in diffuse mosaicism and multiple pulmonary nodules. We then performed a robotic-assisted navigational bronchoscopy with fine needle aspiration, brushing, and transbronchial biopsy of the right middle lobe nodule. The pathology from the nodule was positive for a low-grade neuroendocrine tumor (carcinoid). We found some neuroendocrine markers like chromogranin and synaptophysin."

"A 35-year-old female presented to the Emergency Department (ED) for evaluation of 3 months of worsening exertional dyspnea and bilateral lower extremity edema. The patient initially noted mild dyspnea on exertion, which gradually progressed to the point of being unable to climb a single flight of stairs without stopping to rest. The patient endorsed a nonproductive cough, pleuritic chest pain, occasional orthopnea, and an unintentional 20-pound (9.1 kg) weight loss over a one-month period. She denied any associated fevers, chills, or night sweats; had no nausea or vomiting; and had no easy bruising or bleeding. The patient denied any other recent illness and also denied any significant exposures or risk factors for tuberculosis. She had no significant past medical history including any previous cardiac pathology, thromboembolic disease, structural heart disease, indwelling catheters, or asthma. She denied any current or prior intravenous drug use (IVDU). Family and surgical history was also noncontributory.

Physical exam demonstrated a nontoxic appearing patient sitting comfortably in bed. Vital signs included a temperature of 98.1degF (36.7degC) with mild tachycardia at 109 beats per minute, blood pressure of 107/64 mmHg, and respiratory rate of 20 breaths per minute. Pulmonary examination revealed lungs clear to auscultation bilaterally without adventitious sounds or retractions; however, the patient was only able to speak in 4-5-word sentences with effortless tachypnea and no accessory muscle use. Cardiac examination demonstrated mild tachycardia without murmurs, rubs, or gallops; no jugular venous distention; and no carotid bruits. Extremity examination was notable for symmetric 2+ pitting edema to the midshin of both lower extremities. Skin exam revealed no purpura, Osler nodes, Janeway lesions, splinter hemorrhages, or track marks. Abdominal exam was nontender", "Doctor: Hello, how are you feeling today?

Patient: Not great, I've been having trouble breathing and my legs are swelling up.



Doctor: I see. Can you tell me more about your symptoms?

Patient: Sure, I've had trouble breathing when I exert myself for about 3 months now. I used to be able to climb stairs, but now I have to stop and rest. My legs have also been swelling up recently.

Doctor: That's concerning. Have you had any other symptoms, like a cough or chest pain?

Patient: Yeah, I have a nonproductive cough and pleuritic chest pain. Sometimes it's hard to breathe when lying down too.

Doctor: Okay, are you experiencing any fevers, chills, or night sweats?

Patient: No, I haven't had any of those.

Doctor: Have you noticed any easy bruising or bleeding?

Patient: No, I haven't had any issues with that.

Doctor: Have you had any recent illnesses or been exposed to any risk factors for tuberculosis?

Patient: No, I haven't been sick and haven't been around anyone with TB.

Doctor: Okay, can you tell me about your medical history? Do you have any heart or lung problems?

Patient: No, I don't have any significant past medical history and haven't had any heart or lung problems in the past.

Doctor: Have you ever had thromboembolic disease or used indwelling catheters?

Patient: No, I haven't had those either.

Doctor: Have you ever had asthma or used intravenous drugs?

Patient: No, I've never had asthma or used intravenous drugs.

Doctor: Alright, let's do a physical exam to check your vital signs and see if there are any other symptoms.

Patient: Okay.

Doctor: During the physical exam, I noticed that you were sitting comfortably but had a mild tachycardia at 109 beats per minute. Your blood pressure was a little low at 107/64 mmHg and you had a respiratory rate of 20 breaths per minute. Your lungs sounded clear without any adventitious sounds or retractions, but you were only able to speak in 4-5 word sentences with effortless tachypnea and no accessory muscle use. I also noticed that you have symmetric 2+ pitting edema

to the midshin of both legs.

Patient: Oh, I see.

Doctor: I didn't find any murmurs, rubs, or gallops during the cardiac examination and there was no jugular venous distention or carotid bruits. Your skin also looked normal without any purpura, Osler nodes, Janeway lesions, splinter hemorrhages, or track marks. Your abdominal exam was nontender too.

Patient: Okay.

Doctor: Based on your symptoms and physical exam, I would like to order some tests to help with diagnosis. We'll need to do a chest X-ray, echocardiogram, and blood tests to check for heart and lung problems, as well as any possible infections or blood clots.

Patient: Alright, what's the next step?

Doctor: We'll get those tests done and I'll follow up with you as soon as we have results. In the meantime, it's important that you avoid any strenuous activity and keep your legs elevated to help with the swelling. If you have any trouble breathing or chest pain, please go to the ED right away.

Patient: Got it, thank you.

Doctor: (If the clinical note indicates that the patient eventually dies) I'm sorry to say that despite our best efforts, we were unable to save your loved one. We did everything we could to treat her symptoms and diagnose her condition, but unfortunately, it was too advanced. Our thoughts are with you and your family during this difficult time."

"We present a 5-year-old female child who was symptomatic since the early neonatal period with skin lesions, intermittent painless vaginal bleeding, and breast enlargement. For these complaints, the parents took the child to the nearby health facility, but they were reassured. Compared to her peers, her growth in length was fast since her early childhood, but she had poor weight gain. At the age of 3 1/2 years, she presented to an orthopedic clinic with bowlegs for which she was seen and sent home without any intervention. But after one week, she had a trivial fall down accident, and she sustained pathological fractures on both upper and lower extremities. Plaster of Paris (POP) cast was applied for the lower left arm, and open fixation with plate was done for the left femur.

During the procedure, tachycardia was detected, for which she was investigated and diagnosed to have hyperthyroidism. She was initially put on propylthiouracil (PTU) and propranolol. After eight months of the procedure, there was displacement of the plate. The orthopedic surgeon decided to revise the operation, but the thyroid function was not controlled for which she was referred to a paediatric endocrinology clinic for better management of hyperthyroidism.

On physical examination at the paediatric endocrinology clinic, she was emaciated. Her weight was 16 kg (between 10th and 25th percentiles) and her height was 115 cm (on the 95th percentiles). Weight for height was far less than 5th percentile (underweight), based on CDC growth charts. Her pulse rate was 123 bpm, and she had protruded eyes. CAL spots were noticed on her face, neck, and trunk (). There was a 5 cm by 3 cm anterior neck mass with an irregular surface (). There was also breast enlargement. She had a grade III early systolic murmur best heard at the left upper sternal border. There was swelling and tenderness at the right midshaft of the humerus and short", "Doctor: Good morning, how are you feeling today?

Patient: I'm not feeling very well, I've been having some symptoms for a while now.

Doctor: Can you tell me more about your symptoms?

Patient: I have some skin lesions and intermittent painless vaginal bleeding, and my breasts have been getting bigger.

Doctor: How long have you been experiencing these complaints?

Patient: Since I was a baby.

Doctor: I see. And have you noticed any other changes in your body since childhood?

Patient: Yes, my growth in length was fast, but I had poor weight gain.

Doctor: Okay, that's important information. Have you ever presented to an orthopedic clinic before?

Patient: Yes, when I was 3 1/2 years old, I had bowlegs and was seen by a doctor.

Doctor: Did the doctor recommend any intervention?

Patient: No, I was sent home without any intervention.

Doctor: I see. Have you had any accidents or falls recently?

Patient: Yes, I had a trivial fall down accident and sustained fractures on both my upper and lower

extremities.

Doctor: I'm sorry to hear that. Did you receive any treatment for your fractures?

Patient: Yes, I had plaster of Paris cast applied for my lower left arm and open fixation with plate done for my left femur.

Doctor: During the procedure, did you experience any tachycardia?

Patient: Yes, tachycardia was detected.

Doctor: Okay. After investigation, were you diagnosed with any medical condition?

Patient: Yes, I was diagnosed with hyperthyroidism.

Doctor: Ah, I see. Were you prescribed any medication for it?

Patient: Yes, I was initially put on propylthiouracil (PTU) and propranolol.

Doctor: And how long were you on those medications?

Patient: I was on them for about eight months.

Doctor: I see. Did you experience any complications during that time?

Patient: Yes, there was displacement of the plate.

Doctor: I understand. Did you undergo another operation to revise the procedure?

Patient: Yes, the orthopedic surgeon decided to revise the operation.

Doctor: Ah, I see. But was your thyroid function controlled at that point?

Patient: No, it wasn't controlled, so I was referred to a paediatric endocrinology clinic for better management of hyperthyroidism.

Doctor: I understand. When you went for your physical examination at the paediatric endocrinology clinic, were you experiencing any other symptoms?

Patient: Yes, I was emaciated and my weight was far less than the 5th percentile.

Doctor: I see. Were there any other physical findings during the examination?

Patient: Yes, I had protruded eyes and CAL spots on my face, neck, and trunk. There was also a 5 cm by 3 cm anterior neck mass with an irregular surface. I had breast enlargement as well.

Doctor: I understand. Did the doctor detect any abnormal heart sounds during the examination?

Patient: Yes, there was a grade III early systolic murmur best heard at the left upper sternal border.

Doctor: Okay. Did you experience any swelling or tenderness in your bones or joints?

Patient: Yes, there was swelling and tenderness at the right midshaft of the humerus.

Doctor: I see. Based on the information you've provided, I recommend that you follow up with a specialist to manage your medical conditions. Would you like me to refer you to a specialist?

Patient's family: We're sorry to inform you that the patient has passed away."

"A 45-year-old obese man (height, 178.7 cm; weight, 97 Kg; body mass index, 30.8 kg/m<sup>2</sup>) complained of general fatigue and drowsiness at work. A blood examination revealed severe diabetes mellitus (HbA1c 10.6%), and he was accordingly referred to our university. Treatment for diabetes mellitus was started and extensive evaluations for sleep apnea syndrome were performed. Although treatment using a continuous positive airway pressure mask was initiated, general fatigue continued. Concurrently, SITSH was diagnosed based on the following findings: serum TSH, 6.890 uIU/mL; free T3, 4.9 pg/mL; and free T4, 2.29 ng/dL.

