CE

1.5 ANCC Contact Hours

Sickle Cell Disease

Bone, Joint, Muscle, and Motor Complications

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Sickle cell disease (SCD) is a group of inherited disorders caused by a mutation of the hemoglobin gene, resulting in the formation of abnormal, sickle-shaped red blood cells. It is a lifelong condition characterized by anemia, vaso-occlusion, and decreased blood flow to vital tissues. Sickle cell disease affects every major organ and significantly reduces life expectancy of the affected individuals. Patients with SCD are at an increased risk for developing musculoskeletal complications that decrease quality of life and contribute to the significant burden of the disease. Understanding these complications, as well as the genetics, pathophysiology, and epidemiology of SCD, will assist orthopaedic nurses in providing evidence-informed care.

Sickle cell disease (SCD) is a group of inherited disorders that have multiple-system involvement (National Heart, Blood and Lung Institute [NHBLI], 2018). Abnormal sickle hemoglobin, known as hemoglobin S, is found in individuals with SCD. Per NHBLI (2014),

> Sickle cell anemia (SCA) refers to the clinically similar disorders HbSS or HbSβ0-thalassemia. Sickle cell disease (SCD) refers to all disease genotypes, including SCA and compound heterozygous disorders, such as HbSC, HbSD, and HbSβ+-thalassemia. The carrier state for hemoglobin S (HbAS or sickle cell trait) is not a form of SCD. (p. 11)

Sickle cell disease affects every major body system and increases the risk of multiple complications (see Table 1) and early death.

Genetics of Sickle Cell Disease

Sickle cell disease is a genetic condition occurring due to a mutation of the hemoglobin β-chain gene, resulting in abnormal sickle cell hemoglobin (Ware, de Montalembert, Tshilolo, & Abboud, 2017). The most severe form of SCD is sickle cell anemia (i.e., hemoglobin SS or HbSβ0-thalassemia). Individuals with the hemoglobin SS form of sickle cell anemia inherit two abnormal hemoglobin S genes, one from each parent, acquired via autosomal recessive inheritance (Ware et al., 2017). Some other forms of SCD include hemoglobin SC, hemoglobin SβO thalassemia, hemoglobin Sβ+ thalassemia, hemoglobin SD, and hemoglobin SE (NHBLI, 2018).

Sickle Cell Disease Pathology

When exposed to conditions of low oxygen, red blood cells that contain mutated hemoglobin become inflexible and assume a sickle shape (Piel, Steinberg, & Rees, 2017). The increased rigidity of sickle red blood cells impedes blood flow through small capillaries that results in blockage of blood vessels (i.e., vaso-occlusion) and impaired oxygen supply to vital organs (Piel et al., 2017). Repeated sickling causes the cells to become fragile and subject to easy destruction (i.e., hemolysis), which leads to chronic anemia (Ware et al., 2017). Sickle cell disease affects every major organ system, causes significant morbidity, and shortens the life expectancy of the affected patients by approximately 30 years (Benenson, Jadotte, & Echevarria, 2017).

Epidemiology of Sickle Cell Disease

Per the Centers for Disease Control and Prevention (CDC), an estimated 100,000 Americans have SCD. Sickle cell disease occurs in approximately one in 365 African Americans and one in 16,300 Hispanic Americans. Although SCD is more commonly found in individuals with ancestry from sub-Saharan Africa, the Mediterranean region including Greece, Italy, and Turkey, the Middle East including Saudi Arabia, South Asia, South America, the Caribbean, and Central America, it is not exclusively limited to those regional population groups (CDC, 2017).

Sickle Cell Disease Diagnosis

Sickle cell disease is diagnosed via a blood test that checks for hemoglobin S (National Human Genome Research Institute, 2016; NHBLI, 2018). Most people in

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Table 1. Sickle Cell Disease-Related Complications

System	Common Complications
Blood	Anemia
Central nervous system	Stroke Cognitive problems
Lungs	Acute chest syndrome Pulmonary embolism Pulmonary hypertension
Heart	Cardiomyopathy
Kidneys and genitalia	Renal infarction Chronic renal insufficiency Renal medullary carcinoma Priapism
Bones/joints	Vaso-occlusive bone pain Dactylitis Osteoporosis Avascular necrosis Osteomyelitis Gross motor delay Mobility impairment
Spleen	Splenic infarction Impaired immunity (bacterial infections, sepsis)
Eyes	Retinopathy
Skin	Chronic leg ulcers
Mental	Anxiety Depression Sleep disturbances Poor coping

Note. Data from Natrajan and Kutlar (2015); Piel et al. (2017).

the United States with SCD are now identified via newborn screening. If the infant screens positive for SCD, they are retested to confirm the diagnosis. Prenatal testing is possible. Early diagnosis and evidence-based treatment help prevent complications (NHBLI, 2014). Comprehensive SCD treatment centers are located throughout the United States to ideally provide lifelong specialty care to individuals with SCD and their families.

