Vasogenic edema in a patient with sickle cell disease

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Approximately 5-8% of patients with sickle cell disease (SCD) develop symptoms of cerebral disease.[1] Stroke and cerebral thrombo-embolism are commonly seen while sinus thrombosis occurs rarely.[1] These complications have been attributed to the increase in blood flow and viscosity. Vasogenic edema, an increase in the blood brain barrier (BBB) vascular permeability, which contributes to brain tissue damage is rarely reported among patients with SCD.[2]

A 26-year-old Saudi gentleman with SCD was admitted with generalized bone pain, fever, chills, vomiting, shortness of breath, and impaired level of consciousness. Medical history was significant for recurrent episodes of acute chest syndrome and right hip replacement for avascular necrosis. On examination, he was conscious but drowsy. Blood pressure was 120/72 mm Hg, heart rate 92 bpm, respiratory rate 24 breaths per minute, and temperature 37^0C. He had severe scleral icterus, bilateral inspiratory crackles on lung examination, heart and the rest of neurological examination were normal. Initial pulse oximeter reading was 60% on room air, and 92% on 100% oxygen. Significant laboratory results were as follows: white blood cell 32.7 x 10^6/µL, hemoglobin 6.7 g/dL, hematocrit 17.7%, reticulocyte count 5.3% (normal: 0.2-2%), serum urea was 7.4 µmol/L (normal: 62-115 µmol/L), and creatinine was 178 mmol/L (normal: 2.5-6.5 mmol/L), total bilirubin 107 mmol/L (normal: 2-17 mmol/L), direct bilirubin 51 mmol/L (normal: 0-4.5 mmol/L), aspartate amino transferase 183 U/L (normal: 12-37 U/L), and lactate dehydrogenase 1002 U/L (normal: 100-190 U/L). Chest x-ray showed bilateral extensive alveolar infiltrates. While in the emergency room, his level of consciousness deteriorated (Glasgow coma scale of 7), and he became hypoxemic and hypotensive, subsequently he was intubated. Vasopressors were given, and he was transferred to the Medical Intensive Care Unit (MICU). Simple transfusions followed by exchange transfusions were instituted. Hemoglobin fractionation prior to exchange transfusion revealed an HbS of 73%, which was reduced to 38% after therapy. Cardiac vegetations and intramural thrombus were ruled out by transesophageal echocardiography, and fat embolism was ruled out by bronchoalveolar lavage, urine, and retinal examination. The CSF analysis was unremarkable with normal opening pressure. On day 2, his renal functions deteriorated and continuous renal replacement therapy was started. Brain CT scan showed multifocal patchy hypodense areas in subcortical aspects of both hemispheres and the left basal ganglia. Brain MRI showed large patchy confluent lesions of high signal intensity on T2WI and FLAIR sequences predominantly scattered at the subcortical white matter of both cerebral hemispheres with no enhancement suggestive of vasogenic edema. Multiple foci of hemorrhages were noted within the lesion in the left fronto-parietal region (**Figure 1**). The magnetic resonance angiography as well as magnetic resonance venogram were normal. An EEG revealed a marked diffuse slow wave abnormality without epileptiform discharges. He was treated with broad-spectrum antibiotics, systemic steroids, and was started on prophylactic unfractionated heparin. His hemodynamics and renal functions returned to normal. He underwent tracheostomy and was successfully weaned-off from the ventilator 2 weeks later and was transferred from the MICU. Repeat MRI 4 weeks later upon discharge showed marked resolution of his brain edema.

Symptoms and signs that were seen in our patient were not specific. At his initial presentation, our patient showed evidence of increased intra-cranial pressure, headache, visual disturbance, altered alertness, and behavioral changes. His hospital course was complicated by sepsis and multiple organ dysfunction syndrome. The distribution of his MRI abnormalities was suggestive of vasogenic edema involving the white matter, which was reversible in subsequent MRI. Vasogenic edema in general involves white matter more than the grey matter probably due to lower resistance to flow.[2] Foci of hemorrhages were seen in our patient only at the posteroparietal region, which

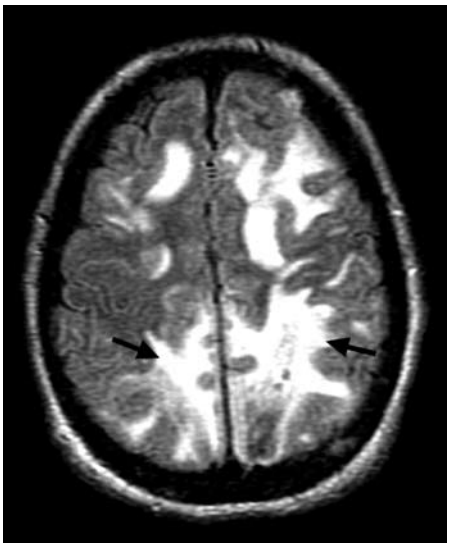

Figure 1 - Axial MRI FLAIR sequence showing patchy confluent lesions and small foci of hemorrhages in the left fronto-parietal region.

can be explained by a thrombosis of small superficial cortical veins; however, these abnormalities were not revealed by MRV. The pathogenesis of vasogenic edema in SCD is not fully understood. It can be due to an acute inflammation resulting from micro thrombosis involving small blood vessels, resulting in perturbation and activation of vascular wall endothelium.[1] This induces a weakening of the tight junction between the endothelial cells resulting in the disruption of BBB with extravasation of fluid and protein. In addition, sicklers have poor cerebrovascular autoregulation leading to hyperperfusion that may result further in breakage of the BBB.[3] The reversibility of the lesion suggests its edematous nature. Moreover, the increase in signal intensity suggests accumulation of fluid in interstitial spaces, which supports the probability of inflammatory venous pathogenesis in the CNS lesion in SCD. These features were described before in cases of vasogenic edema due to other causes.[3-5] The CNS complications remain to be one of the important sequelae of SCD. Vasogenic edema with foci of hemorrhages is rare. This case suggests that, patients with SCD may have reversible illness due to brain edema. Early MRI recognition and application of exchange transfusion along with other supportive therapy is crucial in management of these complications.

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