CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

Case 2-2025: A 21-Year-Old Man with Loss of Consciousness and a Fall

Eric F. Shappell, M.D., Brooks P. Applewhite, M.D., Sharl S. Azar, M.D., and David J. Lin, M.D.

From the Departments of Emergency Medicine (E.F.S.), Radiology (B.P.A.), Medicine (S.S.A.), and Neurology (D.J.L.), Massachusetts General Hospital, and the Departments of Emergency Medicine (E.F.S.), Radiology (B.P.A.), Medicine (S.S.A.), and Neurology (D.J.L.), Harvard Medical School — both in Boston.

N Engl J Med 2025;392:268-76.
DOI: 10.1056/NEJMcpc2412511

PRESENTATION OF CASE

Dr. Kalen N. Wright (Emergency Medicine): A 21-year-old man with sickle cell disease was evaluated in the emergency department of this hospital after loss of consciousness resulting in a fall.

The patient had been in his usual state of health until the week before the current presentation, when he began to have discomfort and pain in the chest, back, arms, and legs. He attributed these symptoms to sickle cell disease and received hydromorphone infusions on an outpatient basis 4 days and 3 days before this evaluation.

On the day of the current presentation, the patient used oral oxycodone and supplemental oxygen for chest pain. In the evening, his family was downstairs in their home when they heard a thud from upstairs; they found the patient lying on the floor of his bedroom. There was no evidence of limb shaking or incontinence. The patient awoke in response to voice but was described as being confused for approximately 1 minute before returning to his baseline mental status. He recalled taking a nap and then feeling dizzy on awakening. The last thing he remembered was trying to walk across his room. Emergency medical services were activated; the fingerstick blood glucose level was normal, and the Glasgow Coma Scale score was 15 (on a scale of 3 to 15, with lower scores indicating greater alteration of consciousness). A cervical collar was applied, and the patient was transported to the emergency department of this hospital.

In the emergency department, a review of systems was notable for head and face pain on the right side from the fall, as well as acute-on-chronic pain involving the chest, back, and right hip and leg that was similar to the patient's previous sickle cell–related pain. He reported no fever, nausea, vomiting, change in bowel habits, dyspnea, rash, weakness, or numbness.

The patient's medical history included homozygous sickle cell disease complicated by vaso-occlusive events, pulmonary embolism and inferior vena cava thrombi, retinal artery occlusion (after which serial blood transfusions were initiated for secondary stroke prophylaxis), sickle cell nephropathy, avascular necrosis of the

hip, cholelithiasis, iron overload, and splenic sequestration resulting in splenectomy. He also had a history of mild persistent asthma and nasal polyps. Medications included apixaban, deferasirox, amoxicillin, gabapentin, cetirizine, montelukast, and famotidine; oxycodone as needed; inhaled albuterol and mometasone–formoterol as needed; and inhaled fluticasone. He used supplementary oxygen through a nasal cannula as needed and received blood transfusions on a regular basis. He was following postsplenectomy vaccination recommendations. Ceftriaxone and methadone had caused rash.

The patient's mother had multiple sclerosis, and she had had petit mal seizures as a child. Multiple relatives had hypertension, and his paternal grandfather had had a stroke. Siblings had asthma, and a first cousin had attention deficit–hyperactivity disorder. The patient worked in the nonprofit sector and lived with his family in an urban area near Boston. He had no history of alcohol, tobacco, or other substance use.

On examination, the temporal temperature was 36.9°C, the heart rate 123 beats per minute, the blood pressure 149/95 mm Hg, the respiratory rate 18 breaths per minute, and the oxygen saturation 97% while the patient was breathing ambient air. An abrasion on the right side of the forehead and swelling of the right cheek were noted. He had no cuts or bleeding in the mouth. The sclerae appeared to be somewhat icteric. The heart was tachycardic with a midsystolic murmur at the base. There was a well-healed surgical scar on the left side of the upper abdomen. Neurologic examination showed right arm weakness that was reported to be chronic; the remainder of the neurologic examination was normal.

Laboratory test results are shown in Table 1. Nucleic acid testing for severe acute respiratory syndrome coronavirus 2 was negative. An electrocardiogram showed sinus tachycardia. Chest radiography showed no abnormalities. Intravenous normal saline and hydromorphone were administered.

Six hours after presentation, on the second hospital day, the patient was witnessed to have an abrupt onset of shaking of the arms and legs with flexion of the arms. The eyes were deviated upward. The event lasted approximately 2 minutes and stopped on its own; intravenous lorazepam was administered 7 minutes after the seizure. The patient was sleepy, but his condition was otherwise unchanged from the previous examination. Laboratory test results are shown in Table 1. Urine toxicology testing was negative except for the detection of oxycodone. Blood cultures were obtained.

