

Specialist Annotation	LLM Output for Evaluation
Case 1	
<p>'Vitals_Hema': ['Vital signs Pulse rate, 83 beats per minute; blood pressure, 100/70 mmHg; respiratory rate, 13 breaths per minute; and temperature, 37 Â° C Anthropometric parameters Weight, 47.1 kg; height, 160 cm; MUAC, 19.3; BMI, 18.4; height / age, -1.7 SD; BMI / age, -0.9 SD'],</p> <p>'Neuro': ['speaking difficulties', 'speaking difficulties', 'delayed walking until the age of 2 years', 'brain magnetic resonance imaging was normal'],</p> <p>'EENT': ['hearing loss, speaking difficulties', 'corneal arcus', 'hearing loss and speaking difficulties', 'ears are of abnormal shape and size. Eyes Bilateral corneal arcus; moderate exophthalmos; asymmetrical corneal light reflex. Ophthalmoscopic examination showed bilateral swelling of the optic disc. Visual acuity is normal. Hearing assessment Severe hearing loss', 'pure tone audiometry found bilateral profound mixed hearing loss'],</p> <p>'CVS': ['nonpitting edema of the ankles'],</p> <p>'RESP': [],</p> <p>'GI': ['Mild hepatosplenomegaly', 'mild hepatosplenomegaly'],</p> <p>'GU': ['hypospadias'],</p>	<p>'Vitals_Hema': { ['temperature: 37°C', 'pulse: 83 beats per minute', 'respiratory rate: 13 breaths per minute', 'blood_pressure: 100/70 mmHg', 'hematological_conditions: Mild microcytic anemia']},</p> <p>'Neuro': { ['neurological: Moderate exophthalmos', 'neurological: Asymmetrical corneal light reflex', 'neurological: Bilateral swelling of the optic disc']},</p> <p>'EENT': { ['eyes: Bilateral corneal arcus; moderate exophthalmos; asymmetrical corneal light reflex. Ophthalmoscopic examination showed bilateral swelling of the optic disc.', 'ears: Severe hearing loss']},</p> <p>'CVS': { ['cardiac: Normal heart', 'vascular: Large hyperpigmented patches overlying with hypertrichosis involving the medial aspects of the thighs and extending to the posterior aspects of the legs', 'vascular: Dorsa of the feet are also involved with well-demarcated, large, hyperpigmented patches']},</p> <p>'RESP': { ['respiratory: Respiratory rate, 13 breaths per minute']},</p> <p>'GI': { []},</p> <p>'GU': { ['genital: Hypospadias']},</p> <p>'MSK': { ['skeletal: Bilateral hallux valgus deformity, with fixed flexion contractures, in the interphalangeal joints of the toes and the little fingers', 'skeletal: Nonpitting edema of the ankles']},</p>

<p>'hypospadias', 'Hypospadias; pubic hair presents in normal distribution; scrotal examination is normal'],</p> <p>'MSK': ['finger and toe deformities (hallux valgus)', 'Bilateral hallux valgus deformity, with fixed flexion contractures, in the interphalangeal joints of the toes and the little fingers', 'Hallux valgus deformity, with flexion contractures of the toes and little fingers'],</p> <p>'DERM': ['hyperpigmented patches symmetrically overlying with hypertrichosis involving the inner aspects of his thighs. These lesions progressed slowly over 6 years, starting first as hypertrichosis and then with indurated hyperpigmented patches gradually developing', 'premature graying of the hair', 'Large hyperpigmented indurated patches overlying with hypertrichosis, symmetrically involving the medial aspects of the thighs and extending to the posterior aspects of the legs. The dorsa of the feet are also involved with well - demarcated, large, hyperpigmented patches. However, the pigmented patches spare the buttocks and knees (see Fig 1). There are both hypo- and hyperpigmented lesions on the face, neck, and upper chest. Hair Shows salt - and - pepper gray hair', 'face looks flat; ears are of abnormal shape and size', 'Bilateral gynecomastia', 'Large, hyperpigmented patches overlying symmetrically with hypertrichosis involving the inner aspect of the thighs, both calves, and the dorsa of the feet, while sparing the knees', 'salt - and - pepper gray hair',</p>	<p>DERM': { ['skin_conditions: Large hyperpigmented indurated patches overlying with hypertrichosis, symmetrically involving the medial aspects of the thighs and extending to the posterior aspects of the legs.', 'skin_conditions: Well-demarcated, large, hyperpigmented patches on the dorsa of the feet.', 'facial_features: Hypo- and hyperpigmented lesions on the face, neck, and upper chest.', 'breast_conditions: Bilateral gynecomastia']},</p> <p>'Lab_Image': { ['Lab_Image: Erythrocyte sedimentation rate: 93 mm/h', 'Lab_Image: Serum cortisol: 1030 nmol/L', 'Lab_Image: Serum testosterone level: 2.63 ng/mL', 'Lab_Image: Hemoglobin: (no specific value mentioned)', 'Lab_Image: WBC count: (no specific value mentioned)', 'Lab_Image: Platelet count: (no specific value mentioned)', 'Lab_Image: Ophthalmoscopic examination: Bilateral swelling of the optic disc', 'Lab_Image: Visual acuity is normal', 'Lab_Image: Hearing assessment: Severe hearing loss', 'Lab_Image: Pure tone audiometry: Bilateral profound mixed hearing loss', 'Lab_Image: Echocardiography was normal', 'Lab_Image: Electrocardiogram was normal', 'Lab_Image: Skin biopsy: Widespread fibrosis and thickened collagen bundles in the papillary and mid dermis; striking infiltrates of CD68 + histiocytes.']],</p> <p>'LYMPH': { ['lymph_nodes: Severely enlarged inguinal lymph nodes, with tenderness on palpation', 'spleen: Mild hepatosplenomegaly']},</p> <p>'History': { ['history_of_present_illness: Gradual onset of hyperpigmented patches symmetrically overlying with hypertrichosis involving the inner aspects of his thighs, starting at age 10', 'family_and_genetics_history: Born of first-cousin parents', 'family_and_genetics_history: Older brother has bilateral swelling of</p>
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<p>'Histopathology findings showed widespread fibrosis and thickened collagen bundles in the papillary and mid dermis and striking infiltrates of CD68 + histiocytes',</p> <p>'Immunohistochemistry stain shows diffuse infiltration of histiocytes'],</p> <p>'Lab_Image': ['elevated erythrocyte sedimentation rate of 93 (normal range, 0–15 mm / h), elevated serum cortisol of 1030 nmol / L (normal range at morning, 171 - 536 nmol / L), and decreased serum testosterone level of 2.63 ng / mL (normal range, 2.8 - 8 ng / mL). Complete blood count showed mild microcytic anemia. Thyroid function tests, liver function tests, renal function tests, serum electrolytes, vitamin B12, serum ferritin, serum iron, antinuclear antibodies, anti – double - stranded DNA, anti - cyclic citrullinated peptide, and lipid profile all were normal',</p> <p>'Echocardiography and electrocardiogram were normal, abdominal ultrasound scan found mild hepatosplenomegaly, brain magnetic resonance imaging was normal',</p> <p>'Histopathology findings showed widespread fibrosis and thickened collagen bundles in the papillary and mid dermis and striking infiltrates of CD68 + histiocytes',</p> <p>'Immunohistochemistry stain shows diffuse infiltration of histiocytes'],</p> <p>'LYMPH': ['Lymph nodes Severely enlarged inguinal lymph nodes, with tenderness on palpation'],</p> <p>'History': ["A 16 - year - old Iraqi boy, born of first - cousin parents, presented to our outpatient clinic at Al - Sadr Teaching Hospital with hyperpigmented patches symmetrically overlying with hypertrichosis involving the inner aspects of his thighs. These lesions</p>	<p>the feet and deformities of the toes']],</p> <p>'ENDO': { ['endocrine_glands: Elevated serum cortisol of 1030 nmol/L', 'endocrine_glands: Decreased serum testosterone level of 2.63 ng/mL']},</p> <p>'Pregnancy': { []}</p>
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<p>ns progressed slowly over 6 years, starting first as hypertrichosis and then with indurated hyperpigmented patches gradually developing. He also had hearing loss, speaking difficulties, premature graying of the hair, gynecomastia, corneal arcus, hypospadias, and finger and toe deformities (hallux valgus). These features started at age 10, except for the hypospadias, which was present since birth, and the hearing loss and speaking difficulties, which were diagnosed in early childhood. The mother stated that the child delayed walking until the age of 2 years, and she reported that he had a severe ear infection by the age of 6. The patient has 3 brothers and 2 sisters; his older brother has bilateral swelling of the feet and deformities of the toes, but the patient 's other siblings are all healthy"],</p> <p>'ENDO': ['gynecomastia', 'pubic hair presents in normal distribution', 'elevated serum cortisol of 1030 nmol / L (normal range at morning, 171 - 536 nmol / L), and decreased serum testosterone level of 2.63 ng / mL (normal range, 2.8 - 8 ng / mL)'],</p> <p>'Pregnancy': []}</p>	
<p>Original Text (PMCID: 6453830)</p> <p>'Case report': "A 16-year-old Iraqi boy, born of first-cousin parents, presented to our outpatient clinic at Al-Sadr Teaching Hospital with hyperpigmented patches symmetrically overlying with hypertrichosis involving the inner aspects of his thighs. These lesions progressed slowly over 6 years, starting first as hypertrichosis and then with indurated hyperpigmented patches gradually developing. He also had hearing loss, speaking difficulties, premature graying of the hair, gynecomastia, corneal arcus, hypospadias, and finger and toe deformities (hallux valgus). These features started at age 10, except for the hypospadias, which was present since birth, and the hearing loss and speaking difficulties, which were diagnosed in early childhood. The mother stated that the child delayed walking until the age of 2 years, and she reported that he had a severe ear infection by the age of 6. The patient has 3 brothers and 2 sisters; his older brother has bilateral swelling of the feet and deformities of the toes, but the patient's other siblings are all healthy. See T</p>	

