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Clinical Review

EMERGENCY MEDICINE MANAGEMENT OF SICKLE CELL DISEASE COMPLICATIONS: AN EVIDENCE-BASED UPDATE

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☐ **Abstract—Background: Sickle cell disease (SCD) affects approximately 100,000 individuals in the United States. Due to alterations in the structural conformation of hemoglobin molecules under deoxygenated conditions, patients with SCD are predisposed to numerous sequelae, many of which require acute intervention. Objective: Our aim was to provide emergency physicians with an evidence-based update regarding the diagnosis and management of SCD complications. Discussion: SCD patients experience significant morbidity and mortality secondary to cerebrovascular accident, acute chest syndrome, acute vaso-occlusive pain crises, SCD-related multi-organ failure, cholecystitis, acute intrahepatic cholestasis, acute sickle hepatic crisis, acute hepatic sequestration, priapism, and renal disease. Emergency physicians must recognize acute manifestations of SCD in order to deliver timely management and determine patient disposition. Conclusions: A comprehensive review of the emergency department management of acute SCD complications is provided. Comprehensive understanding of these aspects of SCD can assist physicians in expediting patient evaluation and treatment, thus decreasing the morbidity and mortality associated with this hemoglobinopathy.** © 2016 Elsevier Inc. All rights reserved.

☐ **Keywords—sickle cell disease; acute chest; acute pain crisis; cerebrovascular accident; transfusion**

INTRODUCTION

Sickle cell disease (SCD) affects nearly 100,000 individuals in the United States, and approximately 2 million Americans carry the sickle cell trait. SCD is prevalent in persons of African, Mediterranean, Indian, and Middle Eastern descent (1–3). The sickle cell mutation is inherited in an autosomal recessive fashion; homozygotes exhibit sickle cell disease (SCD or HbSS) and heterozygotes exhibit sickle cell trait (SCT). Assuming that they have not inherited a second abnormal hemoglobin (Hb) chain, individuals with SCT are commonly asymptomatic and possess a normal lifespan, while those with SCD are predisposed to severe infections, complications associated with repetitive capillary obstruction, painful vaso-occlusive crises, and multi-system organ damage (1,2).

Complications of SCD occur secondary to the sickle cell mutation: a sixth codon substitution of the B-globin chain, replacing hydrophobic valine with hydrophilic glutamic acid, thereby causing sickling of the Hb molecule under de-oxygenated conditions. The congregation of these sickled cells results in microvascular sludging and vascular obstruction, leading to the acute manifestations (1,2).

As SCD is a component of American newborn screening, the discovery of undiagnosed SCD in the emergency department (ED) is relatively uncommon. More frequently, patients with known SCD present to the ED for evaluation secondary to sequelae of the disease after the fourth month of life (decline in fetal hemoglobin concentration) (3).

Emergency physicians are adept at managing multiple disease processes; however, given the range of

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pathophysiologic manifestations of SCD, encounters with these patients often prove challenging. This review seeks to provide emergency physicians with an improved understanding of SCD complications and an evidence-based approach to their management.

MANAGING ACUTE COMPLICATIONS OF SCD: VASO-OCCLUSIVE CRISES AND SEQUELAE OF HEMOGLOBINOPATHY

Vaso-Occlusive Crises

Cerebrovascular accident: Ischemic stroke and intracranial hemorrhage. Cerebrovascular accident (CVA), including ischemic stroke and subsequent intracranial hemorrhage due to hemorrhagic conversion of the ischemic stroke, is a major complication of SCD. Patients presenting to the ED for assessment will display symptoms that vary according to the anatomic location of the infarct or hemorrhage. Small infarcts in the adult and pediatric populations are relatively common and involve the basal ganglia and deep white matter within the anterior circulation (4). Risk factors for CVA in patients with SCD include low Hb, history of acute chest syndrome (ACS), and history of hypertension (4). The pathophysiology regarding anemia and a history of ACS as CVA risk factors is poorly understood. SCD experts hypothesize severe anemia as precipitating increased cerebral blood flow and increased cerebral flow velocity, thereby predisposing SCD patients (the majority experiencing chronic anemia) to cerebrovascular damage. Scientists also postulate the temporal association between ACS and CVAs as resulting from repetitive episodes of hypoxia in the setting of ACS. This hypoxia likely causes additional damage to cerebral vessels, previously injured by microvascular insults (5). In the assessment of adult and pediatric patients presenting with symptoms concerning for acute intracranial pathology, neuroimaging is key. Initial evaluation of the adult patient commonly includes non-contrast head computed tomography (CT), subsequently followed by CT angiography or magnetic resonance angiography (MRA) during the inpatient course.

Goals for the acute treatment of ischemic stroke in the adult SCD patient include limiting injury due to the CVA and establishing secondary prevention through the optimization of cerebral perfusion (maintenance of euglycemia and normothermia and avoidance of hypoxia) (6). Caution is advised when considering the administration of thrombolytics to adult SCD patients experiencing an acute ischemic CVA. Increased rates of intracranial hemorrhage have been reported in this patient population (6). Similar to adult patients without a medical history of SCD, antiplatelet and statin therapy should be considered after an ischemic CVA (6). In addition to the strategies mentioned for secondary CVA prevention, experts also recommend regular transfusions to maintain Hb S < 30%; however, data supporting this intervention was collected in young adults with SCD having experienced their first CVA during childhood (hence its employment in the pediatric population, as discussed later) (6).

In contrast to adults, magnetic resonance imaging (MRI) with diffusion-weighted imaging and MRA of the head and neck should be performed in pediatric patients with suspected acute ischemic stroke, as a non-contrast head CT will miss early signs of ischemic infarct (5). All pediatric patients diagnosed with an ischemic stroke thought secondary to SCD should receive intravenous (IV) fluids and undergo exchange transfusion to achieve an Hb S level of < 30% (5). This procedure should be performed in consultation with a hematologist. If an exchange transfusion cannot be arranged, a simple transfusion should be performed (5). A maximum Hb of 13 g/dL status post transfusion is the recommended target, as pediatric children with SCD may be at risk for recurrent ischemia secondary to increased blood viscosity (5). Currently, thrombolysis is not recommended in pediatric SCD patients presenting with ischemic CVAs (5). One key point that the emergency physician must consider when evaluating the pediatric SCD patient is that hemorrhagic transformation occurs in 30% of children with arterial ischemic and is frequently asymptomatic (7).

To date, there are no published studies regarding the management of hemorrhagic CVA in adult or pediatric SCD patients (6). Previously recognized efficacious treatments for acute intracranial hemorrhage in the general adult and pediatric population include reversal of anticoagulation, treatment in an intensive care unit (ICU), treatment of seizures with antiepileptic agents, and appropriate management of blood pressure (BP) (6).

While BP management in acute CVA is well addressed in adult emergency medicine literature, the management of pediatric hypertension in the setting of CVA is not as well studied. Hypertension in children, defined as BP > 95th percentile for age, within the first 72 h after ischemic stroke is associated with an increased risk of death (8). In the pediatric population, a BP goal of the 50–95th percentile for age and height, with permissive hypertension up to 20% > 95th percentile, should be targeted (6). Pediatric experts recommend use of labetolol or an angiotensin-converting enzyme inhibitor to lower BP by 25%, though renal function should be considered (6,9).

Of note, seizures are common after pediatric neurologic injury (10). Patients with persistent lethargy or altered mental status should be evaluated with electroencephalography for subclinical seizure activity (7).