Dr. Brooks P. Applewhite: Approximately 7 hours after the witnessed episode of shaking, magnetic resonance imaging (MRI) of the head and magnetic resonance angiography of the head were performed. MRI revealed regions of cortical and subcortical signal hyperintensity on T2-weighted fluid-attenuated inversion recovery (FLAIR) imaging, findings that were consistent with vasogenic edema (Fig. 1A, 1B, and 1C). The hyperintensity was seen predominantly in the posterior portion of the supratentorial parenchyma and involved the bilateral posterior frontal, parietal, occipital, and temporal lobes; the left lenticulocapsular region and right cerebellar hemisphere also showed hyperintensity on FLAIR imaging, with overall mild, localized mass effect. Diffusion-weighted imaging (Fig. 1D) showed no restricted diffusion. T1-weighted imaging, performed after the intravenous administration of contrast material (Fig. 1E), revealed regions of irregular enhancement that corresponded to some of the sites of hyperintensity on FLAIR imaging that were consistent with vasogenic edema; these findings suggested a breakdown of the blood–brain barrier. The dural venous sinuses appeared patent.

Susceptibility-weighted imaging (Fig. 1F) revealed numerous punctate foci of hypointense paramagnetic susceptibility effect throughout the brain parenchyma that were consistent with nonspecific microhemorrhages; these foci were present both within and beyond the regions of abnormal hyperintense signal on FLAIR imaging. Foci of susceptibility effect outside regions of signal abnormalities on FLAIR imaging are typically consistent with nonspecific chronic microhemorrhages, whereas those within regions of abnormal signal intensity on FLAIR imaging could reflect acute petechial hemorrhage or additional sites of chronic microhemorrhage. Magnetic resonance angiography showed no abnormalities.

Dr. Wright: A diagnosis and management decisions were made.

Table 1. Laboratory Data.*

Variable	Reference Range, Adults†	On Initial Presentation	Second Hospital Day
Hemoglobin (g/dl)	13.5–17.5	9.8	8.2
Hematocrit (%)	41.0–53.0	28.3	24.3
White-cell count (per μl)	4500–11,000	20,860	22,380
Differential count (per μl)			
Neutrophils	1800–7700	15,650	15,890
Lymphocytes	1000–4800	1670	5370
Monocytes	200–1200	2290	900
Platelet count (per μl)	150,000–400,000	254,000	230,000
Peripheral-blood smear	Normal	Sickle cells, target cells, burr cells, Howell–Jolly bodies	—
Reticulocyte count (%)	0.5–2.5	14.2	—
Sodium (mmol/liter)	135–145	134	138
Potassium (mmol/liter)	3.4–5.0	3.7	3.0
Chloride (mmol/liter)	98–108	93	97
Carbon dioxide (mmol/liter)	23–32	15	15
Urea nitrogen (mg/dl)	8–25	13	10
Creatinine (mg/dl)	0.60–1.50	1.52	1.38
Glucose (mg/dl)	70–110	81	108
High-sensitivity troponin T (ng/liter)	0–14	<6	—
Creatine kinase (U/liter)	60–400	—	4431
Lactate (mmol/liter)	0.5–2.0	—	12.7
D-dimer (ng/ml)	<500	—	>10,000

* To convert the values for urea nitrogen to millimoles per liter, multiply by 0.357. To convert the values for creatinine to micromoles per liter, multiply by 88.4. To convert the values for glucose to millimoles per liter, multiply by 0.05551. To convert the values for lactate to milligrams per deciliter, divide by 0.1110.

† Reference values are affected by many variables, including the patient population and the laboratory methods used. The ranges used at Massachusetts General Hospital are for adults who are not pregnant and do not have medical conditions that could affect the results. They may therefore not be appropriate for all patients.

DIFFERENTIAL DIAGNOSIS

Dr. Eric F. Shappell: This patient is a 21-year-old man with sickle cell disease and a 1-week history of symptoms that were similar to the vaso-occlusive events he typically had. He presented to the emergency department after having a sensation of dizziness followed by loss of consciousness and a fall (during which we can infer that he struck his head) when he attempted to walk across a room. In cases of loss of consciousness, there are two priorities: diagnosis and treatment of the cause of the loss of consciousness and diagnosis and treatment of any injuries resulting from the loss of consciousness.