Table I for clinical examination findings (Fig 1, Fig 2, Fig 3). Table I Findings on examination Examination Findings Vital signs Pulse rate, 83 beats per minute; blood pressure, 100/70 mmHg; respiratory rate, 13 breaths per minute; and temperature, 37°C Anthropometric parameters Weight, 47.1 kg; height, 160 cm; MUAC, 19.3; BMI, 18.4; height/age, -1.7 SD; BMI/age, -0.9 SD Skin Large hyperpigmented indurated patches overlying with hypertrichosis, symmetrically involving the medial aspects of the thighs and extending to the posterior aspects of the legs. The dorsa of the feet are also involved with well-demarcated, large, hyperpigmented patches. However, the pigmented patches spare the buttocks and knees (see Fig 1). There are both hypo- and hyperpigmented lesions on the face, neck, and upper chest. Hair Shows salt-and-pepper gray hair (see Fig 2) Head OFC, 51 cm (-2.8 SD, <1 st percentile); face looks flat; ears are of abnormal shape and size. Eyes Bilateral corneal arcus; moderate exophthalmos; asymmetrical corneal light reflex. Ophthalmoscopic examination showed bilateral swelling of the optic disc. Visual acuity is normal. Hearing assessment Severe hearing loss Breast Bilateral gynecomastia Heart Normal Abdomen Mild hepatosplenomegaly Lymph nodes Severely enlarged inguinal lymph nodes, with tenderness on palpation Genitourinary Hypospadias; pubic hair presents in normal distribution; scrotal examination is normal. Musculoskeletal Bilateral hallux valgus deformity, with fixed flexion contractures, in the interphalangeal joints of the toes and the little fingers (see Fig 3). There is also a nonpitting edema of the ankles. BMI, Body mass index; MUAC, mid-upper arm circumference; OFC, occipitofrontal circumference. Fig 1 Large, hyperpigmented patches overlying symmetrically with hypertrichosis involving the inner aspect of the thighs, both calves, and the dorsa of the feet, while sparing the knees. Fig 2 Posterior view of the patient's head shows salt-and-pepper gray hair. Fig 3 Hallux valgus deformity, with flexion contractures of the toes and little fingers. Laboratory test results showed elevated erythrocyte sedimentation rate of 93 (normal range, 0–15 mm/h), elevated serum cortisol of 1030 nmol/L (normal range at morning, 171-536 nmol/L), and decreased serum testosterone level of 2.63 ng/mL (normal range, 2.8-8 ng/mL). Complete blood count showed mild microcytic anemia. Thyroid function tests, liver function tests, renal function tests, serum electrolytes, vitamin B12, serum ferritin, serum iron, antinuclear antibodies, anti-double-stranded DNA, anti-cyclic citrullinated peptide, and lipid profile all were normal. Echocardiography and electrocardiogram were normal, abdominal ultrasound scan found mild hepatosplenomegaly, brain magnetic resonance imaging was normal, and pure tone audiometry found bilateral profound mixed hearing loss. Histopathology findings showed widespread fibrosis and thickened collagen bundles in the papillary and mid dermis and striking infiltrates of CD68 + histiocytes (see Fig 4). The biopsy was taken from the hyperpigmented patch on the medial aspect of the right thigh. Fig 4 Immunohistochemistry stain shows diffuse infiltration of histiocytes. (CD68 + ; original magnification: ×400.)"