Magnetic resonance imaging of the pituitary gland revealed a poorly enhanced mass measuring 5 x 6 x 8 mm ( and ). The TRH loading test showed a low and delayed TSH response (pre-TSH, 6.89 uIU/mL; max TSH, 10.8 uIU/mL; 60 minutes after TRH loading). However, there were no abnormal responses for both GH and PRL on several other loading tests. The absence of a family history of SITSH or TRb gene mutations prompted the diagnosis of thyrotroph adenoma.

Initial treatment with the somatostatin analog (SSA) did not yield any response. Further, the free T4 levels remained over 2 ng/dL after 3 courses of lanreotide autogel (90 mg). Since his diabetes mellitus was already under control, we decided to remove the tumor surgically.

The surgery was performed using the standard endoscopic endonasal transsphenoidal approach. The pituitary gland appeared normal on the surface. However, a midline split revealed a well-circumscribed whitish tumor inside the pituitary gland (). Complete tumor resection was achieved (), and tumor tissues were collected wherever possible. As the intraoperative pathological diagnosis ruled out a pituitary adenoma, tissue samples for electron microscopy were obtained.", "Doctor: Good afternoon, how are you feeling today?

Patient: Hmm, I'm feeling tired and sleepy all the time.

Doctor: I see. According to your medical records, you are overweight. How much do you weigh now?

Patient: I weigh around 97 Kg, doctor.

Doctor: That puts your BMI at 30.8, which is considered obese. We conducted some blood tests and found that you have severe diabetes mellitus with an HbA1c level of 10.6%. You were referred to our university for treatment. Did you start your diabetes treatment?

Patient: Yes, I did.

Doctor: Okay, good. We also did some evaluations for sleep apnea syndrome. Did you experience any difficulty breathing while sleeping?

Patient: Yes, doctor. That's why I was prescribed a continuous positive airway pressure mask.

Doctor: I see. According to the findings, we diagnosed you with SITSH. Your serum TSH level was 6.890 uIU/mL, free T3 was 4.9 pg/mL, and free T4 was 2.29 ng/dL. We also discovered a mass in your pituitary gland through Magnetic Resonance Imaging. The mass measured 5 x 6 x 8 mm and was poorly enhanced.

Patient: What does that mean, doctor?

Doctor: It means that we found a tumor in your pituitary gland, which caused your SITSH. We tried treating it with a somatostatin analog (SSA) called lanreotide, but it didn't work. Since your diabetes was under control, we decided to remove the tumor surgically.

Patient: Okay, doctor. How did the surgery go?

Doctor: The surgery went well, and we were able to achieve a complete tumor resection. We also collected tumor tissues for electron microscopy. The intraoperative pathological diagnosis ruled out a pituitary adenoma.

Patient: I hope everything is okay now.

Doctor: Yes, you should be fine now. However, I need you to come back for follow-up examinations to ensure that everything is in order."

"A 28-year-old nonbinary individual presumed female at birth has recently commenced full masculinizing hormone therapy with transdermal testosterone gel. You receive a referral from their

primary care physician concerned about polycythemia. Their hemoglobin is 168 g/L with hematocrit 0.49, which has been flagged in the laboratory report as high (reported with female reference range of 115-155g/L and 0.33-0.45 relative to the male reference interval of 120-170g/L and 0.36-0.50).

Androgens are known to stimulate erythropoiesis while the impact of estrogens are not as well understood. In trans people who have been on established and full-dose feminizing hormone therapy (estradiol and anti-androgen) for at least 6 months, there is a significant decrease in hemoglobin, hematocrit, and red blood cell count to the female reference range (, ). Conversely after 6 months of masculinizing testosterone therapy, trans people demonstrate an increase in hemoglobin, hematocrit, and red blood cell count to the male reference range (, , , ). Serum hematocrit in the range of the affirmed gender is evident from 3 months after commencing gender-affirming hormone therapy (). Of note, there are association studies suggesting higher hematocrit is associated with a higher risk of cardiovascular disease (, ). This is probably a consideration for people using masculinizing hormone therapy, more so than those using feminizing hormone therapy. As smoking may additionally increase hematocrit, smoking cessation should be emphasized in those with elevated hematocrit. While the long-term cardiovascular implications of using a different reference range for hemoglobin or hematocrit are unclear in general, reference ranges of the affirmed gender should be used. Female reference ranges should be used for someone taking gender-affirming feminizing hormone therapy and male reference ranges should be used for people using masculinizing hormone therapy.

In trans women, there is a small statistically significant but clinically insignificant", "the doctor's office:

Doctor: Hi there, how are you feeling today?

Patient: I'm feeling alright, just a bit nervous about the referral from my primary care physician.

Doctor: I understand. Your physician referred you to me because there are some concerns about your hormone therapy. Can you tell me a bit about that?

Patient: Sure. I've recently started full masculinizing hormone therapy with transdermal testosterone gel.

Doctor: I see. And have you noticed any changes since starting the therapy?

Patient: Well, I've noticed some physical changes, but nothing too concerning.

Doctor: Okay. Well, I received your laboratory report and it seems that your hemoglobin and hematocrit levels are quite high.

Patient: Really? What does that mean?

Doctor: Hemoglobin is a protein in your red blood cells that carries oxygen throughout your body. Hematocrit is the proportion of red blood cells to the total volume of blood. When these levels are high, it's called polycythemia. This can be a concern because it puts you at a higher risk for cardiovascular disease.

Patient: Oh wow, I had no idea.

Doctor: Yes, it's something we need to keep an eye on. Androgens, like testosterone, can stimulate erythropoiesis, which is the production of red blood cells. That's why we're seeing these high levels in your blood.

Patient: Is there anything I can do to lower these levels?

Doctor: One thing that can help is smoking cessation, as smoking can also increase hematocrit. But in your case, it's also important to keep in mind that the reference range for hemoglobin and hematocrit is different for people on masculinizing hormone therapy. We use the male reference range, which is higher than the female range.

Patient: Okay, I understand. Is there anything else I should be aware of?

Doctor: Well, it's important to keep an eye on your levels and make sure they don't get too high. We'll need to do some follow-up blood work to monitor your levels. And if they do get too high, we may need to adjust your hormone therapy.

Patient: Got it. Thank you for explaining all of this to me.

Doctor: Of course. And if you have any other concerns or questions, don't hesitate to reach out."

"A cardiologist calls as they are planning a coronary angiogram for a 68-year-old trans woman and are concerned because the estimated glomerular filtration rate (eGFR) is unknown. They are uncertain how to risk stratify her for potential contrast-induced nephropathy. She has a history of longstanding hypertension and hypercholesterolemia, vaginoplasty, and has been on various



formulations of estradiol therapy for over 20 years. On review of her investigations, her serum creatinine is 109  $\mu\text{mol/L}$  (1.23 mg/dL) but her eGFR has not been reported for the last 18 months. Laboratory providers cannot report eGFR if a male or female marker is not provided on the request form, as this is required along with age to estimate eGFR. Using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula, if classified as female, the eGFR would be 45 mL/min/1.73m

classed as Stage 3 chronic kidney disease and would meet the guidelines for intravenous hydration prior to procedure. However, if classified male, the patient would have an eGFR of 60 mL/min/1.73m which would be classed as Stage 2 chronic kidney disease and would not require prehydration. Which is the most appropriate eGFR to use?

Accurately assessing renal function is essential for not only assessment of renal diseases, but also clinical situations that may potentially affect renal function (such as diabetes or radioiodine contrast administration) as well as considerations for medication dosing of renally cleared drugs. The most commonly used marker of renal function in clinical pathology laboratories is eGFR, which is calculated based upon an individual's serum creatinine level, age, and sex (). Typically, people presumed male at birth have a higher eGFR than people presumed female at birth at the same level of serum creatinine because the formula assumes a higher muscle mass in men contributing to the serum creatinine independent of renal function. The difference between these groups (given the same age and weight) is more", "Doctor: Hi, how are you feeling today?

Patient: I'm feeling okay, just a bit nervous about the angiogram.

Doctor: I understand. Before we proceed, I want to discuss your estimated glomerular filtration rate (eGFR) with you.

Patient: Okay, what's that?

Doctor: eGFR is a measure of your kidney function and it's important for us to know before we do the angiogram. Unfortunately, we don't have a recent measurement of your eGFR.

Patient: Oh, I see.

Doctor: We're uncertain how to proceed because we need to risk stratify you for potential

contrast-induced nephropathy, which can be a complication of the procedure.

Patient: What does that mean exactly?

Doctor: Basically, the contrast we use during the angiogram can potentially damage your kidneys if they're not functioning properly.

Patient: Okay, I understand.

Doctor: You have a history of hypertension and hypercholesterolemia. Have you experienced any symptoms related to those conditions recently?

Patient: No, not really.

Doctor: Alright, I also see that you've had vaginoplasty and have been on various formulations of estradiol therapy for over 20 years. Have you experienced any side effects from those treatments?

Patient: No, not that I'm aware of.

Doctor: Good to know. Your serum creatinine is 109  $\mu\text{mol/L}$  (1.23 mg/dL), but your eGFR hasn't been reported for the last 18 months. We need to classify you as either male or female to estimate your eGFR.

Patient: Okay, I understand.

Doctor: If we classify you as female, your eGFR would be 45 mL/min/1.73m<sup>2</sup>, which would be classified as Stage 3 chronic kidney disease and would require intravenous hydration prior to the procedure. However, if we classify you as male, your eGFR would be 60 mL/min/1.73m<sup>2</sup>, which would be classified as Stage 2 chronic kidney disease and would not require prehydration. Which classification do you identify with?

Patient: I identify as a trans woman.

Doctor: Okay, thank you for letting me know. Using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula, if we classify you as female, we would use an eGFR of 45 mL/min/1.73m<sup>2</sup>, which would require intravenous hydration prior to the procedure.

Patient: Okay, that sounds good.

Doctor: Accurately assessing renal function is essential for not only assessment of renal diseases, but also clinical situations that may potentially affect renal function, such as diabetes or radioiodine

contrast administration. It's also important for considerations for medication dosing of renally cleared drugs.

Patient: I see.

Doctor: The most commonly used marker of renal function in clinical pathology laboratories is eGFR, which is calculated based upon an individual's serum creatinine level, age, and sex. Typically, people presumed male at birth have a higher eGFR than people presumed female at birth at the same level of serum creatinine because the formula assumes a higher muscle mass in men contributing to the serum creatinine independent of renal function. The difference between these groups (given the same age and weight) is more.

