Abstract:
Sickle cell disease is the most common blood disorder in the United States, affecting 100 000 people. A genetic mutation creates hemoglobin S. In the deoxygenated state, hemoglobin S polymerizes, creating sickled hemoglobin. Sickled hemoglobin causes a cascade of complex pathophysiologic events that lead to hemolysis, chronic anemia and endothelial damage. This results in clinical complications, end organ dysfunction and a shortened life expectancy. The acute nature of many sickle cell complications makes the emergency department a common setting where sickle cell patients present. Common complications (vaso-occlusive episode, fever, acute chest syndrome, stroke) and less common complications (splenic sequestration, priapism, aplastic crisis, ocular emergencies) will be discussed. Public health implications will be discussed briefly.

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Keywords:
sickle cell disease; anemia; complications; vaso occlusive crisis; vaso occlusive episode; acute chest syndrome; stroke; splenic sequestration; priapism; aplastic crisis

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Sickle Cell Disease in the Emergency Department: Complications and Management

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Sickle cell disease (SCD) is the most common blood disorder in the United States, affecting approximately 100 000 people nationwide.[1] Sickle cell disease is a genetic condition. Inheritance of the sickle cell gene creates an abnormal hemoglobin, hemoglobin S.[2] There are various sickle cell genotypes and phenotypes. The most severe type, hemoglobin SS, is the homozygous form. Other forms of sickle cell disease include hemoglobin S in combination with other variant hemoglobins such as hemoglobin C or thalassemia. Phenotype varies, even among those with the same genotype, with some having more severe disease than others. In the deoxygenated state, hemoglobin S polymerizes, creating sickled hemoglobin. Sickled hemoglobin causes a cascade of complex pathophysiologic events that lead to hemolysis, chronic anemia and endothelial damage. This results in clinical complications, end organ dysfunction and a shortened life expectancy. Various sickle cell complications that may present in the emergency department will be discussed.

In 2014, the National Heart, Lung, and Blood Institute (NHLBI) published updated guidelines, Evidence-Based Management of Sickle Cell Disease.[3] One of the more notable guidelines is the recommendation to offer hydroxyurea to all sickle cell patients

age 9 months and older regardless of disease severity to reduce complications. Hydroxyurea is the only widely available Food and Drug Administration (FDA) approved disease-modifying medication for sickle cell anemia. Hydroxyurea increases fetal hemoglobin, which has anti-sickling properties and reduces disease complications and mortality.[4,5] The NHLBI guidelines increased hydroxyurea use among sickle cell patients, therefore emergency care providers are likely to encounter patients on hydroxyurea in the emergency department. The medication has a favorable side effect profile with transient myelosuppression being the most common side effect.[4] Treatment of acute sickle cell complications does not need to be tailored to a patient's use of hydroxyurea.

Stem cell transplant is currently the only curative option for sickle cell patients. The field of stem cell transplantation for sickle cell patients has evolved over the last 2 decades. The expansion of stem cell transplant to include matched unrelated donors and half-matched (haplo-identical) family members in addition to matched siblings makes this a viable treatment option for more sickle cell patients. Matched sibling bone marrow transplantation for sickle cell anemia achieves high success rates with >90% 5 year overall survival.[6] Matched unrelated bone marrow transplantation for this group has 79% overall survival at two years.[6] Newer potentially curative options including gene therapy are currently under investigation. Details are outside of the scope of this article.

EMERGENCY DEPARTMENT UTILIZATION

The acute nature of many sickle cell complications makes the emergency department (ED) a common place sickle cell patients present. Programs such as the Center for Disease Control and Prevention's (CDC) Sickle Cell Data Collection Program contain ED utilization data. Data is primarily available at the state level although there are plans to expand to comprehensive national data collection.[7] A recent study by Paulukonis et al. analyzed ED utilization by pediatric and adult sickle cell patients in California between 2005 and 2014.[8] There were 90 904 ED visits during the study period and 2.1 annual mean visits per person.[8] The frequency of ED visits varied by age group with young adults having higher ED utilization than children, 3.0 mean annual visits for patients 18–30 years of age, compared to 0.5 mean annual visits for patients ages 1–9 years and 0.8 mean annual visits for patients ages 10 to 17 years. This trend is similar to previously published data by Brousseau et al. on ED utilization in 8 states.[9] Data on prevalence of pediatric sickle cell patients with high ED utilization showed approximately 5% of patients under age 20 had 4–10 ED visits in a single year and< 1% of patients had >11 visits in a year.[8]

INTERPRETATION OF COMPLETE BLOOD AND RETICULOCYTE COUNTS

Most sickle cell patients in the ED should have a complete blood count (CBC) and reticulocyte count in additional to other labs as indicated. It will be useful to know the patient's baseline hemoglobin which can be obtained from the patient, their hematologist or primary provider. Typical ranges for baseline hemoglobin are 6-8 g/dl for HbSS, 10-15 g/dl for HbSC and 9-12 g/dL for HbSBeta+ thalassemia, though patients with HbSS on hydroxyurea may achieve a baseline hemoglobin up to 10-11 g/dL.[3] Reticulocytes are young red blood cells (RBCs). The reticulocyte count is a useful indicator of how well the body makes new RBCs. This is important in a disease such as sickle cell where chronic hemolysis and increased turnover of RBCs requires an active production of new RBCs. Typically, sickle cell patients have elevated reticulocyte count at baseline and further elevation during vaso-occlusive pain crisis. Low reticulocyte count can be seen in conditions such as aplastic crisis, and may be notice for concern.

RECOGNITION AND MANAGEMENT OF COMMON COMPLICATIONS

Vaso-Occlusive Crisis (Pain Crisis)

Chief complaint: sickle cell patient with arm and leg pain.

Vaso-occlusive crisis (VOC), also known as vaso-occlussive episode or pain crisis, is the most common acute complication of sickle cell disease. A study by Gill et al. observed the natural history of a pediatric sickle cell cohort.[10] Patients had a pain crisis as early as within the first year of life and half of HbSS patients experience their first pain crisis by age 4.9 years. Intravascular sickling and resultant tissue and bone infarction cause VOC.[2] Pain typically occurs in the extremities but may occur in other locations. While some patients have visible discomfort during a VOC, others with severe pain may lack the typical physiologic and behavioral manifestations of pain. This phenomenon is seen in other conditions with recurrent pain.[11] Documented autonomic nervous system dysfunction in sickle