<p>Case 2</p> <p>'Vitals_Hema': ['microcytic anemia with hemoglobin levels of 10.1 g / dl, and a platelet count of 5.14 lakhs / cu.mm'],</p> <p>'Neuro': ['her other developmental milestones were normal', 'bilateral sensorineural hearing loss'],</p> <p>'EENT': ['bilateral hearing loss was present since 5 years of age', 'proptosis,', 'Auditory evaluation revealed bilateral sensorineural hearing loss'],</p> <p>'CVS': ['swelling of legs'],</p> <p>'RESP': [],</p> <p>'GI': ['hepatomegaly', 'hepatomegaly'],</p> <p>'GU': ['menarche at 11 years of age and has had regular menstrual cycles', 'normal genitalia'],</p> <p>'MSK': ['low height for age', 'Skeletal examination was normal'],</p> <p>'DERM': ['hyperpigmentation over the thighs', 'skin thickening over the buttocks, thighs, and legs', 'proptosis, webbing of neck', 'well - defined, bilaterally symmetrical hyperpigmented, indurated plaques with hypertrichosis were present over medial and lateral aspect of thighs and legs sparing knees and feet. Similar lesions were present over the gluteal region bilaterally', 'Skin biopsy showed thickened collagen bundles with lymphocytic and histiocytic infiltrates in the dermis extending to the subcutaneous tissue with few areas of fibrosis. Immunohistochemistry studies showed CD68 positivity in dermal perivascular histiocytic infiltrate'],</p> <p>'Lab_Image': ['ESR - 75, CRP - 81, microcytic anemia with hemoglobin levels of 10.1 g / dl, and a platelet count of 5.14 lakhs / cu.mm. Serum protein electrophoresis showed increased gamma fraction of 29.8 suggestive of polyclonal gammopathy. Investigations for the cause of fever revealed</p>	<p>'Vitals_Hema': { ['microcytic anemia']},</p> <p>'Neuro': { ['Bilateral sensorineural hearing loss']},</p> <p>'EENT': { ['proptosis', 'bilateral sensorineural hearing loss']},</p> <p>'CVS': { ['Anomalous drainage of left pulmonary vein to innominate vein']},</p> <p>'RESP': { []},</p> <p>'GI': { []},</p> <p>'GU': { ['Normal genitalia']},</p> <p>'MSK': { ['Skeletal examination was normal']},</p> <p>'DERM': { ['Well-defined, bilaterally symmetrical hyperpigmented, indurated plaques with hypertrichosis were present over medial and lateral aspect of thighs and legs sparing knees and feet. Similar lesions were present over the gluteal region bilaterally.', 'Normal genitalia']},</p> <p>'Lab_Image': { ['Hemoglobin: 10.1 g/dl', 'Platelet count: 5.14 lakhs/cu.mm', 'Echocardiography revealed anomalous drainage of left pulmonary vein to innominate vein', 'Chest radiography: Normal', 'Echocardiography: Anomalous drainage of left pulmonary vein to innominate vein']},</p>
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<p>no positive findings. Thyroid profile, fasting, and post - prandial blood sugar levels were normal. Anti - nuclear antibodies ' titer was negative',</p> <p>'Skin biopsy showed thickened collagen bundles with lymphocytic and histiocytic infiltrates in the dermis extending to the subcutaneous tissue with few areas of fibrosis. Immunohistochemistry studies showed CD68 positivity in dermal perivascular histiocytic infiltrate',</p> <p>'An ultrasound abdomen revealed hepatomegaly. Chest radiography was normal, and an echocardiography revealed anomalous drainage of left pulmonary vein to innominate vein'],</p> <p>'LYMPH': ['webbing of neck'],</p> <p>'History': ['A 12 - year - old girl, first born of second degree consanguineous marriage presented with a history of hyperpigmentation over the thighs from birth. History of skin thickening over the buttocks, thighs, and legs was present for past 3 months. There was also a history of recurrent fever associated with swelling of legs. History of bilateral hearing loss was present since 5 years of age, and her other developmental milestones were normal. She had attained her menarche at 11 years of age and has had regular menstrual cycles. There was no history of a similar illness in the family'],</p> <p>'ENDO': ['Thyroid profile, fasting, and post - prandial blood sugar levels were normal'],</p> <p>'Pregnancy': []}</p>	<p>'Skin biopsy: Thickened collagen bundles with lymphocytic and histiocytic infiltrates in the dermis extending to the subcutaneous tissue with few areas of fibrosis.',</p> <p>'Immunohistochemistry studies showed CD68 positivity in dermal perivascular histiocytic infiltrate.',</p> <p>'Thyroid profile: Normal',</p> <p>'Fasting and post-prandial blood sugar levels: Normal']},</p> <p>'LYMPH': { ['Skin biopsy showed thickened collagen bundles with lymphocytic and histiocytic infiltrates in the dermis extending to the subcutaneous tissue with few areas of fibrosis.',</p> <p>'Hepatomegaly detected',</p> <p>'Immunohistochemistry studies showed CD68 positivity in dermal perivascular histiocytic infiltrate.'],</p> <p>'History': { ['History of skin thickening over the buttocks, thighs, and legs was present for past 3 months.',</p> <p>'Recurrent fever associated with swelling of legs.',</p> <p>'First born of second degree consanguineous marriage',</p> <p>'No history of a similar illness in the family']},</p> <p>'ENDO': { []},</p> <p>'Pregnancy': { []}}</p>
<p>Original Text (PMCID: 6536078)</p> <p>Case History: 'A 12-year-old girl, first born of second degree consanguineous marriage presented with a history of hyperpigmentation over the thighs from birth. History of skin thickening over the buttocks, thighs, and legs was present for past 3 months. There was also a history of recurrent fever associated with swelling of legs. History of bilateral hearing loss was present since 5 years of age, and her other developmental milestones were normal. She had attained her menarche at 11 years of age and has had regular menstrual cycles. There was no history of a similar illness in the family. Her general physical examination showed low height for age, propt</p>	

osis, webbing of neck, hepatomegaly, and normal genitalia. Skeletal examination was normal. Auditory evaluation revealed bilateral sensorineural hearing loss. On mucocutaneous examination well-defined, bilaterally symmetrical hyperpigmented, indurated plaques with hypertrichosis were present over medial and lateral aspect of thighs and legs sparing knees and feet. Similar lesions were present over the gluteal region bilaterally. Routine laboratory investigations revealed ESR - 75, CRP - 81, microcytic anemia with hemoglobin levels of 10.1 g/dl, and a platelet count of 5.14 lakhs/cu.mm. Serum protein electrophoresis showed increased gamma fraction of 29.8 suggestive of polyclonal gammopathy. Investigations for the cause of fever revealed no positive findings. Thyroid profile, fasting, and post-prandial blood sugar levels were normal. Anti-nuclear antibodies' titer was negative. Skin biopsy showed thickened collagen bundles with lymphocytic and histiocytic infiltrates in the dermis extending to the subcutaneous tissue with few areas of fibrosis. Immunohistochemistry studies showed CD68 positivity in dermal perivascular histiocytic infiltrate. An ultrasound abdomen revealed hepatomegaly. Chest radiography was normal, and an echocardiography revealed anomalous drainage of left pulmonary vein to innominate vein. In view of the constellation of findings summarized in Table 1, we made the diagnosis of H syndrome.'