LOSS OF CONSCIOUSNESS

This patient's presentation has features that are consistent with both syncope and seizure. The association of loss of consciousness with a change in position (standing to walk across a room) is suggestive of syncope resulting from orthostatic hypotension but is not sufficient to rule out seizure or other causes of syncope. The patient had a period of confusion after regaining consciousness, which could indicate a postictal state; however, a very short duration of confusion (approximately 1 minute in this case) can also occur after syncope. Although he did not have lateral tongue biting or incontinence, both of which are more specifically associated with

seizure than with syncope, the absence of these findings is not sufficiently sensitive to rule out seizure.

The differential diagnosis for the patient's prodrome of dizziness is broad, given that the term "dizzy" is used to describe an array of symptoms including lightheadedness, vertigo, and disequilibrium. Lightheadedness may suggest decreased perfusion of the central nervous system caused by global or focal processes such as orthostasis, increased vagal tone, thromboembolic phenomena, dysrhythmia, blood loss, or other triggers. Vertigo and disequilibrium may suggest disorders affecting the posterior circulation of the central nervous system such as transient ischemic attack, ischemic or hemorrhagic cerebrovascular accident, cerebral venous sinus thrombosis, a space-occupying lesion, an infectious or inflammatory

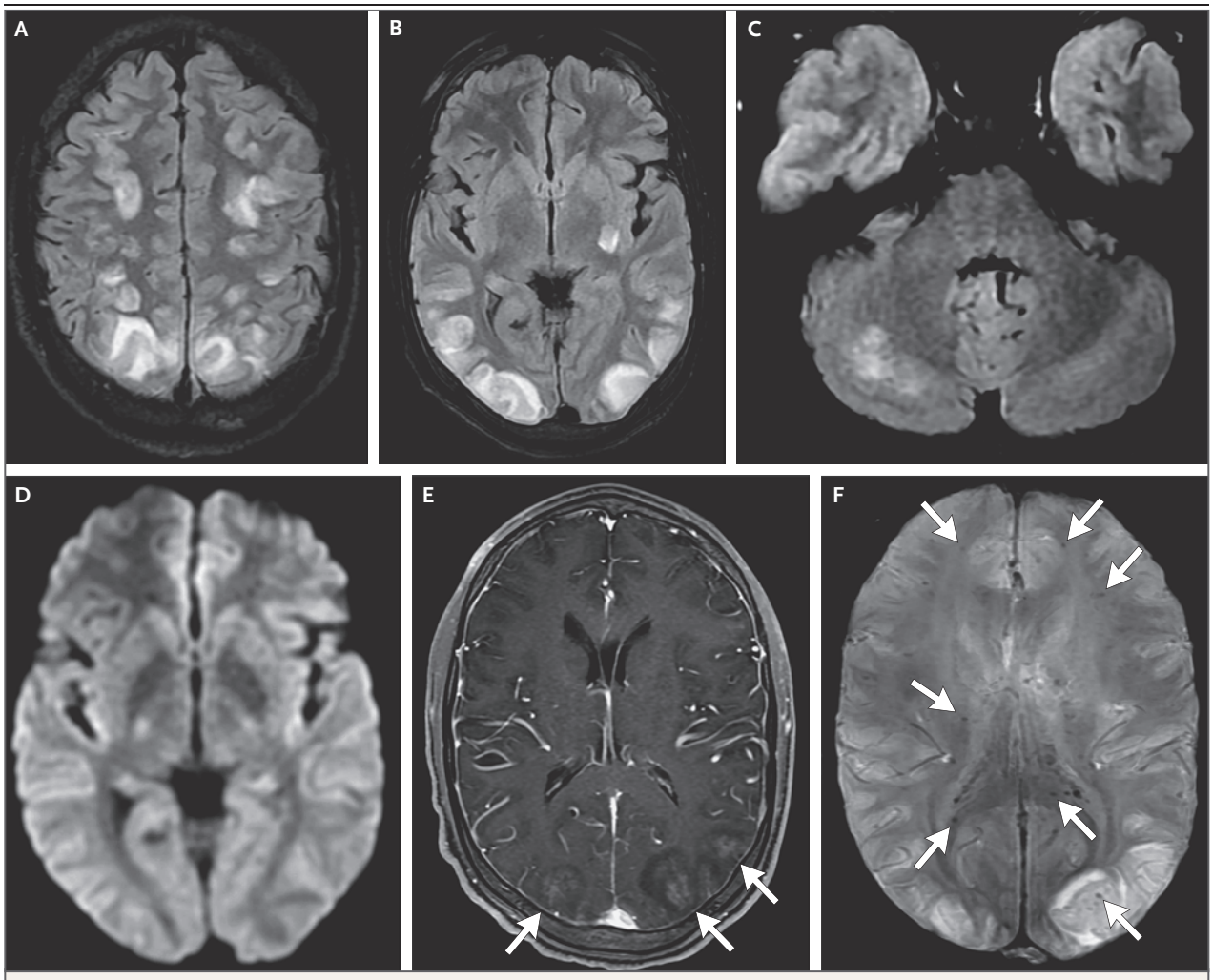

Figure 1. Initial MRI of the Head.