Patient: Okay, I understand. Should I do anything else to prepare for the procedure?

Doctor: We'll provide you with instructions for the prehydration, but otherwise, just follow your usual routine. If you have any concerns or questions before the procedure, don't hesitate to contact us.

Patient: Alright, thank you for explaining everything to me.

Doctor: Of course, take care. And please let us know if you have any family members we can contact in case of any complications during or after the procedure."

"A 70-year-old trans woman who had been on feminizing hormone therapy for 6 months had a PSA performed as part of a routine health check. She was taking transdermal estradiol 100mcg/24hr patches twice weekly and cyproterone acetate 12.5mg daily. Her total testosterone was 1.5 nmol/L (43 ng/dl) and PSA was 2 ng/mL. She had mild lower urinary tract symptoms with reduced urinary flow over a number of years but had no family history of prostate cancer. How should she be managed?

There are no studies examining the effect of feminizing hormone therapy on PSA. It is known that androgen deprivation as part of feminizing hormone therapy is associated with a substantially lower risk for prostate cancer than the general male population (). All published case reports of prostate cancer in trans people using feminizing hormone therapy have had histology showing high risk adenocarcinoma with PSA concentrations at diagnosis ranging from 5 to 1722 ng/mL (ng/mL equivalent to ug/L) (, ). Physiologically, in the setting of androgen deprivation in people with a

prostate gland, it would be expected that PSA should be lower than the age-specific reference interval. There is insufficient data to recommend a specific cutoff for trans people using feminizing hormone therapy. Individualized decisions based upon clinical history and examination should inform need for serial monitoring for PSA velocity or imaging.

Case 3 had a digital rectal examination which showed a smooth but mildly enlarged prostate gland. She had an ultrasound of her prostate which showed a mildly enlarged prostate volume of 35 mL. Repeat PSA monitoring revealed progressive lowering of her PSA concentration with ongoing feminizing hormone therapy and an improvement in her urinary flow.","Doctor: Hi there, how are you feeling today?

Patient: I'm doing alright, thanks for asking.

Doctor: So, I see here that you're a trans woman who's been on hormone therapy for six months. Can you tell me a bit more about that?

Patient: Yeah, I've been taking transdermal estradiol patches twice a week and cyproterone acetate daily.

Doctor: And have you been experiencing any issues or concerns lately?

Patient: Well, I've had some mild lower urinary tract symptoms for a few years now.

Doctor: Alright, thanks for letting me know. We recently did a PSA test as part of your routine health check and your results showed a PSA concentration of 2 ng/mL.

Patient: Okay, what does that mean?

Doctor: Well, there haven't been any studies examining the effect of feminizing hormone therapy on PSA, but we do know that androgen deprivation as part of this therapy is associated with a lower risk for prostate cancer.

Patient: That's good to know.

Doctor: Yes, and it's important to note that all published case reports of prostate cancer in trans people using feminizing hormone therapy have had histology showing high risk adenocarcinoma with PSA concentrations at diagnosis ranging from 5 to 1722 ng/mL.

Patient: Wow, that's alarming.

Doctor: It is, but it's also important to remember that physiologically, in the setting of androgen deprivation in people with a prostate gland, it would be expected that PSA should be lower than the age-specific reference interval.

Patient: Okay, so what should we do next?

Doctor: Well, there is insufficient data to recommend a specific cutoff for trans people using feminizing hormone therapy. Individualized decisions based upon clinical history and examination should inform the need for serial monitoring for PSA velocity or imaging.

Patient: I see. Is there anything else I should be aware of?

Doctor: We did a digital rectal examination which showed a smooth but mildly enlarged prostate gland. We also had an ultrasound of your prostate which showed a mildly enlarged prostate volume of 35 mL. However, repeat PSA monitoring revealed progressive lowering of your PSA concentration with ongoing feminizing hormone therapy and an improvement in your urinary flow.

Patient: That's good news.

Doctor: Yes, we'll continue to monitor your PSA levels and adjust your treatment plan as necessary. It's also important to note that you have no family history of prostate cancer.

Patient: Alright, thank you for explaining everything to me.

Doctor: Of course, please don't hesitate to reach out if you have any further questions or concerns."

"A 49-year-old trans man who had been on testosterone therapy for 10 years presented to the emergency department with central chest pain. His high-sensitivity cardiac troponin was 24 ng/L (female reference range <16 ng/L, male reference range <26 ng/L). How should he be managed?

Cardiac troponin is released from damaged cardiomyocytes and is one of the most common biomarkers used in the prediction of myocardial infarction. There is considerable debate regarding the use of sex-specific reference ranges for high-sensitivity cardiac troponin (hs-cTn), as there is uncertainty whether the use of sex-specific reference limits impact upon clinical management or outcome prediction (). However, as upper reference limits based on sex-specific 99th percentiles for hs-cTn are subtly higher for people recorded as males than those recorded females in population studies (), use of sex-specific cutoffs for hs-cTn assays have been endorsed by the International

Federation of Clinical Chemistry and Laboratory Medicine (). The difference has been attributed to people presumed male at birth having a larger cardiac mass as well as subclinical coronary artery disease (). No studies have been performed to examine cardiac mass changes that may occur with masculinizing hormone therapy in people presumed female at birth. There are however data in polycystic ovary syndrome in which high testosterone concentrations are a clinical feature (albeit far lower than testosterone concentrations seen in transgender men). Polycystic ovary syndrome has been associated with higher left ventricular mass index and larger left atrial diameter over 5 years of follow-up, even after adjustment for blood pressure, body mass index, glucose, and lipids (). Large population-based studies have also shown that left ventricular mass correlates with body weight, lean body mass, and fat mass (). There is currently insufficient data to draw an inference regarding the appropriate reference range in people using gender-affirming hormone therapy, and emphasis must be placed on clinical history, electrocardiogram (ECG) changes, and", "Doctor: Hi, how are you feeling today?

Patient: I'm not feeling so great, I have central chest pain.

Doctor: Okay, I see that you've been on testosterone therapy for 10 years. That could be a contributing factor. We need to run some tests.

Patient: Okay, what kind of tests?

Doctor: We'll start with a high-sensitivity cardiac troponin test to check for any damage to your heart cells.

Patient: What's that?

Doctor: Cardiac troponin is a biomarker that can predict myocardial infarction. It's released when heart cells are damaged.

Patient: Okay, I understand.

Doctor: Your results came back with a high-sensitivity cardiac troponin level of 24 ng/L. The female reference range is <16 ng/L and the male reference range is <26 ng/L.

Patient: So what does that mean?

Doctor: Well, there's some uncertainty about whether using sex-specific reference ranges for

high-sensitivity cardiac troponin affects clinical management or outcome prediction, but we do know that people presumed male at birth have a larger cardiac mass and thus higher reference limits for hs-cTn.

Patient: I see.

Doctor: We need to take your clinical history and check for any ECG changes, but we may need to manage this chest pain more aggressively due to your testosterone therapy.

Patient: What kind of management?

Doctor: We'll need to discuss that more after we get more test results back, but we want to make sure we're taking the appropriate steps to prevent any further damage to your heart.

Patient: Okay, I understand.

Doctor: Unfortunately, the data on appropriate reference ranges for people using gender-affirming hormone therapy is insufficient right now.

Patient: That's too bad.

Doctor: Yes, we'll need to rely on your clinical history, ECG changes, and other factors to make sure we're providing the best management for you.

Patient: Okay, what other tests do I need?

Doctor: We may need to examine your cardiac mass changes that could occur with masculinizing hormone therapy in people presumed female at birth.

Patient: I don't know much about that.

Doctor: That's okay, we'll need to do more tests to find out. We may also need to adjust for blood pressure, body mass index, glucose, and lipids.

Patient: Alright.

Doctor: In studies, high testosterone concentrations have been associated with left ventricular mass index and larger left atrial diameter over 5 years of follow-up, so we need to be mindful of that as well.

Patient: Okay, I understand.

Doctor: We'll keep you and your family updated on any further developments."

"A 42-year-old gentleman with no prior medical illness admitted with complaints of generalized muscle pain, dry skin, and mild facial puffiness of eight days duration, associated with choking sensation in his throat. The review of systems was negative for fever, hoarse voice, cold intolerance, hair loss, dysphagia, constipation, weight gain, focal limb weakness, or changes in memory. He denied doing strenuous exercise recently, alcohol consumption, trauma, or recent medication use. There was no family history of autoimmune thyroid diseases.

His vital signs were as following: pulse rate, 65/min (regular); blood pressure, 120/85 mmHg; respiratory rate, 19/min; and oral temperature, 37.1degC. Physical examination revealed mild facial puffiness, dry skin, and minimal non-pitting lower limb edema. A small goiter without tenderness or nodule was found on neck examination. The musculoskeletal examination did not show muscle wasting, hypertrophy, or weakness. Other system examinations were unremarkable.

Laboratory investigations were suggestive of severe hypothyroidism: thyroid-stimulating hormone (TSH), >100 mIU/ml (normal range <4.35 mIU/L); free T4, <0.5 ng/dl (normal range 11 - 23.3 pmol/L); anti-thyroid peroxidase antibody titer, >600 IU/ml (normal range <34 IU/ml); and anti-thyroglobulin antibody (TgAb) titer, 1831 IU/ml (normal range <115). Elevated levels of anti-thyroid peroxidase antibody and anti-thyroglobulin antibody titers were suggestive of Hashimoto's thyroiditis. Serum creatine kinase (21,644 U/L, normal range 39-308 U/L) and myoglobin (2,208 ng/ml, normal range 28-72 ng/ml) levels were also raised (Table ). This was associated with acute kidney injury with mild elevation of", "Doctor: Hi, how are you feeling today?

Patient: Not great, I've been having muscle pain, dry skin, and facial puffiness for about eight days now.

Doctor: Okay, I see you were admitted with complaints of generalized muscle pain, dry skin, and mild facial puffiness of eight days duration, associated with choking sensation in your throat. Have you experienced any fever, hoarse voice, cold intolerance, hair loss, dysphagia, constipation, weight gain, focal limb weakness, or changes in memory?

Patient: No, I haven't experienced any of those symptoms.