<p>Case 3:</p> <p>'Vitals_Hema': ['Her height was 110 cm (10 - 25th percentile), weight 23 kg (75 - 90th percentile).', "Her body weight, length and head circumference were 2900, 51 cm and 33.5 cm, all of them were beneath the 5 th percentiles. Her blood pressure was 60/40 mmHg, respiratory rate was 39 / min, pulse rate was 112 / min and body temperature was 37.1 Â° C. "],</p> <p>'Neuro': ['lethargy', 'lethargic', 'lethargic', 'depressed fontanele'],</p> <p>'EENT': ['mild hyperpigmentation, including oral cavity.'],</p> <p>'CVS': ['high blood pressure', 'mild dehydration and decreased skin turgor.'],</p> <p>'RESP': [],</p> <p>'GI': ['poor weight gain', 'without history of vomiting or diarrhea'],</p> <p>'GU': ['small hypoplastic uterus (6 * 7 * 3 ml) or atretic ovaries', 'hyponatremia, hyperkalemia', 'testicles in the abdominal cavity and uterus was not detected in pelvis', 'External genitalia seemed normal female type with no ambiguity'],</p> <p>'MSK': [],</p> <p>'DERM': ['no hyperpigmentation', 'decreased skin turgor.', 'mild hyperpigmentation, including oral cavity.'],</p> <p>'Lab_Image': ['Ultrasonographic examination revealed small hypoplastic uterus (6 * 7 * 3 ml) or atretic ovaries and adrenal glands had normal sizes', 'normal laboratory results except for 17 OHP which was lower during the period', 'Renal Doppler ultrasonography and scan was performed which was normal', 'Ultrasonography revealed the testicles in the abdominal cavity and uterus was not detected in pelvis', 'Chromosome study showed 46XY pattern', 'Na : 142 mmol / l, K : 4.5 mmol / l, 17OHP : 0.1 ng / ml, ACTH : 22 pg / ml, Renin:50.8 pg / ml, Aldosterone : 105 pg / ml'],</p>	<p>'Vitals_Hema': { ['temperature: 37.1°C', 'pulse: 112/min', 'respiratory_rate: 39/min', 'blood_pressure: 60/40 mmHg']},</p> <p>'Neuro': { []},</p> <p>'EENT': { []},</p> <p>'CVS': { ['vascular: High blood pressure', 'cardiac: Pulse rate was 112/min']},</p> <p>'RESP': { ['respiratory: Respiratory rate was 39/min']},</p> <p>'GI': { []},</p> <p>'GU': { ['genital: Ultrasonography revealed testicles in the abdominal cavity', 'genital: Uterus was not detected in pelvis', 'genital: External genitalia seemed normal female type with no ambiguity']},</p> <p>'MSK': { []},</p> <p>'DERM': { ['skin_conditions: Mild hyperpigmentation, including oral cavity']},</p> <p>'Lab_Image': { ['Lab_Image: Na: 142 mmol/l', 'Lab_Image: K: 4.5 mmol/l', 'Lab_Image: 17OHP: 0.1 ng/ml', 'Lab_Image: ACTH: 22 pg/ml', 'Lab_Image: Renin:50.8 pg/ml', 'Lab_Image: Aldosterone: 105 pg/ml', 'Lab_Image: At the time of admission, she was lethargic without history of vomiting or diarrhea.', 'Lab_Image: Renal Doppler ultrasonography: Normal', 'Lab_Image: 17 OHP: 0.1 ng/ml']}</p>
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<p>'LYMPH': [],</p> <p>'History': ['Orchiectomy', 'A 28 - day - old phenotypic female infant was admitted to pediatric endocrinology clinic of Al - Zahra Hospital, affiliated to Isfahan University of Medical Sciences, because of poor weight gain and lethargy. She was a full - term infant with a birth weight of 3250 gr (50 th percentile), length of 51 cm (50 th percentile) and head circumference of 34 cm (50 th percentile).The patient had no perinatal problem. She was the 1 st child of non consanguineous parents. At the time of admission, she was lethargic without history of vomiting or diarrhea. There was not any familial history of similar presentation or features endocrine disease. She had no history of drug consumption except vitamin A+D.'],</p> <p>'ENDO': ['adrenal glands had normal sizes', 'decreased cortisol level and increased ACTH level', 'adrenal insufficiency'],</p> <p>'Pregnancy': ['full - term infant with a birth weight of 3250 gr (50 th percentile), length of 51 cm (50 th percentile) and head circumference of 34 cm (50 th percentile).The patient had no perinatal problem.']]</p>	<p>', 'Lab_Image: ACTH: 22 pg/ml', 'Lab_Image: Renin:50.8 pg/ml', 'Lab_Image: Aldosterone: 105 pg/ml']}, 'LYMPH': { ['bone_marrow: Bone marrow study showed 46XY pattern', 'immune_cells: Mild dehydration and decreased skin turgor']}, 'History': { ['past_medical_history: Hyponatremia', 'past_medical_history: Hyperkalemia', 'past_medical_history: Metabolic acidosis', 'past_medical_history: Decreased cortisol level', 'past_medical_history: Increased ACTH level', 'past_surgical_history: Orchiectomy at age 6 years', 'family_and_genetics_history: Father had colon cancer', 'family_and_genetics_history: Sister diagnosed with breast cancer at age 50', 'history_of_present_illness: Poor weight gain and lethargy', 'family_and_genetics_history: No familial history of similar presentation or features endocrine disease', 'chief_complaint: Poor weight gain and lethargy']},</p> <p>'ENDO': { ['endocrine_glands: Adrenal insufficiency observed', 'endocrine_glands: Decreased cortisol level', 'endocrine_glands: Increased ACTH level']},</p> <p>'Pregnancy': { ['maternal_health: Hyponatremia', 'maternal_health: Hyperkalemia', 'maternal_health: Metabolic acidosis', 'maternal_health: Decreased cortisol level', 'neonatal_health: Poor weight gain observed', 'neonatal_health: Lethargy without history of vomiting or diarrhea', 'neonatal_health: Depressed fontanelle observed', 'neonatal_health: Mild dehydration and decreased skin turgor', 'maternal_health: Mild dehydration diagnosed', 'maternal_health: Decreased skin turgor']</p>
Original Text (PMCID 3415193)	