Bone, Joint, Muscle, and Motor Complications in Sickle Cell Disease

Significant musculoskeletal complications may occur in individuals with SCD including vaso-occlusive episodes and bone pain, dactylitis, growth retardation and atypical skeletal development, osteomyelitis and septic arthritis, bone demineralization, and motor/mobility impairment.

Vaso-Occlusive Episodes and Bone Pain

Vaso-occlusive pain episodes are the hallmark of SCD that is most commonly manifested by bone pain. Individuals with SCD experience recurrent pain episodes, and up to 30% of patients report daily symptoms (Smith et al., 2008). Sickle cell disease pain may last for hours to days, and some SCD individuals are never completely pain-free (Smith et al., 2008). Sluggish blood flow through the bone marrow and a relatively low oxygen environment of the bone tissue increase the likelihood of red cell sickling and vaso-occlusion (Natrajan & Kutlar, 2015). Repeated vaso-occlusion leads to inadequate blood supply to the bone, bone infarction (i.e., tissue death), and bone pain. Typically, patients present with deep-seated pain in the extremities and low back that may range from mild to excruciating (Natrajan & Kutlar, 2015). Symptoms may be triggered by dehydration or infection, although in most cases, no precipitating factors are identified. Sickle cell pain often becomes chronic, resulting in poor quality of life (Yawn et al., 2014). Pain episodes can occur in early infancy and into adulthood and are a major cause of hospitalization for individuals with SCD (Yawn et al., 2014).

Vaso-occlusive pain is often unrecognized, underrated, and undertreated by health care professionals. Perceived discrepancies between patient behavior and pain scores have been documented in the care of patients with SCD and lead to mistrust between patients and their providers (Zempsky, 2010). Patients are often perceived as drug seekers or substance abusers, who inappropriately utilize healthcare services, despite a lack of evidence to support this belief (Benenson et al., 2017). In fact, less than 10% of patients with SCD are addicted, a percentage comparable for persons with other diseases (Natrajan & Kutlar, 2015).

Patients with SCD who are perceived as "drug addicts" are usually undertreated for pain. Treatment with inadequate doses of opioids leaves the patients with the alternative of either suffering or asking for more medications, complaining about their treatment, and perhaps visiting other healthcare facilities for pain management (Shapiro, Benjamin, Payne, & Heidrich, 1997). These behaviors (known as pseudo addiction) are a consequence of unsatisfactory pain relief. When viewed with an underlying suspicion of substance abuse, however, these behaviors can be interpreted as proof of the underlying perception (Shapiro et al., 1997). From the patient standpoint, however, inadequate treatment of pain is a cause of needless suffering and negative attitudes toward healthcare professionals and institutions.

Early and aggressive management of acute sickle cell pain may reduce the development of pseudo addiction and chronic pain (Yawn et al., 2014). Patients presenting with vaso-occlusive pain require rapid triage, evaluation, and administration of analgesics. The American Pain Society and the NHLBI urge that patients with SCD receive an initial analgesic within 30 minutes of arrival (Tanabe, Hafner, Martinovich, & Artz, 2012). Although there is no standard protocol of pain management, timely administration of pain medications is an important benchmark of healthcare quality and a key outcome from a patient perspective (Tanabe et al., 2012).

It is important that the preferences and needs of the individual with SCD seeking care be heard, respected, and responded to with the same attention as applied to any other individual with serious physiological pain (Yawn et al., 2014). Pain management should include parenteral opioids for severe pain administered in a timely manner, guided by an individualized treatment protocol written by the patient with his or her practitioner or an institutional SCD-specific protocol

when an individual protocol is not available (Yawn et al., 2014). Frequent pain reassessment with appropriate administration of medications until pain relief is obtained is important. Opioid side effects, especially depression of respiratory drive, should be monitored and treated without delay. Oral or intravenous hydration should be initiated to minimize the effect of sickling (Natrajan & Kutlar, 2015). Routine use of oxygen supplementation during an acute vaso-occlusive pain episode is not indicated unless there is evidence of low oxygen saturation. There is no role for routine blood transfusion in the setting of an isolated pain crisis. Transfusion may be necessary if vaso-occlusive pain is accompanied by another complication such as stroke or acute chest syndrome (Yawn et al., 2014). Patients with acute pain are better managed in specialty centers and units dedicated to care of patients with SCD (Natrajan & Kutlar, 2015). A multidisciplinary team that includes primary care providers, hematologists, social workers, case managers, and school nurses may improve SCD pain management, especially when chronic pain is an issue (Yawn et al., 2014).