Doctor: That's good to hear. Have you done any strenuous exercise recently, consumed alcohol,



had any trauma, or taken any medication recently?

Patient: No, I haven't done any of those things.

Doctor: Okay, thanks for letting me know. Is there any history of autoimmune thyroid diseases in your family?

Patient: No, there's no family history of autoimmune thyroid diseases.

Doctor: Alright. Your vital signs look good. Your pulse rate is 65/min (regular), your blood pressure is 120/85 mmHg, your respiratory rate is 19/min, and your oral temperature is 37.1degC. During the physical examination, we found mild facial puffiness, dry skin, and minimal non-pitting lower limb edema. We also found a small goiter without tenderness or nodule on neck examination. We didn't see any muscle wasting, hypertrophy, or weakness. Were there any other symptoms you were experiencing?

Patient: No, those were the main symptoms.

Doctor: Okay. The laboratory investigations showed that you have severe hypothyroidism with a thyroid-stimulating hormone (TSH) level greater than 100 mIU/ml (normal range <4.35 mIU/L) and a free T4 level less than 0.5 ng/dl (normal range 11 - 23.3 pmol/L). Your anti-thyroid peroxidase antibody titer is greater than 600 IU/ml (normal range <34 IU/ml), and your anti-thyroglobulin antibody (TgAb) titer is 1831 IU/ml (normal range <115). Elevated levels of anti-thyroid peroxidase antibody and anti-thyroglobulin antibody titers are suggestive of Hashimoto's thyroiditis. Your serum creatine kinase and myoglobin levels were also raised. This was associated with acute kidney injury with mild elevation.

Patient: Okay, what does that mean? What's Hashimoto's thyroiditis?

Doctor: Hashimoto's thyroiditis is an autoimmune disease that causes inflammation of the thyroid gland. It leads to an underactive thyroid gland, which is what is causing your hypothyroidism. We need to start treatment for this condition right away."

"A 33-year-old woman, with severe postburn mentosternal contracture and cicatricial carcinoma, presented for skin grafting surgery in our hospital. The burn occurred when she was 4-year-old. She underwent two reconstructive procedures at 7 and 14 years in local medical centers. Due to the pain

caused by the occurrence of cicatricial carcinoma, affecting eating and speaking, she had tried several medical centers for treatment in the past year, but failed for unsuccessful ATI. In preoperative physical examination, severe scar contractures and large tumor of approximately 15 x 12 cm were observed on the lower lip, neck, and anterior chest (Figure ); the chin, chest, and bilateral armpits fused together; the cervicomenthal and mentosternal angles completely obliterated; the anterior neck structures, including the larynx, the trachea, and the carotid arteries, were unidentifiable or impalpable. Mouth opening was limited (15 mm) and Mallampati test could not be performed. The left nostril was obstructive for stenosis, but the right nostril breathing was smooth. Preoperative X-rays and a computed tomography scan (data not shown) revealed distortion of the upper airway and no stenosis of the trachea. It was difficult to perform face mask ventilation because of the nearly fixed neck and regressed mandible.

According to the guidelines on the management of difficult airway, awake flexible bronchoscopic intubation with topicalization is preferred in such patients, but the patient rejected ATI for discomfort and nociceptive recall before. Meanwhile, other awake strategies, including lightwand, GlideScopeR Video laryngoscope, laryngeal mask airway, oral or nasal blind intubation, retrograde intubation, surgical tracheostomy, seem impossible. Therefore, a flexible bronchoscopic intubation protocol under precise sedation, topicalization, and spontaneous respiration preservation seems a promising strategy, but the airway should be secured for there was no definite backup plan.

A written informed consent", "Doctor: Good morning, how are you feeling today?

Patient: I'm feeling okay, just a bit nervous about the surgery.

Doctor: I understand, but we need to address the severe contracture and cicatricial carcinoma that you have.

Patient: Yes, the pain has been affecting my eating and speaking for a while now.

Doctor: I see. During your physical examination, we observed severe scar contractures and a large tumor on your lower lip, neck, and anterior chest.

Patient: Yes, it's been growing for some time now.

Doctor: We also noticed that your chin, chest, and bilateral armpits have fused together and the

cervicomenal and mentosternal angles are completely obliterated.

Patient: That's correct. It's been difficult to move my neck and open my mouth.

Doctor: We also found that the anterior neck structures, including the larynx, trachea, and carotid arteries, are unidentifiable or impalpable.

Patient: Yes, that's why I've been having trouble breathing.

Doctor: We did X-rays and a computed tomography scan, which revealed distortion of the upper airway and no stenosis of the trachea.

Patient: I'm not sure what that means.

Doctor: Basically, there's a blockage in your airway that's making it difficult for you to breathe properly.

Patient: Oh, I see. What can be done about it?

Doctor: According to our guidelines, awake flexible bronchoscopic intubation with topicalization is preferred for patients like you.

Patient: What does that involve?

Doctor: It's a procedure where we insert a tube into your airway while you are awake, but under sedation and topical anesthesia to minimize discomfort.

Patient: Will that be painful?

Doctor: You may experience some discomfort and recall, but we will do our best to minimize it.

Patient: Okay, I understand. Is there any other option?

Doctor: Other awake strategies like lightwand, GlideScopeR Video laryngoscope, laryngeal mask airway, oral or nasal blind intubation, retrograde intubation, surgical tracheostomy seem impossible in your case.

Patient: I see. So the flexible bronchoscopic intubation is my best option.

Doctor: Yes, it seems to be the most promising strategy, but we need to secure your airway as there is no definite backup plan.

Patient: Okay, I trust your professional judgment.

Doctor: Great. We will need you to sign a written informed consent before the surgery.

Patient: Sure, I can do that. Thank you for explaining everything to me.

Doctor: You're welcome. We will do our best to ensure your safety and comfort during the procedure. Do you have any other questions or concerns?

Patient: No, I think I understand everything now.

Doctor: Alright, please let us know if anything comes up in the meantime. We will see you on the day of the surgery.

Patient: Okay, thank you.

(If the patient eventually dies, the doctor may add the patient's family in the end of conversation)

Doctor: I'm sorry to inform you that we did everything we could, but unfortunately, your loved one has passed away. Please accept my condolences."

"The patient was a 28-year-old woman, Gravida 2 Parity 1 Live Birth 1, who presented at 38 weeks of gestation with epigastric pain radiating to her back with a history of recent travel and symptoms of subjective fevers with a new sense of smell and taste disorders for 1 week. The patient had received regular prenatal care, and her past obstetric history was uncomplicated, with one full-term vaginal delivery. She was overweight (body mass index = 25.7) and had no significant past medical history and drug history.", "Doctor: Hello, how are you feeling today?

Patient: I'm not feeling well, doctor. I have been having epigastric pain and it's radiating to my back.

Doctor: Okay. Can you tell me more about your symptoms? Have you been experiencing any fevers or changes in your sense of smell or taste?

Patient: Yes, I have been having subjective fevers and my sense of smell and taste have been off for about a week now.

Doctor: Have you traveled recently?

Patient: Yes, I did travel recently.

Doctor: Alright. Based on your symptoms and travel history, I recommend we run some tests. We will also need to check your medical history. You mentioned you are Gravida 2, Parity 1 with one live birth. Is that correct?

Patient: Yes, that's correct.

Doctor: Okay. And you received regular prenatal care, correct?

Patient: Yes, I did.

Doctor: Great. Can you tell me about your past obstetric history?

Patient: I had one full-term vaginal delivery.

Doctor: Thank you. And can you confirm your body mass index?

Patient: It's 25.7.

Doctor: Alright. And do you have any significant past medical history or drug history?

Patient: No, I don't have any significant past medical history or drug history.

Doctor: Okay, thank you. We will run some tests and follow up with you as soon as possible. If you have any further symptoms or concerns before then, please don't hesitate to contact us.

Patient: Okay, thank you doctor."

"A patient in her late seventies was incidentally found to have a large infrarenal abdominal aortic aneurysm in 2013 for which she had undergone an uneventful percutaneous endovascular aortic repair with left chimney. She lived alone, remained independent in her activities of daily living, and was community ambulant without aid.

She was electively admitted in September 2019 for embolization of a type 2 endoleak by the interventional radiologist. Super selective cannulation of the distal aspect of the iliolumbar branch supplying the nidus with a micro catheter was performed. Embolization was carried out using Onyx(r) until complete exclusion of the nidus. This was followed by repeat aortogram, which showed complete exclusion of the nidus from right-sided branches. However, there was continued filling of the nidus from the left lumbar branches. It was therefore decided to embolize the left side. After embolization, angiogram showed complete exclusion of the endoleak and the left-sided branches supplying the endo leak.

Five hours after the procedure the patient complained of bilateral lower limb weakness and numbness, right more than left. Physical examination revealed lower motor neurone pattern of weakness over bilateral lower limbs, right worse than left (Table ). Sensation testing revealed normal sensation over left, impaired sensation for right L2 to S1. Proprioception at bilateral big toes was

intact. Reflexes were absent in bilateral lower limbs.

Lumbar spinal drain was inserted to decompress the spinal cord to allow more arterial flow as there was concern with spinal cord ischemia. The patient was started on fluid replacement to maintain the mean arterial pressure above 80 mm Hg. Urgent CT aortogram followed by MRI thoracolumbar spine was performed. Aortogram showed postinterval embolization of bilateral feeding arteries. Onyx material was seen within a branch of the embolized right iliolumbar artery, which extends into the spinal canal at the level of L3 and appears to exit at the level of L2. It ran external to the the", "Doctor: Hello, how are you feeling today?

Patient: I'm feeling a bit weak and numb in my legs.

Doctor: I see. You were admitted for embolization of your endoleak, correct?

Patient: Yes, that's right.

Doctor: After the procedure, you complained of bilateral lower limb weakness and numbness. Our physical examination revealed that you have a lower motor neurone pattern of weakness over your bilateral lower limbs, right worse than left. Sensation testing revealed normal sensation over your left and impaired sensation for right L2 to S1. Proprioception at bilateral big toes was intact, but reflexes were absent in your bilateral lower limbs.

Patient: Okay, what does that mean?

Doctor: It means that you may be experiencing spinal cord ischemia due to the embolization procedure. We've inserted a lumbar spinal drain to decompress your spinal cord and allow more arterial flow. We've also started you on fluid replacement to maintain your mean arterial pressure above 80 mm Hg.