'Radiological findings': 'Ultrasonographic examination revealed small hypoplastic uterus (6*7*3 ml) or atretic ovaries and adrenal glands had normal sizes. Clinical Course and Follow-up First, the patient hydrated with normal saline. Thereafter, considering hyponatremia, hyperkalemia, metabolic acidosis and decreased cortisol level and increased ACTH level, lipoid CAH was diagnosed and replacement therapy with standard doses of glucocorticoid (hydrocortisone) and mineralocorticoid (fludrocortisone) and sodium chloride was initiated. After replacement therapy, electrolyte abnormalities were corrected during first week and the patient was discharged from hospital with good clinical condition. She recommended referring for follow up. During follow-up, she had good clinical condition, with normal laboratory results except for 17 OHP which was lower during the period. At 6-years old, the patient referred with high blood pressure and adrenal insufficiency because of arbitrary drug discontinuation by mother. Renal Doppler ultrasonography and scan was performed which was normal. Regarding the recommendation of pediatric nephrologist fludrocortisone and sodium chloride was discontinued and treatment continued with hydrocortisone. Ultrasonography revealed the testicles in the abdominal cavity and uterus was not detected in pelvis. Orchiectomy was performed. Chromosome study showed 46XY pattern. On her most recent visit at the age of 6 years, the patient had no hyperpigmentation. Her height was 110 cm (10-25th percentile), weight 23 kg (75-90th percentile). Her last laboratory tests results were as follows; Na: 142 mmol/l, K: 4.5 mmol/l, 17OHP: 0.1 ng/ml, ACTH: 22 pg/ml, Renin: 50.8 pg/ml, Aldosterone: 105 pg/ml.', 'CASE REPORT': 'A 28-day-old phenotypic female infant was admitted to pediatric endocrinology clinic of Al-Zahra Hospital, affiliated to Isfahan University of Medical Sciences, because of poor weight gain and lethargy. She was a full-term infant with a birth weight of 3250 gr (50th percentile), length of 51 cm (50th percentile) and head circumference of 34 cm (50th percentile). The patient had no perinatal problem. She was the 1st child of nonconsanguineous parents. At the time of admission, she was lethargic without history of vomiting or diarrhea. There was not any familial history of similar presentation or features endocrine disease. She had no history of drug consumption except vitamin A+D.', 'Physical examination': 'She was lethargic, had depressed fontanelle. She had mild dehydration and decreased skin turgor. In skin examination, she had mild hyperpigmentation, including oral cavity. External genitalia seemed normal female type with no ambiguity. There was not any abdominal or inguinal mass in abdominal examination. Her body weight, length and head circumference were 2900, 51 cm and 33.5 cm, all of them were beneath the 5th percentiles. Her blood pressure was 60/40 mmHg, respiratory rate was 39/min, pulse rate was 112/min and body temperature was 37.1°C.'

