Sickle cell disease, fat embolism syndrome, and “starfield” pattern on MRI

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A 45-year-old man with history of hemoglobin sickle cell disease (SCD) was admitted to the medical intensive care unit from an outside hospital with a several-day history of progressive chest and extremity pain, fever, tachycardia, tachypnea, and hypoxemia, and underwent red cell exchange for acute chest syndrome. He concomitantly developed progressive decline in mental status over several hours. His examination was notable for Glasgow Coma Scale 5 with no motor response to pain, and he was subsequently intubated.

MRI revealed innumerable foci of restricted diffusion and susceptibility throughout the supratentorial brain and cerebellum, as well as scattered T2 hyperintense foci prominently in the frontal white matter (figure). MRI angiography was unremarkable. The MRI findings were typical of a “starfield” pattern of multifocal small cerebral emboli with a differential that included cardiogenic, septic, or fat emboli; vasculitis; diffuse axonal injury; and tiny hemorrhagic metastases.¹ While transthoracic echocardiogram was negative for presence of microcavitation, this patient had a grade 3 right-to-left shunt identified on transcranial Doppler ultrasound. Given the clinical picture and presence of shunt, the MRI findings were believed to be consistent with fat embolism syndrome.¹

Vaso-occlusive sickle cell crises can lead to generalized bone marrow necrosis and bone infarction with subsequent fat embolism syndrome.¹ The features of fat embolism syndrome are respiratory distress, altered mental status, and petechiae, as well as acute kidney injury, anemia, thrombocytopenia, fever, tachycardia, and jaundice.¹ These are all secondary sequelae to fat emboli from bone marrow necrosis entering osseous venous channels and entering the lungs, or crossing a right-to-left intracardiac or pulmonary shunt to enter the brain or kidneys.¹

A prior study showed that fat embolism accounts for 44% of acute chest syndrome, and patients who have this have more complicated hospital courses, neurologic complications, and extremity pain, which implies bone marrow necrosis.² Moreover, a cross-sectional study of 170 patients with SCD determined that the presence of a right-to-left shunt is higher in patients who experience stroke than those who do not (45.6% vs 23.6%, $p < 0.001$), and intrapulmonary shunting in particular (not intracardiac) is more prevalent.³ The authors of this study concluded that patients with SCD and stroke are 2.7 times more likely to have a right-to-left shunt (95% confidence interval 1.6–4.6).³

Typical MRI findings of fat embolism syndrome include innumerable bright, punctate restricted diffusion and T2 hyperintensities in a starfield pattern throughout the brain. This is thought to reflect numerous sites of cytotoxic edema related to hemorrhage and infarction from cerebral vessel occlusion by fat emboli.^{1,4} Gradient-echo images and susceptibility-weighted images frequently demonstrate corresponding foci of susceptibility artifact representing microhemorrhage.⁵

The treatment is typically red cell exchange transfusion and supportive care.⁶ Although prognosis is variable, this complication can be neurologically devastating and is helped with early time to

PRACTICAL IMPLICATIONS

Consider fat embolism syndrome as the cause of acute encephalopathy in patients with hemoglobin SS or SC disease in vaso-occlusive crisis.

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Axial brain MRI shows innumerable areas of punctate diffusion restriction (A), microhemorrhages (B), and T2 hyperintensities (C).

treatment.⁷ Notably, despite early, gold standard treatment for our patient (red cell exchange), the patient still did poorly, requiring a tracheostomy and percutaneous endoscopic gastrostomy tube. On discharge, he was unable to do no more than move his eyes to voice.

While the majority of SCD-related stroke is attributed to moyamoya-like vasculopathy, this case report emphasizes that fat embolism syndrome is an additionally important and potentially devastating cause of stroke that may be underdiagnosed in these patients. Patients with SCD who present with vaso-occlusive crises are at risk of fat embolism syndrome, which can cause cerebral microinfarctions due to diffuse embolism of nonthrombotic material. Bone marrow necrosis with subsequent pulmonary emboli in the presence of right-to-left shunt results in embolic phenomenon to the brain, which presumably occludes capillaries and small arteries, causing subsequent inflammation.¹ The starfield pattern on MRI supports diagnosis in the appropriate clinical context and presence of shunt. Right-to-left shunts, and pulmonary shunts in particular, are more common in patients with SCD and stroke. In the setting of acute change in mental status in a patient with vaso-occlusive crisis, there

should be high suspicion for fat embolism syndrome. Early recognition and intervention with exchange transfusion can be life-saving.

Author contributions

J.H. Kang: drafting of manuscript. C.W. Hargett: critical revision of manuscript for intellectual content. T. Sevilis: critical revision of manuscript for intellectual content. M. Luedke: critical revision of manuscript for intellectual content.

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