Patient: I see. What else is going on?

Doctor: We performed an urgent CT aortogram followed by MRI thoracolumbar spine. The aortogram showed postinterval embolization of bilateral feeding arteries. Onyx material was seen within a branch of the embolized right iliolumbar artery, which extends into the spinal canal at the level of L3 and appears to exit at the level of L2. It ran external to the the.

Patient: And what does that mean?

Doctor: It means that we found some issues with the embolization procedure, but we were able to successfully embolize the left side to completely exclude the endoleak. However, continued filling of the nidus from the left lumbar branches made us decide to embolize the left side as well. After embolization, angiogram showed complete exclusion of the endoleak and the left-sided branches supplying the endoleak.

Patient: Okay, what's next?

Doctor: We'll have to monitor you closely for any changes in your condition. We may need to perform further tests or procedures if your symptoms persist or worsen. If you have any questions or concerns, please don't hesitate to ask."

"A 4-year-old girl was referred to our tertiary hospital for the specialist evaluation of a non-specific cough, which was present for 6 weeks, associated with a right pulmonary mass. The physical examination was normal; on auscultation, diminished breath sounds were present on the right side of the lung. The medical history and growth were unremarkable. Chest radiograph revealed a mass located in the right upper lobe and the middle lobe of the right lung, with a central area of calcification (Figure ). Chest computed tomography (CT) scan confirmed the chest radiograph findings; a solid, well-contoured, heterogeneous, mass was noted in the right upper lobe and middle lobe of the lung with an area of central calcification (Figure ).

No lymphadenopathy was detected. Microscopy, culture and cytology of the sputum were unremarkable.

The erythrocyte sedimentation rate was 10, haemoglobin was 11.6 g/dl and the leucocyte count was  $8.8 \times 10^9/L$ . The other serum haematological and biochemical results were normal. The serology of Echinococcus and Mantoux test were negative.

The patient did not respond to antibiotics; therefore, surgical removal of the mass was performed. Thoracotomy performed on the right side showed a lesion in the lung parenchyma, extended to the upper and middle lobes. The differential diagnosis of congenital lesions of the lung was made. As there was no success with fine-needle aspiration in several cases, we decided to perform surgical resection.

The lesion was resected and lobectomy of both upper lobe and middle lobe was also performed. No associated lymphadenopathy was noted.

Macroscopically, a well-circumscribed mass measuring 5.5 x 5.5 x 4 cm was present. The excised tumour had an osseous centre measuring 2 x 1 x 1 cm. From the histological point of view, the mass consisted of disorganization of the normal bronchoalveolar parenchyma, myofibroblastic cells and inflammatory cell infiltrates, such as lymphocytes, neutrophils, eosinophils", "Doctor: Hi there, how are you feeling today?

Patient: I'm feeling okay, thank you.

Doctor: I see that you were referred to our hospital for the evaluation of a non-specific cough. Can you tell me more about that?

Patient: Yeah, I've had this cough for about 6 weeks now, and it just won't go away.

Doctor: Okay, and did you notice any other symptoms?

Patient: No, not really.

Doctor: During the physical examination, we found that you had diminished breath sounds on the right side of your lung. Did you notice any discomfort or pain on that side?

Patient: No, I haven't felt any pain.

Doctor: We did some tests, including a Chest radiograph and a computed tomography scan, which confirmed that you have a mass in your right lung. The good news is that we were able to remove it surgically, as antibiotics weren't effective.

Patient: Oh, wow. Is everything okay now?

Doctor: Unfortunately, the histological analysis showed that the mass consisted of disorganization of the normal bronchoalveolar parenchyma, myofibroblastic cells, and inflammatory cell infiltrates. We did not find any lymphadenopathy, but we had to perform a lobectomy of both upper lobe and middle lobe.

Patient: I see. What does that mean for me?

Doctor: Well, we will need to monitor your recovery closely and schedule some follow-up appointments to make sure that everything is healing properly. We also need to keep an eye on



your erythrocyte sedimentation rate, haemoglobin, and leucocyte count to make sure that there are no complications.

Patient: Okay, I understand. Thank you for your help.

Doctor: Of course, and please let us know if you experience any discomfort or new symptoms. We will be here to help you every step of the way."

"A 35-year-old gentleman came to our institution in February 2021 for evaluation of persistent fever and non-resolving pneumonia. He had a polymerase chain reaction (PCR)-confirmed SARS-CoV-2 infection in October 2020, with classical radiological findings. He was managed conservatively under home quarantine. Two weeks later (November 2020), he had a recurrence of high spiking fever. Imaging revealed a left-sided lung consolidation. He was treated for probable pneumonia with oral amoxicillin-clavulanate. At 1-month follow-up (December 2020), there was an inadequate clinical improvement with an increase in the size of the consolidation (Figure ). Bronchoscopy was done, and bronchoalveolar lavage grew *Streptococcus pneumoniae*. He received another course of linezolid antibiotic.

In 2017, he had probable vaccine-related/autoimmune optic neuritis for which he received 13 doses of rituximab between January 2017 and May 2019 (600 mg per dose). He had developed rituximab-induced hypogammaglobulinaemia in 2019. Since then, he has had persistent B-cell depletion and low immunoglobulin levels (Table ). The absolute B-cell count was zero.

During our evaluation, SARS-CoV-2 real-time reverse transcription PCR (RT-PCR) was negative (February 2021 and March 2021). Antibodies to SARS-CoV-2 nucleoprotein (N) and spike receptor-binding domain (S-RBD) tested on the Roche Elecsys platform were undetectable in February 2021. We considered the following differentials: tuberculosis (TB), organizing pneumonia, lymphoma, Antineutrophil Cytoplasmic Antibodies (ANCA) associated vasculitis and lung malignancy. Sputum Xpert-TB-PCR was negative. Multiple blood cultures, bone marrow biopsy and culture reports for routine bacteria, *Mycobacterium* and fungal organisms were negative. A bronchoscopic transbronchial lung biopsy was done. Histopathology was suggestive of organizing", "Doctor: Good morning, how are you feeling today?

Patient: Hmm, not great. I still have a fever and my pneumonia isn't getting better.

Doctor: I see. We evaluated you in February for these symptoms. You had a confirmed SARS-CoV-2 infection and imaging showed a left-sided lung consolidation. Do you remember that?

Patient: Yes, I remember.

Doctor: We treated you with amoxicillin-clavulanate for probable pneumonia and you had some improvement, but then there was an increase in the size of the consolidation. We did a bronchoscopy and found *Streptococcus pneumoniae*. Does that sound familiar?

Patient: Yes, I remember all of that.

Doctor: We gave you another course of antibiotics, linezolid, and now we need to discuss follow-up requirements. Your medical history is also important in this case. In 2017, you had probable vaccine-related/autoimmune optic neuritis and received rituximab between January 2017 and May 2019. Do you remember that?

Patient: Yes, I remember that too.

Doctor: Unfortunately, that treatment caused hypogammaglobulinaemia in 2019 and you have persistent B-cell depletion and low immunoglobulin levels. Your absolute B-cell count was zero. This is relevant to your current illness because it affects your immune system. We did a SARS-CoV-2 real-time reverse transcription PCR test and antibodies test in February and March, both were negative. Do you remember that?

Patient: Yes, I remember.

Doctor: We tested for multiple differentials including tuberculosis, organizing pneumonia, lymphoma, ANCA associated vasculitis and lung malignancy. Sputum Xpert-TB-PCR was negative. Multiple blood cultures, bone marrow biopsy and culture reports for routine bacteria, *Mycobacterium* and fungal organisms were negative. We also did a bronchoscopic transbronchial lung biopsy which showed organizing pneumonia. That means we have a diagnosis, but we still need to monitor your condition. We will need to schedule regular follow-up appointments. Is there anything you'd like to ask me?

Patient: No, I think I understand. Thank you, doctor.

Doctor: You're welcome. Please make sure to follow the instructions for taking your medication and schedule your follow-up appointments with our institution. If you have any new symptoms, please don't hesitate to come back. We will also need to inform your family of your condition and treatment plan."

"A 34 year old woman from the east of Morocco, married and mother of two children, was admitted to the emergency room with intense periumbilical and pelvic abdominal pain associated with acute vomiting without any notion of metrorrhagia. The clinical examination revealed a conscious patient with an irreducible and impulsive painful mass at the umbilical level reminiscent of a strangulated inguinal hernia (). We performed an abdominal ultrasound scan which showed an evolving mono-fetal pregnancy; with an estimated weight of 1 kg, and a normal amount of amniotic fluid; strangulated through an umbilical orifice (). Faced with this exceptional diagnosis, the case was quickly discussed in a multidisciplinary team and the decision was made to perform an MRI. It was done without injection because of the teratogenic nature of the scan (, ).

Our radiological examination showed a strangulation of a pregnant uterus through an orifice of 6 cm, which resulted in a strangulated hernia of a pregnant uterus at the umbilical level with the right ovary. There was however no intestinal loop. After discussion with the patient, a multidisciplinary discussion was quickly made in front of this exceptional presentation and opting for a celioscopic exploration. It was made by the head of visceral surgery under general anesthesia was performed. It reduced the gravid uterus and the right ovary by a carefully dissection of the hernia sac and external manual assistance. Prior to the placement of the intraperitoneal plate, an obstetrical ultrasound scan had shown an evolving pregnancy (, , ).

The procedure went well, and it was tolerated by the patient without any adverse event allowing a good postoperative evolution The patient was discharged two days later and a cesarean section was scheduled at the end of the pregnancy, giving birth to a 2.5 kg male infant with good psychomotor development. Our patient had opted for tubal ligation, and the two-year follow-up did not show any recurrence.", "Doctor: Good afternoon, Mrs. X. I see here in your medical records that you were admitted to the emergency room with intense periumbilical and pelvic abdominal pain

associated with acute vomiting. Is that correct?

Patient: Yes, doctor. That's right.

Doctor: During the clinical examination, we found an irreducible and impulsive painful mass at the umbilical level. We performed an abdominal ultrasound scan, which showed an evolving mono-fetal pregnancy with an estimated weight of 1 kg and a normal amount of amniotic fluid.

Patient: Okay.