<p>Case 4</p> <p>'Vitals_Hema': [],</p> <p>'Neuro': [],</p> <p>'EENT': ['The ophthalmologic examination was normal', 'The eye examination was normal'],</p> <p>'CVS': ['Echocardiography was unremarkable', 'hypertension', 'hypertension'],</p> <p>'RESP': ['chronic obstructive pulmonary disease', 'asthma'],</p> <p>'GI': ['inflammatory bowel syndrome'],</p> <p>'GU': [],</p> <p>'MSK': ['osteoarthritis', 'rheumatoid arthritis'],</p> <p>'DERM': ['asymptomatic eruption on the neck.', 'numerous soft, oval - to - round, tan papules, measured few millimeters in diameter, with a symmetric distribution around the neck area', 'A skin punch biopsy was performed, and the hematoxylin and eosin (H and E) sections revealed a normal - appearing epidermis. The dermis was also relatively normal. An elastin stain was performed and revealed the absence of elastic fibers in the papillary dermis. The reticular dermis showed irregular, variably thickened, and distorted elastic fibers. No associated calcification was encountered.', 'H and E section and elastin stain revealed increased elastic fibers in the mid and deep dermis, with no calcification being evident', 'asymptomatic cutaneous lesions', 'numerous tan to yellowish soft papules over the lateral side of the patient's neck, measuring 2–3 mm', 'slowly progressive itchy skin lesions after spraying perfumes', 'multiple symmetrically distributed, skin - colored to yellowish papules, around 2–3 mm, on the lateral and anterior sides of the patient's neck, upper chest, and the antecubital fossa of both forearms',</p>	<p>'Vitals_Hema': { []},</p> <p>'Neuro': { []},</p> <p>'EENT': { ['eyes: The ophthalmologic examination was normal.', 'eyes: The eye examination was normal.']}},</p> <p>'CVS': { ['vascular: Irregular, variably thickened, and distorted elastic fibers in the reticular dermis', 'vascular: Increased elastic fibers in the mid and deep dermis']}},</p> <p>'RESP': { ['respiratory: Chronic obstructive pulmonary disease (COPD)', 'respiratory: Asthma']}},</p> <p>'GI': { []},</p> <p>'GU': { []},</p> <p>'MSK': { ['skeletal: Osteoarthritis']}},</p> <p>'DERM': { ['skin_conditions: Numerous soft, oval-to-round, tan papules on the neck area', 'skin_conditions: Normal-appearing epidermis', 'skin_conditions: Absence of elastic fibers in papillary dermis', 'skin_conditions: Irregular, variably thickened, and distorted elastic fibers in reticular dermis', 'skin_conditions: Asymptomatic skin-colored to yellow papules coalescing into plaques on both sides of the neck']}},</p> <p>'Lab_Image': { ['Lab_Image: H and E section and elastin stain revealed increased elastic fibers in the mid and deep dermis, with n</p>
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<p>"gradual appearance of small skin - colored papules, measuring 2–3 mm, with a cobblestone appearance covering the patient's neck and the upper chest bilaterally.",</p> <p>'psoriasis',</p> <p>'asymptomatic skin - colored to yellow papules coalescing into plaques on both sides of the neck. No other body sites were involved.'],</p> <p>'Lab_Image': ['Echocardiography was unremarkable',</p> <p>'A skin punch biopsy was performed, and the hematoxylin and eosin (H and E) sections revealed a normal - appearing epidermis. The dermis was also relatively normal. An elastin stain was performed and revealed the absence of elastic fibers in the papillary dermis. The reticular dermis showed irregular, variably thickened, and distorted elastic fibers. No associated calcification was encountered',</p> <p>'H and E section and elastin stain revealed increased elastic fibers in the mid and deep dermis, with no calcification being evident'],</p> <p>'LYMPH': [],</p> <p>'History': ['A 62 - year - old female patient, a heavy smoker for 40 years and a known case of chronic obstructive pulmonary disease, visited the clinic with a 5 - year history of an asymptomatic eruption on the neck',</p> <p>'no family history of similar skin conditions was recorded, and no history of sun exposure preceded the eruption',</p> <p>'A 68 - year - old female with no significant medical history presented to the clinic with asymptomatic cutaneous lesions for around 16 years',</p> <p>'The patient had no systemic symptoms and was otherwise healthy',</p> <p>'A 61 - year - old female patient presented to the clinic with a 2 - year history of slowly progressive itchy skin lesions after spraying perfumes. Her medical history included diabetes mellitus Type 2, hypertension, asthma, and osteoarthritis',</p> <p>'There was no history of sun exposure or family history of similar cutaneous manifestation',</p> <p>"A 77 - year - old female presented with a 4 - year history of gradual appearance of small skin - colored papules, measuring 2–3 mm, with a cobblestone appearance covering the patient's neck and the upper chest bilaterally. Her medical history included rheumatoid arthritis, psoriasis, inflammatory bowel syndrome, and hypertension",</p>	<p>o calcification being evident.', 'Lab_Image: Echocardiography was unremarkable', 'Lab_Image: inflammatory bowel syndrome', 'Lab_Image: Skin punch biopsy: Normal-appearing epidermis', 'Lab_Image: Elastin stain: Absence of elastic fibers in papillary dermis', 'Lab_Image: Elastin stain: Irregular, variably thickened, and distorted elastic fibers in reticular dermis', 'Lab_Image: H and E section: Increased elastic fibers in mid and deep dermis', 'Lab_Image: Elastin stain: No calcification evident', 'Lab_Image: Ophthalmology consult: normal eye examination']},</p> <p>'LYMPH': { ['immune_cells: No relevant information available', "spleen: Soft papules over the lateral side of the patient's neck, measuring 2–3 mm", 'immune_cells: Multiple symmetrically distributed, skin-colored to yellowish papules']}, 'History': { ['past_medical_history: Chronic obstructive pulmonary disease', 'history_of_present_illness: 5-year history of an asymptomatic eruption on the neck', 'social_history: Heavy smoker for 40 years', 'history_of_present_illness: Asymptomatic cutaneous lesions for around 16 years', 'past_medical_history: Diabetes mellitus Type 2', 'past_medical_history: Hypertension', 'past_medical_history: Asthma', 'past_medical_history: Osteoarthritis', 'history_of_present_illness: 2-year history of slowly progressive itchy skin lesions after spraying perfumes', 'family_and_genetics_history: No family history of similar cutaneous manifestation', 'chief_complaint: Patient presented to the clinic with a 2-year history of slowly progressive itchy skin lesions', 'past_medical_history: Rheumatoid arthritis', 'past_medical_history: Psoriasis', 'past_medical_history: Inflammatory bowel syndrome', 'past_medical_history: Hypertension', 'history_of_present_illness: 4-year history of gradual appearance of small skin-colored papules, measuring 2–3 mm, with a cobblestone appearance covering the patient's neck and the upper chest b</p>
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<p>'A 71 - year - old female presented with a 1–2 - year history of asymptomatic skin - colored to yellow papules coalescing into plaques on both sides of the neck. No other body sites were involved. The patient was otherwise healthy, with no other systemic complaints'],</p> <p>'ENDO': ['diabetes mellitus Type 2,'],</p> <p>'Pregnancy': []]</p>	<p>ilaterally", 'family_and_genetics_history: Father had colon cancer', 'family_and_genetics_history: Sister diagnosed with breast cancer at age 50', 'history_of_present_illness: A 1-2 year history of asymptomatic skin-colored to yellow papules coalescing into plaques on both sides of the neck']},</p> <p>'ENDO': { []},</p> <p>'Pregnancy': { []}</p>
<p>Original Text (PMCID:6862365)- Case series</p> <p>'Case 5': 'A 62-year-old female patient, a heavy smoker for 40 years and a known case of chronic obstructive pulmonary disease, visited the clinic with a 5-year history of an asymptomatic eruption on the neck. Physical examination revealed numerous soft, oval-to-round, tan papules, measured few millimeters in diameter, with a symmetric distribution around the neck area. Echocardiography was unremarkable. The ophthalmologic examination was normal. Moreover, no family history of similar skin conditions was recorded, and no history of sun exposure preceded the eruption.', 'Histopathology of cases (1–3)': 'A skin punch biopsy was performed, and the hematoxylin and eosin (H and E) sections revealed a normal-appearing epidermis. The dermis was also relatively normal. An elastin stain was performed and revealed the absence of elastic fibers in the papillary dermis. The reticular dermis showed irregular, variably thickened, and distorted elastic fibers. No associated calcification was encountered.', 'Histopathology of case 4 and 5': 'H and E section and elastin stain revealed increased elastic fibers in the mid and deep dermis, with no calcification being evident.', 'Case 3': "A 68-year-old female with no significant medical history presented to the clinic with asymptomatic cutaneous lesions for around 16 years. Physical examination revealed numerous tan to yellowish soft papules over the lateral side of the patient's neck, measuring 2–3 mm. The patient had no systemic symptoms and was otherwise healthy.", 'Case 4': "A 61-year-old female patient presented to the clinic with a 2-year history of slowly progressive itchy skin lesions after spraying perfumes. Her medical history included diabetes mellitus Type 2, hypertension, asthma, and osteoarthritis. On physical examination, there were multiple symmetrically distributed, skin-colored to yellowish papules, around 2–3 mm, on the lateral and anterior sides of the patient's neck, upper chest, and the antecubital fossa of both forearms. There was no history of sun exposure or family history of similar cutaneous manifestation.", 'Case 2': "A 77-year-old female presented with a 4-year history of gradual appearance of small skin-colored papules, measuring 2–3 mm, with a cobblestone appearance covering the patient's neck and the upper chest bilaterally. Her medical history included rheumatoid arthritis, psoriasis, inflammatory bowel syndrome, and hypertension. However, other systemic examinations were unremarkable, especially</p>	

ally for eye, cardiac, or gastrointestinal systems.", 'Case 1': 'A 71-year-old female presented with a 1–2-year history of asymptomatic skin-colored to yellow papules coalescing into plaques on both sides of the neck. No other body sites were involved. The patient was otherwise healthy, with no other systemic complaints. Given the clinical resemblance to PXE, an ophthalmology consult was performed to rule out the presence of angioid streaks. The eye examination was normal.

Case 5

'Vitals_Hema': ['His heart rate was 120 beats per minute and his blood pressure was 100/65 mmHg. His weight and height were 12.8 kg (1.5 SDS) and 86 cm (2 SDS), respectively', 'his body weight and length were 16.7 kg (0.5 SDS) and 99.7 cm (1.5 SDS), respectively'],

'Neuro': ['He was able to ascend stairs with the support of a hand grasp. He could stack 3 cubes, eat without assistance, and pronounce 10 words, meaning that the patient's developmental status was normal for his age', 'normal growth and development'],

'EENT': [],

'CVS': ['A grade 2 systolic murmur was heard in the left upper sternal border and echocardiography revealed a patent ductus arteriosus', 'hypotensive'],

'RESP': [],

'GI': ['imperforate anus', 'tracheoesophageal fistula was not suspected clinically', 'anal atresia', 'abdomen was distended and discolored', 'bowel necrosis', 'peritonitis', 'peritonitis', 'occasional nausea and vomiting'],

'GU': ['normal male genitalia, with both testes palpable', 'Bilateral grade 3 vesicoureteral reflux (VUR) was revealed via voiding cystourethrography', 'renal anomalies', 'normal male genitalia'],

'Vitals_Hema': { ['pulse: 120 beats per minute', 'blood_pressure: 100/65 mmHg']},

'Neuro': { ['cognitive: Normal developmental status for age']},

'EENT': { ['missing_k']},

'CVS': { ['cardiac: Grade 2 systolic murmur was heard in the left upper sternal border', 'cardiac: Patent ductus arteriosus']},