Despite significant burden of the disease, the majority of patients with SCD manage their pain at home. The pain treatment plan should be tailored to the individual and may vary depending on the daily symptoms, opioid tolerance, and comorbidities such as renal insufficiency (Yawn et al., 2014). Access to short-acting and long-acting opioids at home should be part of the SCD pain plan. Alternative therapies such as relaxation, breathing exercises, yoga, and self-hypnosis may be helpful (Williams & Tanabe, 2016). Some patients with SCD may benefit from hydration and local heat applications. Ice packs and cold compresses should be avoided because cold may precipitate sickling.

Patients with severe and frequent episodes of vaso-occlusive pain are candidates for hydroxyurea therapy (Yawn et al., 2014). Hydroxyurea increases the level of fetal hemoglobin. Fetal hemoglobin does not contain β-chains and therefore does not sickle. Hydroxyurea therapy substantially reduces the frequency of painful vaso-occlusive episodes and the need for hospitalizations in adults and children with SCD (Yawn et al., 2014). When taken orally once daily, hydroxyurea is well tolerated but may cause a decrease in white blood cells and platelets (Yawn et al., 2014). Close monitoring of blood cell count (by obtaining a complete blood cell count) is necessary, and a reduction in dose or temporary discontinuation of the hydroxyurea medication is needed if neutropenia (low white blood cell count) or thrombocytopenia (low platelet count) occurs.

Recurrent acute and chronic pain is commonly associated with psychosocial complications such as sleep disturbances, anxiety, and depression. Up to 30% of patients with SCD are diagnosed with depression, which is five times as high as that of the general population (Adam et al., 2017). Many patients commonly report low self-esteem and feeling of hopelessness as a result of pain, hospitalizations, and loss of schooling (for children) or employment (for adults) (Anie, 2005). Chronic pain and excessive burden of the disease negatively affect health-related quality of life of individuals with SCD, which closely resemble quality-of-life outcomes for patients undergoing dialysis (Adam et al., 2017). Mental health conditions contribute to poor disease self-management, low adherence to medical directives, and decreased capacity to cope with pain (Adam et al., 2017). Sickle cell disease-affected individuals with recurrent or chronic vaso-occlusive pain should be screened for psychiatric complications and psychosocial distress. They may benefit from interventions such as psychoeducation and cognitive-behavioral therapy (Anie, 2005).

Dactylitis

Along with fatigue or irritability from anemia and jaundice from hemolysis, dactylitis is one of the early indications of SCD (NHBLI, 2018). Dactylitis or hand and foot syndrome typically occurs in young children between 6 months and 7 years of age but may also occur later, beyond the earlier noted age points (Vaishya, Agarwal, Edomwonyi, & Vijay, 2015). Painful, warm, erythematous swelling of one or both hands and/or one or both feet follow microinfarcts. Fever and increased white blood cells may also be present. Dactylitis is generally self-limiting with a usual resolution within 1 month of onset. Treatment includes bed rest, elevation, immobilization, pain relief, and mild heat. Recognition of safety concerns with pain relief (e.g., increased adverse effect risk) and application of heat (e.g., increased thermal injury risk) in young children are important.

Growth Retardation and Atypical Skeletal Development

Children with SCD often experience growth impairment and skeletal immaturity (Vaishya et al, 2015). These complications are related to bone marrow hyperplasia and subsequent ischemia as well as localized anoxic events that precede epiphysis closure and may result in long bone asymmetry. Frontal bossing due to expansion of the skull bones related to increased hematopoietic activity is often observed (Vaishya et al, 2015).

Children and adolescents with SCD tend to be shorter and weigh less than their nonaffected peers. Anemia may cause infants to feed poorly due to fatigue, and the resultant impaired nutritional intake may affect overall growth (NHBLI, 2018). Hydroxyurea, which is used to decrease crises in individuals with severe SCD, supports growth and development in school-aged and young children (Agrawal, Patel, Shah, Nainiwal, & Trivedi, 2014).