MRI of the head was performed on presentation. A T2-weighted fluid-attenuated inversion recovery (FLAIR) sequence (Panels A through C) shows regions of cortical and subcortical hyperintense signal predominantly involving the posterior portion of the supratentorial parenchyma, findings that are consistent with vasogenic edema with resultant mild, localized mass effect. A diffusion-weighted image (Panel D) shows no restricted diffusion. A T1-weighted image, obtained after the administration of contrast material (Panel E), shows regions of irregular enhancement that correspond to some of the sites of hyperintensity on FLAIR imaging that were suggestive of vasogenic edema (arrows). On a susceptibility-weighted image (Panel F), numerous subtle punctate foci of hypointense susceptibility effect are seen throughout the brain parenchyma, both within and beyond the regions of abnormal hyperintense signal on FLAIR imaging (arrows). Foci of susceptibility effect outside regions of signal abnormalities on FLAIR imaging are typically consistent with nonspecific chronic microhemorrhages, whereas those within regions of abnormal signal intensity on FLAIR imaging could reflect acute petechial hemorrhage or additional sites of chronic microhemorrhage.

process (e.g., meningitis or encephalitis), or a vascular phenomenon such as posterior reversible encephalopathy syndrome (PRES) or reversible cerebral vasoconstriction syndrome (RCVS).

TRAUMATIC INJURY

The patient sustained a fall associated with loss of consciousness, which caused headache and blunt head trauma. The use of oral anticoagulant therapy in this patient places him at increased risk for traumatic intracranial hemorrhage from this injury. Therefore, traumatic intracranial hemorrhage as a possible secondary pathologic process in this case should be considered. Additional consideration will be given to evaluation for other traumatic consequences of the fall.

SEIZURE

Six hours after presentation, the patient again lost consciousness. This episode was witnessed in sufficient detail to diagnose seizure (tonic–clonic activity with a postictal period). Although this event increases the likelihood that the initial episode of loss of consciousness was also seizure, it is possible that the initial episode was syncopal in nature and that this seizure episode involved a separate process, such as seizure due to traumatic intracranial hemorrhage from the fall.

The seizure activity was not associated with evidence of global malperfusion (e.g., systemic hypotension). The lack of such evidence suggests a primary neurologic process (e.g., hemorrhage, ischemia, inflammation, or a vascular condition) a metabolic derangement (e.g., hyponatremia, hypocalcemia, or uremia), a hematologic disorder (e.g., thrombotic thrombocytopenic purpura or disseminated intravascular coagulation [DIC]), or a toxin-mediated condition.

Fat embolism syndrome is often associated with traumatic injuries and orthopedic procedures. However, it is also a potential complication of sickle cell disease that can result in seizure. Patients with fat embolism syndrome can present with neurologic findings including seizure caused by fat emboli from bone entering the central nervous system through pulmonary and intracardiac shunts. However, most fat emboli typically end up in the pulmonary circulation and cause clinically significant respiratory symptoms that precede or coincide with neurologic symptoms. Such respiratory symptoms are not consistent with this patient's presentation.[1-3] In addition, this patient did not have petechiae that are commonly associated with fat embolism syndrome when they appear in a distribution unrelated to gravity.

LABORATORY TESTING

The patient's initial laboratory findings, including normal blood levels of glucose, sodium, and urea nitrogen, are not suggestive of metabolic derangement. Hematologic findings (including moderate anemia and the presence of sickle cells, Howell–Jolly bodies, target cells, and burr cells) are consistent with sickle cell disease after splenectomy, without evidence of aplastic crisis. The platelet count was normal, and no schistocytes or immature cells were present on the peripheral-blood smear — findings that make hematologic processes such as thrombotic thrombocytopenic purpura, DIC, a hematologic cancer, and hyperhemolysis syndrome (a condition marked by hemolysis after blood transfusion) unlikely in this patient. His negative urine toxicology screen combined with the absence of known exposures or a toxidrome on examination make toxin-mediated disorders unlikely.

On the basis of the second set of blood samples, which was obtained shortly after the patient had had the witnessed seizure, the creatine kinase level was moderately elevated and the lactate level was markedly elevated, findings that together are consistent with seizure activity. An elevated creatine kinase level can also occur in association with processes that cause muscle breakdown, including myositis (e.g., infectious or autoimmune) and rhabdomyolysis (e.g., caused by exercise or medications), but this patient's history is not suggestive of these processes. The presence of lactate levels greater than 10 mmol per liter in patients with normal hepatic function and without evidence of ischemic processes (e.g., mesenteric ischemia or ischemic limb) or overt critical illness is uncommon, although such levels can be seen with toxic effects caused by metformin[4]; however, this patient did not receive treatment with metformin.