'RESP': { []},

'GI': { []},

'GU': { ['urinary: Bilateral grade 3 vesicoureteral reflux (VUR) was revealed via voiding cystourethrography.', 'genital: Normal male genitalia, with both testes palpable']},

'MSK': { ['skeletal: postaxial polydactyly of the left foot']},

'DERM': { ["skin_conditions: slight bronzing of the patient's skin", 'skin_conditions: generalized hyperpigmentation']},

'Lab_Image': { ['Lab_Image: Echocardiography revealed a patent ductus arteriosus', 'Lab_Image: Voiding cystourethrography revealed']},

<p>'slightly decreased sodium level (132 mmol / L) but normal potassium (4.8 mEq / L)', 'no abnormalities, such as adrenal enlargement, hydronephrosis, distal ureter dilatation'],</p> <p>'MSK': ['postaxial polydactyly of the left foot', 'Spine ultrasound revealed no vertebral anomalies', 'limb abnormalities', 'postaxial polydactyly of the left foot'],</p> <p>'DERM': ['slight bronzing of the patient 's skin after repeated surgeries', 'generalized hyperpigmentation', "child 's hyperpigmentation was markedly exacerbated after explorator y laparotomy for the episode of peritonitis with sepsis", 'hyperpigmentation', 'generalized hyperpigmentation', 'generalized hyperpigmentation had improved'],</p> <p>'Lab_Image': ['echocardiography revealed a patent ductus arteriosus', 'Bilateral grade 3 vesicoureteral reflux (VUR) was revealed via voiding cystourethrography. Spine ultrasound revealed no vertebral anomalies, and tracheoesophageal fistula was not suspected clinically', 'Laboratory test results, including electrolyte levels, were normal. Neonatal screening tests for metabolic disease were also normal, including the 17 - alpha - hydroxyprogesterone level. Chromosome analysis revealed a 46, XY karyotype.', "Laboratory investigations revealed a slightly decreased sodium level (132 mmol / L) but normal potassium (4.8 mEq / L) and glucose (86 mg / dL) levels; complete blood count, blood gas profile, hepatic and renal function, thyroid function test and sex hormone levels were obtained. Decreased cortisol (1.0 Î¼g / dL) and markedly elevated adrenocorticotrophic hormone (ACTH) (16,064 pg / mL) levels were noted. The patient 's cortisol levels did not respond to stimulation with ACTH (125 Î¼g) (Table 1). Meanwhile, he presented a normal 17 - hydroxyprogesterone level (0.42 ng / mL). Plasma renin activity and aldosterone levels were 7.28 ng / mL / hr (normal range, 1.0â€“6.5 ng / mL / hr) and 0.1 ng / dL (normal range, 3â€“35 ng / dL), respectively",</p>	<p>aled bilateral grade 3 vesicoureteral reflux (VUR)', 'Lab_Image: Spine ultrasound revealed no vertebral anomalies', 'Lab_Image: Bowel necrosis', 'Lab_Image: Short-bowel syndrome', 'Lab_Image: Voiding cystourethrography: Bilateral grade 3 vesicoureteral reflux (VUR)', 'Lab_Image: Thyroid function test results: Normal', 'Lab_Image: Cortisol levels did not respond to stimulation with ACTH (125 µg)', 'Lab_Image: Plasma renin activity and aldosterone levels were normal']},</p> <p>'LYMPH': { ['immune_cells: Increased leukocytes in blood test']},</p> <p>'History': { ['past_medical_history: Born with imperforate anus and colostomy performed', 'past_medical_history: Diagnosed with VACTERL association (vertebral defects, anal atresia, cardiac defects, tracheo-esophageal fistula, renal anomalies, and limb abnormalities)', 'past_surgical_history: Colostomy performed the day after birth', 'past_surgical_history: Takedown of colostomy and jejunostomy at 7 months', 'past_surgical_history: Bowel resection with colostomy and jejunostomy due to bowel necrosis', 'history_of_present_illness: Gradual onset of hyperpigmentation over time', 'history_of_present_illness: Episode of sepsis and peritonitis secondary to Acinetobacter baumannii infection at 17 months', 'history_of_present_illness: Occasional nausea and vomiting', 'family_and_genetics_history: Father had colon cancer', 'family_and_genetics_history: Sister diagnosed with breast cancer at age 50', 'chief_complaint: Patient was referred to our department for evaluation of hyperpigmentation']},</p> <p>'ENDO': { ['endocrine_glands: Primary adrenal insufficiency observed', 'endocrine_glands: Decreased cortisol levels (1.0 µg/dL)', 'endocrine_glands: Markedly elevated adrenocorticotrophic hormone</p>
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'The abdominal ultrasound revealed no abnormalities, such as adrenal enlargement, hydronephrosis, distal ureter dilatation, or bowel wall thickening',

'no pathogenic variants were detected in CYP11A1 genes. The exome - sequencing results revealed compound heterozygous mutations for c.653 C > T and c.661G > A (p. Gly221Ser) in exon 6 of the STAR gene. Sanger sequencing confirmed the presence of these variants and each of the same heterozygous variant was found in his father and mother, respectively',

'Laboratory tests revealed normal levels of cortisol (4.6 Î¼g / dL), sodium (139 mmol / L), potassium (4.9 mEq / L), glucose (70 mg / dL), and d ACTH (53.6 pg / mL)',

'LYMPH': [],

'History': ['A male child was born at a gestational age of 39 weeks with no history of antenatal or perinatal problems. Apgar scores were 9 points at one minute and 10 points at 5 minutes. His birth weight and height were 3,800 g (z -score, +1 standard deviation score) and 52.5 cm (z -score, +1.4 SDS), respectively. There was no family history of consanguineous marriages. The patient was born with an imperforate anus and a colostomy was performed the day after birth',

'At the age of 3 months, the patient was admitted to the hospital for colostomy takedown, anorectoplasty, and endoscopic dextranomer / hyaluronic acid copolymer injection for VUR',

'Bowel resection with colostomy and jejunostomy was performed 3 times, which resulted in short - bowel syndrome',

'At the age of 7 months, a takedown of the colostomy and jejunostomy was performed',

'At 17 months of age, the patient had an episode of sepsis and peritonitis secondary to Acinetobacter baumannii infection and an exploratory laparotomy was performed to check for bowel necrosis'],

'ENDO': [],

'Pregnancy': ['born at a gestational age of 39 weeks with no history of antenatal or perinatal problems. Apgar scores were 9 points at one minute and 10 points at 5 minutes. His birth weight and height were 3,800 g (z -score, +1 standard deviation score) and 52.5 cm (z -score, +1.4 SDS), respectively']}]

ne (ACTH) levels (16,064 pg/mL)', 'endocrine_glands: Normal 17-hydroxyprogesterone level (0.42 ng/mL)']}]},