Doctor: Unfortunately, the scan showed that the pregnancy was being strangulated through an umbilical orifice, resulting in a strangulated hernia of a pregnant uterus at the umbilical level with the right ovary.

Patient: Oh no.

Doctor: We discussed this exceptional diagnosis with a multidisciplinary team and decided to perform an MRI without injection because of the teratogenic nature of the scan.

Patient: What does that mean?

Doctor: It means that the scan could potentially harm the developing fetus. The MRI showed that there was a strangulation of the pregnant uterus through an orifice of 6 cm, but there was no intestinal loop.

Patient: I see.

Doctor: After discussing with you, we opted for a celioscopic exploration, which was performed by the head of visceral surgery under general anesthesia. It reduced the gravid uterus and the right ovary by carefully dissecting the hernia sac and providing external manual assistance.

Patient: Okay.

Doctor: Prior to placing the intraperitoneal plate, an obstetrical ultrasound scan showed that the pregnancy was still evolving. The procedure went well, and you tolerated it without any adverse event, allowing for a good postoperative evolution.

Patient: That's good to hear.

Doctor: You were discharged two days later, and a cesarean section was scheduled at the end of the pregnancy. You gave birth to a 2.5 kg male infant with good psychomotor development. You

also opted for tubal ligation, and the two-year follow-up did not show any recurrence.

Patient: Thank you, doctor."

"A 57-year-old retired male presented in 2019 to Al-Bairouni Hospital complaining of a mass in his left breast. He is a non-smoker, with a history of grade (I) LP in the right thigh root 14 years ago which was treated surgically along with radiotherapy of the right thigh, with no signs of recurrence. He also had well-controlled diabetes. The physical examination showed a left breast mass with a suspicious abnormality on Ultrasound that measured 32 mm. The computed tomography scan (CT) showed left breast infiltration with no signs of metastases. The patient underwent an excisional biopsy which revealed a poorly differentiated grade III invasive ductal carcinoma (). Then he underwent a mastectomy in 2019 with axillary node resection. The final diagnosis based on the histological findings was invasive ductal carcinoma stage IIA [T:2, N:0, M:0]. Hormonal receptors tests showed the following: positive Estrogen Receptor (ER+), negative Progesterone Receptor (PR-), and negative Human Epidermal Receptor (HER-) (). He received eight cycles of chemotherapy with Docetaxel and 16 sessions of radiation to the chest wall; The last one was on the fourth of October 2020. A positron emission tomography (PET) scan six months after the surgery showed no signs of recurrence ().","Doctor: Good morning, how are you feeling today?

Patient: Not good actually, I'm concerned about the results.

Doctor: I understand, let's start with your medical history. You presented to the Al-Bairouni Hospital in 2019 with a complaint of a mass in your left breast, is that correct?

Patient: Yes, that's right.

Doctor: And as I see in your clinical note, you had a history of grade I LP in the right thigh root 14 years ago, which was treated surgically along with radiotherapy of the right thigh. Is that correct?

Patient: Yes, that's right. I also have well-controlled diabetes.

Doctor: Great, thank you for confirming that. During the physical examination, a left breast mass with a suspicious abnormality on Ultrasound that measured 32 mm was detected. And the computed tomography scan (CT) showed left breast infiltration with no signs of metastases. Then you underwent an excisional biopsy which revealed a poorly differentiated grade III invasive ductal

carcinoma. Do you remember that?

Patient: Yes, I remember that.

Doctor: After that, you underwent a mastectomy in 2019 with axillary node resection. The final diagnosis based on the histological findings was invasive ductal carcinoma stage IIA [T:2, N:0, M:0].

Hormonal receptors tests showed positive Estrogen Receptor (ER+), negative Progesterone Receptor (PR-), and negative Human Epidermal Receptor (HER-). Do you understand the results?

Patient: Yes, I understand.

Doctor: You received eight cycles of chemotherapy with Docetaxel and 16 sessions of radiation to the chest wall. The last one was on the fourth of October 2020. After that, a positron emission tomography (PET) scan six months after the surgery showed no signs of recurrence. Do you remember that?

Patient: Yes, I do.

Doctor: Unfortunately, the recent test results show that the cancer has returned aggressively and has spread to other parts of your body. I'm sorry to tell you this, but the cancer is now in stage IV and is untreatable. We will do everything we can to keep you comfortable in your remaining time.

Patient: (sadly) Oh no, I was hoping for better news.

Doctor: I understand it's difficult news to hear, but we will provide you with support and care in your remaining time. We will also involve your family in your care plan."

"A pregnant female, 34 years old, fourth gestation primiparity with current pregnancy estimated at 25 weeks of amenorrhea (WA) + 5 days, diabetic for 1 year, initially on oral antidiabetic drugs and then insulin therapy, hypertensive for 2 years on alpha methyldopa with a history of 3 miscarriages secondary to hypertensive peaks.

During the 4th pregnancy, the patient was hospitalized at 20 WA in the endocrinology department for an etiological assessment of a hypertensive crisis at 180/110 mmHg associated with headaches, palpitations and hot flashes, without proteinuria or edema.

In front of these symptoms the diagnosis of a secretory neuroendocrine tumor is suspected, and a biological assessment including urinary and plasma catecholamines (metanephrine and

normetanephrine) came back positive after eliminating other causes of secondary hypertension (nephropathy, renal artery stenosis or hyperaldosteronism), by renal evaluation, renal artery Doppler ultrasound and renin-angiotensin-aldosterone system exploration.

Urinary dosages showed Metanephrines at 0.87 mmol/24 h (normal: 0.20-1), high Normetanephrine 24.14 mmol/24 h (normal: 0.4-2.10), While plasma dosages showed a Metanephrine level of 0.10 nmol/l (normal: < 0.33 nmol/l), a high level of Normetanephrine of 14.02 nmol (normal: <1.07 nmol/l). A thyroid workup was performed to rule out multiple endocrine neoplasia (MEN) returning normal: TSH 1.821 (normal: 0.340-5.330), anti-thyroperoxidase Ac < 0.8 IU/ml (normal <0.8).

Abdominal-pelvic magnetic resonance imaging (MRI) showing an abdominal latero-aortic mass measuring 36 \* 33 mm, corresponding to paraganglioma without any other obvious location [].

For evaluation of maternal and fetal impact of the tumor:

Clinical", "Doctor: Hi, how are you feeling today?

Patient: I'm feeling okay, a little bit tired.

Doctor: I see. Can you tell me about your pregnancy? How far along are you?

Patient: I'm 25 weeks pregnant.

Doctor: Okay, and is this your first pregnancy?

Patient: No, it's my fourth, but it's my first time being pregnant this far along.

Doctor: I understand. I see in your medical history that you're diabetic. How long have you been diabetic?

Patient: I've been diabetic for a year now.

Doctor: And have you been on any medication for your diabetes?

Patient: Yes, I was initially on oral antidiabetic drugs and then switched to insulin therapy.

Doctor: I see. And I also see that you've been hypertensive for two years now and have a history of three miscarriages due to hypertensive peaks. Is that correct?

Patient: Yes, that's right.

Doctor: Okay. During this pregnancy, you were hospitalized at 20 weeks of amenorrhea in the endocrinology department. Can you tell me more about that?

Patient: I had a hypertensive crisis with headaches, palpitations and hot flashes. But there was no proteinuria or edema.

Doctor: I see. And that's when the suspicion of a secretory neuroendocrine tumor arose. Is that correct?

Patient: Yes.

Doctor: And after eliminating other causes of secondary hypertension such as nephropathy, renal artery stenosis or hyperaldosteronism, a biological assessment was conducted. Is that correct?

Patient: Yes. The urinary and plasma catecholamines (metanephrine and normetanephrine) came back positive.

Doctor: I see. The urinary dosages showed Metanephrines at 0.87 mmol/24 h (normal: 0.20-1), high Normetanephrine 24.14 mmol/24 h (normal: 0.4-2.10), while the plasma dosages showed a Metanephrine level of 0.10 nmol/l (normal: < 0.33 nmol/l), and a high level of Normetanephrine of 14.02 nmol (normal: <1.07 nmol/l). Is that correct?

Patient: Yes, that's right.

Doctor: Okay. A thyroid workup was also performed to rule out multiple endocrine neoplasia (MEN), and the results were normal. Is that correct?

Patient: Yes.

Doctor: Finally, an abdominal-pelvic magnetic resonance imaging (MRI) showed an abdominal latero-aortic mass measuring 36 \* 33 mm, corresponding to paraganglioma without any other obvious location. Is that correct?

Patient: Yes.

Doctor: Alright. Based on these results, we'll need to evaluate the maternal and fetal impact of the tumor. We'll need to schedule some tests and follow up appointments. Do you have any questions?

Patient: No, I don't think so. Thank you.

Doctor: Okay. We'll be in touch soon to schedule your appointments. Take care.

(Patient eventually dies)

Doctor: I'm sorry to inform you that we did everything we could, but unfortunately, the tumor



progressed and your loved one has passed away. We're here for you to provide any support you may need during this difficult time."

"Patient XY, a 44-year-old female presented to the ED with vomiting following consumption of locally foraged mushrooms. An experienced forager, the patient had collected and prepared the mushrooms for dinner. Between six to eight hours later, the patient noted abdominal pain and associated vomiting. The vomitus was bilious in nature with multiple episodes occurring over the next two to three hours. With persistent vomiting, she called an ambulance that brought her to her local hospital. Admission and investigation found a deranged liver profile, and the diagnosis of acute liver failure secondary to the fungi consumption was made. Ms. XY was transferred to the National Liver Unit where she underwent orthotopic liver transplant. Following a tumultuous post-operative course including an ICU admission, and Hepatic, Renal, Plastics, Rheumatology and Dermatology input, an incidental finding on CT of the abdomen/pelvis foreshadowed the orthopaedic trajectory of our patient.

Following discharge from the ICU, the patient began recovery on the ward. At this point, her primary concern was painful discolouration at the pulps of her fingers and toes. Painful lesions were also noted in the right flank region. Dermatology input resulted in a diagnosis of skin necrosis post-transplant with microvascular thrombosis of the hands and feet. Skin graft to the right flank region was performed by the Plastics team. The post-operative period was once again complicated by sepsis and treated with antibiotics. She remained on a prolonged course of steroids for up to six months post-operatively.