The D-dimer level was markedly elevated, at a level greater than the upper limit of detection of the assay. Sickle cell disease is associated with elevated D-dimer levels at baseline, and these levels may increase during vaso-occlusive episodes.[5] This patient's markedly high level suggests the possibility of clinically significant

vaso-occlusive activity or an additional process such as acute thrombosis. Although the patient was taking anticoagulant therapy, treatment failure occurs in approximately 2% of patients who receive direct oral anticoagulants for venous thromboembolism.[6-8] Markedly elevated D-dimer levels can also occur in the context of diffuse inflammatory states such as those associated with cancer, sepsis, DIC, or trauma; however, the patient's other laboratory findings and medical history make these diagnoses unlikely.

IMAGING STUDIES

The patient's chest radiography showed no abnormalities, which is consistent with the absence of respiratory symptoms and further decreases the likelihood of fat embolism syndrome or acute chest syndrome due to sickle cell disease. MRI of the head showed no evidence of radiologically significant intracranial hemorrhage, and diffusion-weighted imaging showed no evidence of restricted diffusion — findings that rule out hemorrhage, arterial thrombosis, and an acute embolic event. The susceptibility-weighted images showed scattered punctate foci in a pattern consistent with microhemorrhages associated with cerebral fat embolism. In the context of normal findings on diffusion-weighted imaging, these susceptibility-weighted imaging findings suggest evidence of previous cerebral fat embolism, which is unlikely to be contributory to the patient's current presentation. With acute cerebral fat embolism, a starfield pattern on diffusion-weighted imaging would be expected.[9,10]

The normal-appearing venous circulation rules out a diagnosis of cerebral venous sinus thrombosis, and the normal-appearing arterial circulation without a history of thunderclap headache makes a diagnosis of RCVS unlikely. There was evidence of symmetric vasogenic edema in the frontal, parietal, occipital, and temporal lobes and in the cerebellum. This pattern is consistent with PRES. The absence of involvement of the limbic system decreases the possibility of autoimmune encephalitis, particularly given the absence of typical symptoms including subacute memory and psychiatric changes. The symmetric nature of these findings and the absence of other features suggestive of infection, such as meningeal involvement, decreases the likelihood of infectious encephalitis or cerebritis, particularly in the absence of recent infectious symptoms.

POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME

Overall, the patient's presentation is most consistent with PRES. This syndrome is commonly associated with vision changes, nausea and vomiting, headache, and seizure, although presentations such as this one without typical prodromes have been described. Hypertension is also commonly seen in patients with PRES and has been hypothesized to be contributory to the pathophysiology of the disease; however, cases without hypertension have also been described. Risk factors for PRES include pregnancy, certain medications (e.g., chemotherapy or immunosuppressive therapy), and chronic disease states including autoimmunity, renal dysfunction, and sickle cell disease[11]; this patient has both sickle cell disease and renal dysfunction.

The patient's laboratory findings are consistent with a vaso-occlusive event associated with sickle cell disease and a postictal state. Sickle cell disease is associated with endothelial dysfunction (the cascading effects of which result in elevation of D-dimer levels), and endothelial dysfunction is another hypothesized pathophysiological mechanism of PRES. These laboratory findings, combined with the MRI findings, indicate that PRES is the most likely diagnosis that would explain the patient's presentation.

CLINICAL IMPRESSION

Dr. Sharl S. Azar: In this patient with underlying sickle cell disease complicated by two previous episodes of retinal artery occlusion, the risk of recurrent neurologic complications is high. Retinal artery occlusions are treated in the same way as stroke, and 24% of patients with sickle cell disease will have at least one stroke by their fourth decade of life.[12]

A strong mimic of stroke in patients with sickle cell disease, however, is PRES. Although the risk of PRES is lower than that of stroke in patients with sickle cell disease, the diagnosis of PRES can be missed if it is not considered early.[13] Another consideration is epilepsy, which is two to three times as common in patients with sickle cell disease as in those without the disease[14]; the patient's mother also had a history of epilepsy. We considered whether the seizure that occurred in the hospital could be the first manifestation of an underlying seizure disorder

in this patient. Finally, patients with sickle cell disease are at increased risk for fat embolism syndrome.[13] Although this rare condition is often associated with long-bone fractures, it can manifest in patients with sickle cell disease during times of severe, painful vaso-occlusive events as a result of infarction of the bone marrow or of the bone itself. In the general population, the management of fat embolism syndrome is limited to supportive care, whereas in patients with sickle cell disease, urgent red-cell exchange is recommended.[2]