'Pregnancy': { ['neonatal_health: Imperforate anus', 'neonatal_health: Colostomy performed', 'neonatal_health: Patent ductus arteriosus', 'neonatal_health: Bilateral grade 3 vesicoureteral reflux (VUR)', 'neonatal_health: Postaxial polydactyly of the left foot', 'neonatal_health: Short-bowel syndrome', 'neonatal_health: Bowel resection with colostomy and jejunostomy performed three times', 'neonatal_health: Generalized hyperpigmentation']

Original Text (PMCID: 7136505)

'Case report': "A male child was born at a gestational age of 39 weeks with no history of antenatal or perinatal problems. Apgar scores were 9 points at one minute and 10 points at 5 minutes. His birth weight and height were 3,800 g (z-score, +1 standard deviation score) and 52.5 cm (z-score, +1.4 SDS), respectively. There was no family history of consanguineous marriages. The patient was born with an imperforate anus and a colostomy was performed the day after birth. He had normal male genitalia, with both testes palpable, and postaxial polydactyly of the left foot. A grade 2 systolic murmur was heard in the left upper sternal border and echocardiography revealed a patent ductus arteriosus. Bilateral grade 3 vesicoureteral reflux (VUR) was revealed via voiding cystourethrography. Spine ultrasound revealed no vertebral anomalies, and tracheoesophageal fistula was not suspected clinically. Based on this clinical information, including anal atresia, renal anomalies, and limb abnormalities, he was diagnosed with VACTERL association which is defined by the presence of at least 3 of the following congenital malformations: vertebral defects, anal atresia, cardiac defects, tracheo-esophageal fistula, renal anomalies, and limb abnormalities. Laboratory test results, including electrolyte levels, were normal. Neonatal screening tests for metabolic disease were also normal, including the 17-alpha-hydroxyprogesterone level. Chromosome analysis revealed a 46, XY karyotype. He was discharged from the neonatal intensive care unit at 21 days of age. At the age of 3 months, the patient was admitted to the hospital for colostomy takedown, anorectoplasty, and endoscopic dextranomer/hyaluronic acid copolymer injection for VUR. After the surgery, the patient was febrile and hypotensive and his abdomen was distended and discolored. An exploratory laparotomy revealed bowel necrosis. Bowel resection with colostomy and jejunostomy was performed 3 times, which resulted in short-bowel syndrome. He could not be discharged because parenteral nutrition was required. The remnant small bowel extended from the Treitz ligament to the jejunocolonic anastomosis and the length of the remnant bowel was only 40 cm. At the age of 7 months, a takedown of the colostomy and jejunostomy was performed. The patient's mother observed slight bronzing of the patient's skin after repeated surgeries. At 17 months of age, the patient had an episode of sepsis and peritonitis secondary to *Acinetobacter baumannii* infection and an exploratory laparotomy was performed to check for bowel necrosis. At this time, generalized hyperpigmentation was noted by the doctor and the mother stated that the child's hyperpigmentation was markedly exacerbated after exploratory laparotomy for the episode of peritonitis with sepsis. The patient was referred to our department for the evaluation of the hyperpigmentation. He experienced occasional nausea and vomiting. His heart rate was 120 beats per minute and his blood pressure was 100/65 mmHg. His weight and height were 12.8 kg (1.5 SDS) and 86 cm (2 SDS), respectively. At this point, he was noted to have generalized hyperpigmentation, normal male genitalia, and postaxial polydactyly of the left foot. He was able to ascend stairs with the support of a hand grasp. He could stack 3 cubes, eat without assistance, and pronounce 10 words, meaning that the patient's developmental status was normal for his age. Laboratory investigations revealed a slightly decreased sodium level (132 mmol/L) but normal potassium (4.8 mEq/L) and glucose (86 mg/dL) levels; complete blood count, blood gas profile, hepatic and renal function, thyroid function test and sex hormone levels were obtained. Decreased cortisol (1.0 µg/dL) and markedly elevated adre

nocorticotrophic hormone (ACTH) (16,064 pg/mL) levels were noted. The patient's cortisol levels did not respond to stimulation with ACTH (125 µg) (Table 1). Meanwhile, he presented a normal 17-hydroxyprogesterone level (0.42 ng/mL). Plasma renin activity and aldosterone levels were 7.28 ng/mL/hr (normal range, 1.0–6.5 ng/mL/hr) and 0.1 ng/dL (normal range, 3–35 ng/dL), respectively. The abdominal ultrasound revealed no abnormalities, such as adrenal enlargement, hydronephrosis, distal ureter dilatation, or bowel wall thickening. Based on the patient's symptoms and laboratory results, we considered several genetic causes for primary adrenal insufficiency, and the causative genes of candidate diseases were listed as STAR for NCCLAH and CYP11A1 for congenital adrenal insufficiency. Additionally, melanocortin-2 receptor (MC2R) and MC2R accessory protein for familial glucocorticoid deficiency (FGD) were listed as candidate genes with a low probability because the patient did not have elevated aldosterone. Targeted gene-panel sequencing was performed to check for pathogenic variants in those genes responsible for primary adrenal insufficiency. Genomic DNA was extracted from the peripheral blood of the patient and both parents. Library preparation was done using the TruSight One Sequencing Panel (Illumina, Inc., San Diego, CA, USA), which enriches a 12-Mb region spanning 62,000 target exons of a total of 4,813 genes. Massively parallel sequencing was performed on the Illumina NextSeq platform. Sequence reads were mapped to the UCSC hg19 standard database for comparative analysis. The average depth of the panel was 85.86X, and percentages of bases above 10X of CYP11A1 and STAR were 99.37%, and 100%, respectively. Meanwhile, no pathogenic variants were detected in CYP11A1 genes. The exome-sequencing results revealed compound heterozygous mutations for c.653C>T and c.661G>A (p.Gly221Ser) in exon 6 of the STAR gene. Sanger sequencing confirmed the presence of these variants and each of the same heterozygous variant was found in his father and mother, respectively (Fig. 1). This variant has been previously reported in association with CLAH. Hydrocortisone (7.8 mg/m²/day) and fludrocortisone (50 µg/day) were started as therapy for primary adrenal insufficiency. The dose of hydrocortisone was gradually increased until the age of 24 months for sufficient ACTH suppression and levels of ACTH and cortisol were subsequently decreased to the optimal range (Fig. 2). Finally, at 28 months of age, he was discharged and went home with the attainment of oral feeding without nausea and vomiting. He showed no symptoms of hypoglycemia and continued to show normal growth and development. Our last evaluation of the patient was when he was 36 months of age, during which point, his body weight and length were 16.7 kg (0.5 SDS) and 99.7 cm (1.5 SDS), respectively. Laboratory tests revealed normal levels of cortisol (4.6 µg/dL), sodium (139 mmol/L), potassium (4.9 mEq/L), glucose (70 mg/dL), and ACTH (53.6 pg/mL). The generalized hyperpigmentation had improved, and he continued to visit the outpatient clinic regularly without additional admission."