Hypoxic-ischemic encephalopathy following vaso-occlusive crisis in hemoglobin SC disease

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A 56-year-old African American woman with hemoglobin SC disease, hypertension, and diabetes mellitus presented to the emergency department after she was found unresponsive at home. The patient was last seen normal approximately 8 hours prior to presentation. According to family, she complained of severe arthralgias in her hands and knees for the prior 2 days. Physical examination revealed an obese woman who was unresponsive to verbal stimulus. Blood pressure was 130/70 mm Hg, heart rate was 103 beats per minute, and respirations were 18 per minute and labored. Lung examination revealed diffuse wheezes and decreased breath sounds over the left-upper lobe. On neurologic examination, the patient's brainstem reflexes were intact; her tone and bulk were normal; and equal, purposeless movements were noted in all limbs. She flexed only her upper extremities to painful stimuli.

A complete blood count showed a leukocytosis of 22.0 K/ μ L and hemoglobin of 9.4 g/dL. A chest X-ray film showed hazy opacification of the left hemithorax with an area of confluent density in the left upper lung suggestive of an infiltrate and atelectasis. An urgent noncontrast CT of the head was unremarkable. The patient developed respiratory failure at which point she was intubated and transferred to the intensive care unit. Due to concern for acute chest syndrome, broad-spectrum antibiotics, IV hydration, and a blood transfusion were initiated.

Because the patient's neurologic status failed to improve, neurology was consulted. Repeat neurologic examinations were unchanged with the exceptions of increased tone and hyperreflexivity without clonus in all 4 extremities. Babinski sign was present on the left. A stroke was suspected and MRI of the head was performed on the first full day of admission. Diffusion-weighted imaging (DWI) revealed patchy areas of restricted diffusion involving the gray matter and the gray-white junction of both hemispheres (figure, A). Similarly, the susceptibility-weighted imaging (SWI) showed extensive areas of susceptibility involving the gray matter and gray-white junction of both hemispheres (figure, B). This combination was most consistent with diffuse microcapillary obstruction. Because multiple lesions were present in more than one arterial territory, we also considered emboli from a proximal source, such as endocarditis, left atrial thrombus, or aortic atheromatous disease. However, these were appropriately ruled out by a normal transesophageal echocardiogram and negative blood cultures on

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Figure MRI brain

(A) Diffusion-weighted sequence. (B) Susceptibility-weighted sequence. (C) T2-weighted spin-echo sequence showing normal proximal carotid and basilar arteries. (D) Fluid-attenuated inversion recovery sequence.

days 1 and 4 of admission. Additionally, the proximal carotid and basilar arteries appeared normal and there was no evidence of collateral flow under conventional T2-weighted turbo spin-echo imaging (figure, C).

With the diagnosis of hypoxic-ischemic brain injury confirmed, an exchange transfusion was performed to prevent further infarction; however, the patient's neurologic status did not improve on serial examinations. She was unable to wean from the ventilator and later transferred to long-term acute care.

DISCUSSION

Stroke is a devastating and potentially fatal complication of sickle cell disease.¹ Cerebral infarction typically results from an occlusive vasculopathy of the distal intracranial segments of the internal carotid artery and proximal middle and anterior cerebral arteries.² Stenotic lesions have been demonstrated by cerebral angiography, transcranial Doppler ultrasonography, and MRI.³ Hemoglobin S deoxygenation and polymerization chiefly occurs in the microcirculation and venous system; thus, the macroangiopathy of sickle cell disease is attributed to obstruction of the vasa vasorum and mechanical damage of endothelium by sickle cells, which promote a proinflammatory and hypercoagulable state.²

The present case is unique in that the patient had innumerable, bihemispheric microvascu-

lar occlusions that resulted in acute coma. While small artery occlusion of the brain is not uncommon in sickle cell disease, it often occurs in the context of silent infarcts. These subclinical lesions are small and distributed in the white matter of the frontal and parietal lobes—a pattern distinct from the locations seen in hypertensive patients.⁴ In a prospective, multicenter study of 671 episodes of acute chest syndrome, neurologic events occurred in 11% of patients. Although the most common event was altered mental status, CNS hemorrhage and anoxic brain injury were also rarely reported.⁵

The SWI revealed areas of excess deoxygenation that were either at risk or the result of vaso-occlusion. This clinically manifested as acute encephalopathy. The areas of patchy restricted diffusion on DWI corresponded to the areas of microcapillary obstruction observed on SWI and support the acuity of the lesions. Furthermore, the T2-weighted turbo spin echo and fluid-attenuated inversion recovery sequences (figure, C and D) confirmed that there were not any areas of remote ischemia. SWI takes advantage of the fact that the change from diamagnetic oxyhemoglobin to paramagnetic deoxyhemoglobin results in decreased signal intensity of MRI. This sequence has been used to detect the presence of blood hypoxia in the liver, kidneys, and brain of transgenic mouse models of sickle cell disease⁶ and the corpora cavernosa of a sickle cell patient with megalophallus.⁷ A more recent study showed that SWI is a more sensitive technique than conventional T2-weighted gradient-recalled echo for detecting microhemorrhages associated with hypertension, small-vessel disease, and stroke.⁸

Hypoxic-ischemic encephalopathy is a rare but known neurologic complication of sickle crisis. Using susceptibility-weighted and other MRI techniques, we show that small-vessel occlusions, presumably due to sludging of sickled erythrocytes, are one possible etiology.

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DISCLOSURES

The authors report no disclosures.