Indeed, the American Society of Hematology suggests that patients with sickle cell disease who present with focal neurologic symptoms should receive prompt red-cell exchange as the primary intervention.[15] It is important to emphasize that this guideline does not necessitate identification of a cause for the neurologic symptoms before initiation of red-cell exchange. Clear data to support the use of red-cell exchange to treat seizure alone are lacking, but given the high level of concern about an underlying infarct as the driver of new seizure in this patient, red-cell exchange should be strongly considered as an initial intervention.[16,17] Shortly after the current presentation, the patient received a red-cell exchange, which successfully reduced his hemoglobin S level to 5.9%, well below the 30% hemoglobin S threshold that red-cell exchange is intended to achieve.

CLINICAL DIAGNOSIS

Posterior reversible encephalopathy syndrome in the context of sickle cell vaso-occlusive crisis.

DR. ERIC F. SHAPPELL'S DIAGNOSIS

Posterior reversible encephalopathy syndrome in the context of sickle cell vaso-occlusive crisis and previous cerebral fat embolism.

DISCUSSION OF EMERGENCY MANAGEMENT

Dr. David J. Lin: Seizure is a common occurrence, affecting up to 10% of the general population and accounting for 2% of emergency department visits.[18,19] In this 21-year-old patient who presents with a first-time seizure and has a known history of sickle cell disease and previous arterial and vaso-occlusive events while receiving anticoagulant therapy, stroke (both the ischemic and the hemorrhagic subtype) should be strongly considered. Seizure commonly occurs early after stroke; one study showed that 4% of the patients had seizure within 14 days after stroke.[20] In adults, seizure as the presenting sign at the onset of stroke is relatively rare; it is associated with large, severe stroke[21] and is a contraindication to thrombolytic therapy.[22] In children, however, seizure as the presenting sign of stroke is much more common, occurring in 22% of children with stroke.[23]

Acute management of seizure in the emergency department focuses on airway management and seizure cessation. The decision regarding whether to start an antiseizure medication after a first seizure depends on multiple factors including the cause of the seizure, the clinical stability of the patient, and the risk of recurrent seizure. One study showed that the number of episodes of seizure at presentation, the presence of an underlying neurologic disorder (e.g., a structural abnormality on neuroimaging), or abnormal findings on electroencephalography could be used to predict the risk of future seizure and thus could guide whether to start an antiseizure medication after a first-time seizure in a patient presenting to the emergency department.[24] The choice of antiseizure medication is based on the route of administration, drug interactions, and whether the patient has unacceptable side effects. Given this patient's multiple episodes of seizure on presentation and the abnormalities noted on MRI, levetiracetam was initiated in parallel with ongoing red-cell exchange.

DIAGNOSTIC IMAGING

Dr. Applewhite: On the third hospital day, computed tomography of the pelvis was performed because of hip pain. Subcapital fractures in both femurs and a comminuted displaced acetabular fracture on the right side with an adjacent hematoma were detected.

MRI of the head that was performed 6 weeks after the current presentation showed complete resolution of both the vasogenic edema that had been seen on initial FLAIR imaging and the associated abnormal enhancement (Fig. 2A, 2B, and 2C), without gliosis or focal encephalomalacia. In effect, there was a reversal of previously ob-

served signal abnormalities that were consistent with PRES (Fig. 2D). Susceptibility-weighted imaging showed persistent, diffusely scattered, punctate foci of hypointense susceptibility effect throughout the brain parenchyma that were consistent with chronic microhemorrhages (Fig. 2E and 2F). Because many of these foci of susceptibility were seen on MRI of the head at presentation without associated foci of restricted diffusion on diffusion-weighted imaging, it is postulated that the chronic microhemorrhages may in part reflect chronic consequences of more remote fat emboli.