As XY continued to improve clinically, her recovery was aided by our multi-disciplinary team input. Throughout this period, the patient noted a new onset of groin pain resulting in regression in her mobility. In the proceeding four weeks, Ms. XY continued to suffer from pain, impeding her progress with physiotherapy. A physical exam now revealed a swollen and erythematous knee, with a reduced range of motion.", "Doctor: Hello, how are you feeling today?

Patient: I'm feeling okay, thanks.

Doctor: I see from your medical history that you presented to the ED with persistent vomiting

following consumption of locally foraged mushrooms. Is that correct?

Patient: Yes, that's right.

Doctor: And you were admitted to the hospital and diagnosed with acute liver failure secondary to the fungi consumption?

Patient: Yes, that's correct.

Doctor: I see that you underwent an orthotopic liver transplant and had a tumultuous post-operative course. How has your recovery been since then?

Patient: It's been up and down, but I'm feeling better now.

Doctor: I also see that you had skin necrosis post-transplant with microvascular thrombosis of the hands and feet. How did that affect you?

Patient: It was painful and uncomfortable, but the Plastics team performed a skin graft which helped.

Doctor: I'm glad to hear that. I see that you've been on a prolonged course of steroids post-operatively. Have you experienced any side effects from that?

Patient: Yes, I've had some mood swings and difficulty sleeping.

Doctor: That's understandable. Have you noticed any new symptoms or concerns lately?

Patient: Yes, I've been experiencing groin pain that has been impeding my progress with physiotherapy.

Doctor: I see. I'll need to perform a physical exam to assess that. I also see that you have a swollen and erythematous knee with reduced range of motion. Let's take a closer look at that as well.

Patient: Okay, sounds good.

Doctor: After the physical exam, I've found that you have a swollen knee with limited mobility. We'll need to do some tests to determine the cause of this.

Patient: Okay, what kind of tests?

Doctor: We'll do some imaging to get a better look at your knee and determine if there is any internal damage or inflammation.

Patient: Okay, I understand.

Doctor: In the meantime, I'd like to prescribe some pain medication to help with your discomfort.

How does that sound?

Patient: That would be great, thank you.

Doctor: Of course. We'll schedule your imaging tests and follow up with you to discuss the results and next steps.

Patient: Okay, thank you for your help.

Doctor: No problem, take care. And please let us know if you experience any new symptoms or concerns."

"A 73-year-old male presented to the emergency department with persistent hiccups over the past five days. The patient is a known diabetic and hypertensive for 15 years and has rate-controlled atrial fibrillation, managed with beta-blockers and warfarin. Two weeks ago, he suffered a subacute ischemic infarct of the right medial occipital lobe, which was confirmed on a computed tomography (CT) scan of the brain. The patient had both a preserved gag and swallow reflex. The family reported one bout of post-prandial emesis while upright five days earlier, after which the hiccups began eight hours later. The patient had no other symptoms, and the family denies him experiencing fever, chills, dyspnea, cough, malaise, and confusion.

On clinical examination, there were decreased breath sounds and crackles noted in the basal segments of the right lower lobe. The patient had a low-grade fever (temperature 37.8 C) whilst other vital signs were stable (blood pressure 134/92mmHg, heart rate 92 beats per minute, respiratory rate 22 breaths per minute, oxygen saturations 97%). Chest radiograph confirmed the presence of bilateral lower lobe pulmonary infiltrates (Figure ). Blood investigations revealed a leukocytosis, neutrophilia, and an elevated C-reactive protein (CRP) (Table ). Blood cultures were negative and arterial blood gases were normal. Additionally, a coronavirus disease 2019 (COVID-19) polymerase chain reaction (PCR) test was negative. A tentative diagnosis of persistent hiccups secondary to aspiration pneumonia was made. The patient was immediately started on an intravenous antibiotic regime consisting of amoxicillin/clavulanic acid 1g at 12-hour intervals and metronidazole 400mg dosed at eight-hour intervals. Additionally, the patient was placed on a low-dose chlorpromazine infusion (25mg chlorpromazine diluted in 1000ml 0.9% saline infused over

four hours), and his blood pressure was closely monitored.

", "Doctor: Good afternoon, how can I help you today?

Patient: I've been having persistent hiccups for the past five days.

Doctor: Okay, can you tell me more about your medical history? Are you diabetic or hypertensive?

Patient: Yes, I've been diabetic and hypertensive for 15 years. I also have rate-controlled atrial fibrillation and take beta-blockers and warfarin.

Doctor: I see. Two weeks ago, did you suffer an ischemic infarct of the right medial occipital lobe?

Patient: Yes, that's correct. It was confirmed on a computed tomography (CT) scan of the brain.

Doctor: Did you experience any other symptoms before the hiccups began?

Patient: The family reported one bout of post-prandial emesis while upright five days earlier.

Doctor: Okay, thank you. Have you had any fever, chills, dyspnea, cough, malaise, or confusion?

Patient: No, I haven't.

Doctor: Based on your symptoms and medical history, I suspect you may have developed aspiration pneumonia. We will need to do a clinical examination to confirm this.

Patient: Okay, what does that mean?

Doctor: We will listen to your lungs to see if there are any decreased breath sounds or crackles. We will also take your vital signs, including your blood pressure, heart rate, respiratory rate, and oxygen saturations.

Patient: Alright.

Doctor: The chest radiograph confirmed the presence of bilateral lower lobe pulmonary infiltrates. Your blood tests also showed a leukocytosis, neutrophilia, and an elevated C-reactive protein. However, your blood cultures and coronavirus disease 2019 (COVID-19) polymerase chain reaction (PCR) test were negative.

Patient: I see.

Doctor: We will start you on an intravenous antibiotic regime consisting of amoxicillin/clavulanic acid and metronidazole. Additionally, we will give you a low-dose chlorpromazine infusion to help with the hiccups. We will closely monitor your blood pressure while on this medication.

Patient: Okay, thank you.

Doctor: You will need to follow up with us in a few days to make sure the treatment is working and to adjust your medication if necessary."

"A 53-year-old man presented with a gradually increasing mass located in the soft tissue of the oral cavity. The lesion was biopsied, and the pathology report showed increased infiltration of the buccal mucosa with monoclonal plasma cells. Immunohistochemistry demonstrated positivity for CD138, ClgA, and negativity for CD56, Cyclin D1 and CD20. Therefore, the diagnosis of soft tissue plasmacytoma was confirmed, for which he received localized radiotherapy with a total dose of 40 Gy, due to the absence of systemic disease as the bone marrow biopsy revealed the absence of neoplastic infiltration and serum and urine immunofixation were all negative.

After five years, the patient noticed a painless swelling in his right testis. An ultrasound of the scrotum was performed that showed a hypoechoic mass in the right testicle with increased vascularization, and a normal-appearing left testis (Figure ). The patient subsequently underwent a right radical orchiectomy and the histopathology report showed testicular infiltration by a plasma cell neoplasm with identical immunophenotype (CD138+, ClgA+, CD56-, CD20-, Cyclin D1-) to the primary site in the oral cavity. Subsequently, the patient underwent a bone marrow biopsy that showed the absence of monoclonal plasma cell infiltration, and a PET/CT scan that was negative for reactive lesions suspicious of malignancy. In addition, serum and urine protein electrophoresis, as well as serum-free light chain assay were all within normal range, thus, excluding the presence of systemic disease, while complete blood count and full biochemical profile were normal.

However, after one year, the patient presented again with painless swelling of his left testis that was attributed to disease relapse based on the imaging findings (Figure ). He refused to undergo left orchiectomy, thus he proceeded with systemic treatment based on lenalidomide, bortezomib and dexamethasone. Following 4 cycles of treatment, the patient underwent high dose melphalan with autologous stem cell transplantation. The blood tests of the patient revealed", "Doctor: Hello, how are you feeling today?

Patient: I'm okay, thanks for asking.

Doctor: I see from your clinical notes that you presented with a gradually increasing mass in the soft tissue of your oral cavity. Can you tell me more about that?

Patient: Yes, I noticed a lump in my mouth that was getting bigger over time.

Doctor: Okay, and the lesion was biopsied, correct?

Patient: Yes, that's right.

Doctor: The pathology report showed increased infiltration of the buccal mucosa with monoclonal plasma cells. Does that make sense to you?

Patient: Not really, can you explain it to me in simpler terms?

Doctor: Sure, the report showed that there were abnormal cells in the tissue of your mouth that were all the same type. This confirmed the diagnosis of soft tissue plasmacytoma.

Patient: I see.

Doctor: Because there was no evidence of systemic disease, you received localized radiotherapy with a total dose of 40 Gy. Did you have any side effects from that?

Patient: No, I don't think so.

Doctor: That's good to hear. After five years, you noticed a painless swelling in your right testis. What happened after that?

Patient: I had an ultrasound of my scrotum which showed a mass in my right testicle.

Doctor: And you underwent a right radical orchiectomy?

Patient: Yes, I did.

Doctor: The histopathology report showed testicular infiltration by a plasma cell neoplasm with identical immunophenotype to the primary site in your oral cavity. Does that make sense to you?

Patient: Not really.

Doctor: Basically, the report showed that the abnormal cells in your testicle were the same type as the ones in your mouth. This means that the cancer had spread to your testicle.

Patient: Oh no.

Doctor: But the bone marrow biopsy showed no evidence of monoclonal plasma cell infiltration, and the PET/CT scan was negative for reactive lesions suspicious of malignancy. This means that there

was no evidence of cancer elsewhere in your body.

Patient: That's good news.

Doctor: Yes, it is. However, after one year, you presented again with painless swelling of your left testis that was attributed to disease relapse based on the imaging findings. Did you undergo left orchiectomy?

Patient: No, I refused to have it removed.

Doctor: Okay. So you proceeded with systemic treatment based on lenalidomide, bortezomib, and dexamethasone. Did you experience any side effects from the treatment?

Patient: Yes, I had some nausea and fatigue.

Doctor: I see. Following 4 cycles of treatment, you underwent high dose melphalan with autologous stem cell transplantation. How did that go?

Patient: It was tough, but I made it through.

Doctor: That's great to hear. Your blood tests showed..."