FOLLOW-UP

Dr. Azar: Given the patient's history of retinal artery occlusion, he had been receiving serial transfusion therapy as prophylaxis against secondary stroke. Because of the hip fractures he sustained after his fall at home, and despite undergoing corrective orthopedic surgery during this admission, the patient lived in ongoing severe pain with limited mobility, which made it more difficult for him to travel to and from the clinic where he was receiving transfusion therapy. Therefore, transfusion therapy was stopped,

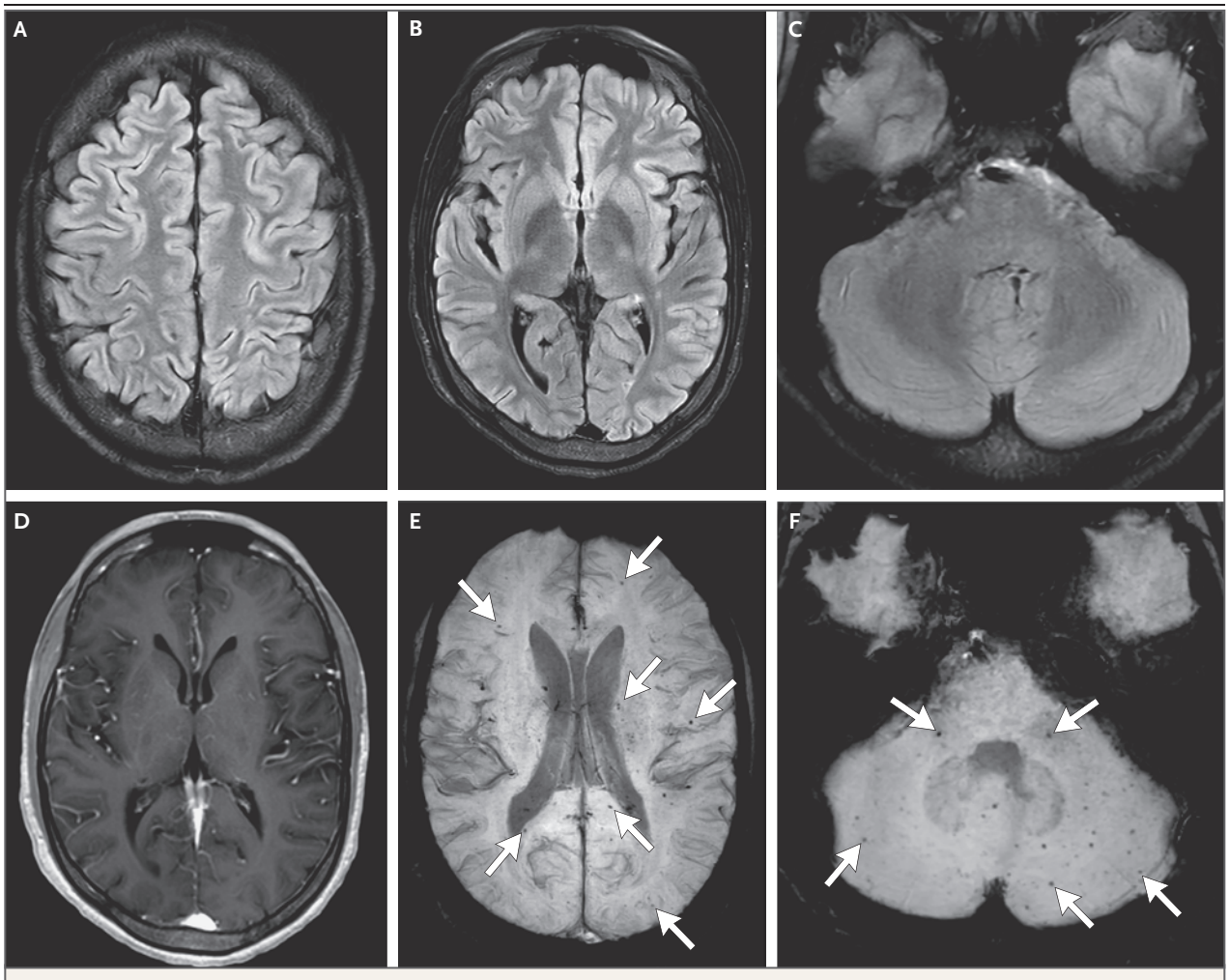

Figure 2. Follow-up MRI of the Head.

MRI of the head was performed 6 weeks after the current presentation. A T2-weighted FLAIR sequence (Panels A through C) shows resolution of previously observed regions of vasogenic edema. A T1-weighted image, obtained after the administration of contrast material (Panel D), shows resolution of previous abnormal enhancement. On minimum-intensity-projection susceptibility-weighted images (Panels E and F), persistent scattered foci of hypointense susceptibility effect are seen throughout the brain parenchyma (arrows); these foci are consistent with sites of chronic microhemorrhage.

and treatment with hydroxyurea was initiated. The patient subsequently had two additional admissions related to suspected osteomyelitis from his hip fractures and then three additional admissions for episodes of seizure that occurred as separate episodes of status epilepticus 9 months after the current presentation. Careful scrutiny of the results of his serial imaging studies over the course of these admissions has revealed the accumulation of innumerable silent cerebral infarcts, which may be the result of fat embolism syndrome or could be the sequelae of progressive sickle cell disease; the role that these infarcts may have played in his repeat presentations is unclear. He is now receiving serial transfusion therapy despite his limited mobility, with the clinic helping to support his monthly transportation.