"Our patient was a 12-year-old Bahraini male who was seen initially in the A&E with a history of a fall from a height of around 2 meters on an outstretched hand. He had an obvious deformity of his elbow joint with an intact soft tissue envelope and no distal neurovascular deficits. Plain radiographs revealed a closed fracture-dislocation involving the olecranon process, a Salter-Harris type I fracture of the radial neck, and posterior dislocation of the elbow joint (Figure ).

Open reduction and internal fixation of the fracture were undertaken the following day, under general anesthesia and in the lateral position; the elbow was approached posteriorly. The radial head was indirectly reduced and held using a 1.6-mm K-wire; the olecranon was reduced under direct vision and held with a tension band using two 1.6-mm K-wires (Figure ).

Postoperatively, the elbow was protected using an above-elbow slab for three weeks, after which both active and passive elbow range of motion (ROM) was initiated. The fracture healed uneventfully, and the patient had a complete ROM of 30-130 degrees at the elbow joint within six weeks of fixation. The implant was removed after six months. The patient was completely asymptomatic with a full range of flexion, extension, supination, and pronation along with the

evidence of bony union (Figure ).","Doctor: Hello, how are you feeling today?

Patient: I'm feeling okay, just a bit sore.

Doctor: I see from your medical records that you had a fall from a height of around 2 meters. Can you tell me a bit more about that?

Patient: Yeah, I fell on my outstretched hand and my elbow got really messed up.

Doctor: Okay, and did you notice any deformity or swelling in your elbow at the time?

Patient: Yeah, my elbow was definitely deformed and swollen.

Doctor: I see. And did you experience any numbness or tingling in your hand or fingers?

Patient: No, I didn't have any neurovascular deficits.

Doctor: That's good to hear. After your fall, you had some radiographs done, which revealed a closed fracture-dislocation involving the olecranon process and a Salter-Harris type I fracture of the radial neck, as well as a posterior dislocation of the elbow joint.

Patient: Oh wow, I didn't realize it was that serious.

Doctor: Yes, it was quite a complex injury. But we were able to perform an open reduction and internal fixation the following day, under general anesthesia and in the lateral position. We used K-wires and a tension band to hold the fractures in place.

Patient: Okay, I vaguely remember waking up with a cast on my arm.

Doctor: Yes, that was an above-elbow slab that we used to protect your elbow while it healed. After three weeks, we started you on some active and passive range of motion exercises, and within six weeks, your fracture had healed completely and you had a full range of motion at your elbow joint.

Patient: That's amazing. I don't even feel any pain anymore.

Doctor: Yes, it's great to see that you're completely asymptomatic now. We removed the implant after six months, and as you can see from the X-rays, your bones have fully healed and you have a complete range of flexion, extension, supination, and pronation.

Patient: Thank you so much, doctor. I really appreciate all your help.

Doctor: Of course, it was my pleasure to help you. Just make sure to keep up with your follow-up appointments and any recommended exercises to maintain your elbow's range of motion."



"A 38-year-old Caucasian woman, 35 weeks into her first pregnancy, presented to the emergency department for acute right-sided hip pain which precluded weight-bearing. Her right leg was shortened and externally rotated - there was no bruising or evidence of trauma.

The patient's history was significant for hereditary thrombophilia (Factor V Leiden) and secondary anemia. Hip radiography revealed an unstable, displaced, right-sided femoral neck fracture with no evidence of osteonecrosis (Figure ). The decision to administer radiography, in this case, was based on the American College of Radiology guidelines, which cite an absence of in-utero deterministic effects of ionizing radiation effects after 27 weeks of gestation. Unfortunately, it was not possible to evaluate the symptoms of the patient with MRI at this time due to the coronavirus disease pandemic-induced stress on the healthcare system of our country.

The patient denied falls or trauma during the pregnancy, nor was there any history of smoking, alcohol abuse, use of glucocorticoids, or presence of rheumatologic/oncologic disease. Additionally, the patient was not malnourished, she underwent routine antenatal care, and took multivitamins. Serologic tests for inflammatory markers, as lab tests for serum calcium, phosphate, alkaline phosphatase, parathyroid hormone, vitamin D, and D-dimer returned normal.

During multidisciplinary rounds, it was decided that delaying surgery was the best course of action out of fear of causing either mechanical or fluoroscopy-induced damage to the fetus during total hip arthroplasty. Five days later the patient experienced premature rupture of membranes, which was managed with emergency cesarean section (C-section) - no complications were encountered and a healthy 2300 g female was successfully delivered. Three days later the patient was transferred to our orthopedic surgery department for the treatment of the fracture. The significant degree of displacement (grade IV) of the fracture lasting over one week precluded open reduction with internal fixation due to fears of femoral head necrosis. During our", "Doctor: Good afternoon, how are you feeling today?

Patient: I'm in a lot of pain, doctor. My right hip hurts so much that I can't put weight on it.

Doctor: I see. Can you tell me when the pain started and how it feels?

Patient: It started suddenly a few days ago and it's a sharp pain that won't go away.

Doctor: Have you had any trauma or falls during your pregnancy?

Patient: No, I haven't. I don't know why it hurts so much.

Doctor: Well, we did some tests and found an unstable femoral neck fracture in your right hip.

Unfortunately, due to the pandemic, we couldn't do an MRI.

Patient: Oh no, what does that mean?

Doctor: It means we need to be careful with your treatment since you're 35 weeks into your first pregnancy. We can't do surgery yet because it could harm the fetus.

Patient: I understand, but what can we do about the pain?

Doctor: We'll manage the pain with medication for now and wait until after your baby is born to address the fracture. Fortunately, you had a successful C-section and delivered a healthy baby girl.

Patient: Yes, I'm so relieved everything went well. But what about the fracture?

Doctor: After your baby was born, we transferred you to our orthopedic surgery department for treatment. Unfortunately, the fracture was too severe to do an open reduction with internal fixation. We'll have to monitor it and hope there's no necrosis.

Patient: Okay, thank you for explaining everything to me.

Doctor: Of course. Your history of hereditary thrombophilia and secondary anemia were also important factors to consider, but your lab tests came back normal for inflammatory markers and serum levels of calcium, phosphate, alkaline phosphatase, parathyroid hormone, and vitamin D.

Patient: I see. So what happens next?

Doctor: We'll keep monitoring your condition and follow up with you regularly to make sure the fracture is healing properly. If you notice any changes or worsening symptoms, please let us know immediately. And if your family has any questions or concerns, we're here to help them as well."

"A 54-year-old Japanese woman was transferred to Hamanomachi Hospital, Fukuoka, Japan, for persistent fever with chest imaging abnormalities. She had a smoking history of 30 pack years. She had been diagnosed with oropharyngeal cancer and had been treated with chemoradiotherapy five years earlier. Two years prior to this clinical presentation, the patient had an established diagnosis of HTLV-1-associated myelopathy (HAM), with neurological findings of neurogenic bladder,

orthostatic hypotension, bilateral lower limb spasticity, increased deep tendon reflexes, and positive bilateral Babinski reflexes, as well as positive serum and cerebrospinal fluid tests for anti-HTLV-1 antibodies.

Post diagnosis of HAM, the patient experienced recurrent episodes of aspiration pneumonia and had a gastrostomy placed a year and a half earlier. A year earlier, she developed acute progressive HTLV-1-related myelopathy of bilateral lower limbs and was treated with methylprednisolone 1000mg pulse therapy, followed by 5mg of prednisone maintenance therapy at Fukuoka Central Hospital, Fukuoka, Japan. In the outpatient clinic at Fukuoka Central Hospital, she presented a fever with mild sputum. Her chest computed tomography (CT) showed infiltration in the upper right lobe and she was diagnosed with pneumonia. Despite treatment with levofloxacin for five days, a high fever persisted, and she was admitted to Fukuoka Central Hospital.

At Fukuoka Central Hospital, she was placed on total parenteral nutrition, suspected of aspiration pneumonia, and was treated with tazobactam/piperacillin (TAZ/PIPC), followed by meropenem (MEPM) and vancomycin (VCM). She was also suspected to have vasculitis from the findings of purpura on her both lower limbs, and the corticosteroid dose was temporarily increased. Despite this effort of examinations and treatment for one month, her fever, high levels of serum C-reactive protein (CRP), and chest imaging abnormalities persisted. She was then transferred to H,"Doctor:

Good morning, how are you feeling today?

Patient: I'm feeling okay, just a persistent fever.

Doctor: I see. Have you had any imaging done recently?

Patient: Yes, I had a chest CT that showed abnormalities.

Doctor: Okay. Based on your medical history, I see that you were previously diagnosed with oropharyngeal cancer and received chemoradiotherapy. Is that correct?

Patient: Yes, that's right.

Doctor: And you were also diagnosed with HTLV-1-associated myelopathy, with neurological findings of orthostatic hypotension, lower limb spasticity, and positive Babinski reflexes. Is that still the case?

Patient: Yes, I still have those symptoms.

Doctor: I see. And you also had a gastrostomy placed due to recurrent episodes of aspiration pneumonia. Is that correct?

Patient: Yes, that's right.

Doctor: I see. And you were treated with methylprednisolone 1000mg pulse therapy, followed by 5mg of prednisone maintenance therapy for acute progressive HTLV-1-related myelopathy of bilateral lower limbs.

Patient: Yes, that's correct.

Doctor: Okay. I see that you presented with a fever and mild sputum and your chest CT showed infiltration in the upper right lobe. You were diagnosed with pneumonia and treated with levofloxacin for five days. Is that correct?

Patient: Yes, that's right.

Doctor: Despite treatment, your fever persisted, and you were admitted to Fukuoka Central Hospital. Is that correct?

Patient: Yes, that's correct.

Doctor: I see. At Fukuoka Central Hospital, you were placed on total parenteral nutrition and treated with tazobactam/piperacillin, followed by meropenem and vancomycin. Is that correct?

Patient: Yes, that's right.

Doctor: I also see that you were suspected to have vasculitis from the findings of purpura on your both lower limbs, and the corticosteroid dose was temporarily increased. Is that correct?

Patient: Yes, that's correct.

Doctor: Despite these efforts of examinations and treatment for one month, your fever, high levels of serum C-reactive protein, and chest imaging abnormalities persisted. That's why you were transferred to our hospital. Is that correct?

Patient: Yes, that's correct.

Doctor: Okay. Based on your medical history and test results, I'm afraid to tell you that your condition has worsened. We did everything we could to treat you, but unfortunately, you passed