FINAL DIAGNOSIS

Posterior reversible encephalopathy syndrome due to sickle cell disease.

This case was presented at Emergency Medicine Grand Rounds.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

REFERENCES

1. Mellor A, Soni N. Fat embolism. Anaesthesia 2001;56:145-54.
2. Tsitsikas DA, Vize J, Abukar J. Fat embolism syndrome in sickle cell disease. J Clin Med 2020;9:3601.
3. Gendreau S, Scholer M, Cecchini J, et al. Cerebral fat embolism in sickle cell disease. Am J Hematol 2020;95(2):E41-E45.
4. Juneja D, Nasa P, Jain R. Metformin toxicity: a meta-summary of case reports. World J Diabetes 2022;13:654-64.
5. Kabrhel C, Mark Courtney D, Camargo CA Jr, et al. Factors associated with positive D-dimer results in patients evaluated for pulmonary embolism. Acad Emerg Med 2010;17:589-97.
6. Agnelli G, Buller HR, Cohen A, et al. Oral apixaban for the treatment of acute venous thromboembolism. N Engl J Med 2013;369:799-808.
7. The EINSTEIN Investigators. Oral rivaroxaban for symptomatic venous thromboembolism. N Engl J Med 2010;363:2499-510.
8. Schulman S, Kearon C, Kakkar AK, et al. Dabigatran versus warfarin in the treatment of acute venous thromboembolism. N Engl J Med 2009;361:2342-52.
9. Parizel PM, Demey HE, Veeckmans G, et al. Early diagnosis of cerebral fat embolism syndrome by diffusion-weighted MRI (starfield pattern). Stroke 2001;32:2942-4.
10. Goenka N, Ropper AH. Cerebral fat embolism. N Engl J Med 2012;367:1045.
11. Geocadin RG. Posterior reversible encephalopathy syndrome. N Engl J Med 2023;388:2171-8.
12. Ohene-Frempong K, Weiner SJ, Sleeper LA, et al. Cerebrovascular accidents in sickle cell disease: rates and risk factors. Blood 1998;91:288-94.
13. Solh Z, Taccone MS, Marin S, Athale U, Breakey VR. Neurological PRESentations in sickle cell patients are not always stroke: a review of posterior reversible encephalopathy syndrome in sickle cell disease. Pediatr Blood Cancer 2016;63:983-9.
14. Ali SB, Reid M, Fraser R, MooSang M, Ali A. Seizures in the Jamaica cohort study of sickle cell disease. Br J Haematol 2010;151:265-72.
15. DeBaun MR, Jordan LC, King AA, et al. American Society of Hematology 2020 guidelines for sickle cell disease: prevention, diagnosis, and treatment of cerebrovascular disease in children and adults. Blood Adv 2020;4:1554-88.
16. Hulbert ML, Scothorn DJ, Panepinto JA, et al. Exchange blood transfusion compared with simple transfusion for first overt stroke is associated with a lower risk of subsequent stroke: a retrospective cohort study of 137 children with sickle cell anemia. J Pediatr 2006;149:710-2.
17. Yawn BP, Buchanan GR, Afenyi-Annan AN, et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members. JAMA 2014;312:1033-48.
18. Annegers JF, Hauser WA, Lee JR, Rocca WA. Incidence of acute symptomatic seizures in Rochester, Minnesota, 1935-1984. Epilepsia 1995;36:327-33.
19. Huff JS, Morris DL, Kothari RU, Gibbs MA, Emergency Medicine Seizure Study Group. Emergency department management of patients with seizures: a multicenter study. Acad Emerg Med 2001;8:622-8.
20. Reith J, Jørgensen HS, Nakayama H, Raaschou HO, Olsen TS. Seizures in acute stroke: predictors and prognostic significance. The Copenhagen Stroke Study. Stroke 1997;28:1585-9.
21. Kim J-W, Stetefeld HR, Fink GR, Malter MP. Seizures at stroke onset: a case-control study. Seizure 2023;113:28-33.
22. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med 1995;333:1581-7.
23. Abend NS, Beslow LA, Smith SE, et al. Seizures as a presenting symptom of acute arterial ischemic stroke in childhood. J Pediatr 2011;159:479-83.
24. Kim LG, Johnson TL, Marson AG, Chadwick DW, MRC MESS Study group. Prediction of risk of seizure recurrence after a single seizure and early epilepsy: further results from the MESS trial. Lancet Neurol 2006;5:317-22.