Osteomyelitis and Septic Arthritis

Osteomyelitis (i.e., infection of the bone) is a common complication of SCD, with a prevalence of 12% (Natrajan & Kutlar, 2015). Decreased blood flow to the bone in combination with impaired ability to fight infections due to splenic infarction contributes to the development of this condition (Natrajan & Kutlar, 2015). *Salmonella* and other gram-negative bacteria are the most common causes of osteomyelitis in patients with SCD (Natrajan & Kutlar, 2015). Septic arthritis is less prevalent. The clinical presentation of osteomyelitis and septic arthritis may be similar to a vaso-occlusive pain episode (Berger, Saunders, Wang, & Friedman, 2009). Infectious episodes are more likely to be associated with a prolonged duration of fever, swelling, and limited range of motion of the

limb (Berger et al., 2009). No single laboratory or imaging test reliably differentiates osteomyelitis from vaso-occlusive episode, and a high level of suspicion is required to make the diagnosis (Berger et al., 2009). The treatment involves prolonged therapy with broad-spectrum antibiotics and possible surgical debridement.

Avascular Necrosis of the Femoral and Humeral Head

Osteonecrosis of the femoral and humeral head (also known as avascular necrosis) is a well-known complication of SCD (Ravikanth, Abraham, & Alapati, 2017). This condition is a result of infarction (i.e., tissue death) of articular surfaces of long bone due to compromised blood supply (Yawn et al., 2014). Avascular necrosis occurs in approximately 10% of patients with SCD (Yawn et al., 2014). Patients present with chronic joint pain, with a progressive decrease in range of motion of affected joints. The main manifestation of osteonecrosis of the femoral head is pain with weight-bearing. Most untreated patients will progress to femoral or humoral head collapse and permanent disability (i.e., decreased mobility, abnormal gait, and limb-length discrepancies) within 5 years (Natrajan & Kutlar, 2015). The diagnosis is made by bone imaging. The initial therapy is usually conservative and includes pain control, reduced weight-bearing, and physical therapy. Core decompression that entails removal of necrotic tissue, with or without bone graft to fill the "cored area," may be attempted (Ravikanth et al., 2017). Joint replacement is generally delayed if possible, given the high rate of artificial joint failure and the increased risk of surgery for individuals with SCD (Ravikanth et al., 2017).

Bone Demineralization

Osteopenia (i.e., decreased bone density) is prevalent in patients with SCD (Yawn et al., 2014). The cause of osteopenia is not completely elucidated but likely to be multifactorial. More than 50% of patients with SCD are vitamin D deficient (Natrajan & Kutlar, 2015). Fractures of the long bones are commonly underdiagnosed, and self-reported rates of fractures in young adults with SCD are high (Natrajan & Kutlar, 2015). High doses of vitamin D supplementation have resulted in improvement in chronic pain and higher levels of physical activity.

Motor Development and Mobility

Brain insult may have a negative impact on an individual's motor development and mobility. Many children with SCD suffer a brain insult between 2 and 9 years of age (NHBLI, 2018). Up to 24% of individuals with SCA have a clinical stroke that may affect balance, strength, and walking before turning 46 years of age.

Silent strokes are the most common cerebral vascular accident in children with SCD. Silent stroke–caused brain injury may affect decision-making and learning. Silent strokes occur in approximately 28% of children with SCD by 6 years of age, with 37% of children with SCD affected by silent stroke by 14 years of age (Kwiatkowski et al., 2009). Minimally, annual stroke prevention screening via transcranial Doppler ultrasound scan for children with SCD should commence at 2 years of age (Mack & Thompson, 2017).

Infants and toddlers with SCD are at high risk for neurodevelopmental delay including motor delay (Glass et al, 2013). Early, intensive, and extended developmental monitoring is warranted. Referral for early intervention services including physical therapy should be considered.

Nursing Interventions of Patients With SCD With Bone, Joint, and Motor Complications

Nursing interventions for individuals with SCD will vary with patient and family preference, acuity, and healthcare setting. Specific nursing interventions for musculoskeletal complications are outlined in Table 2. Patients presenting with acute vaso-occlusive pain should be quickly evaluated in an unbiased manner. Pain should be assessed using standardized age-appropriate pain assessment tools (e.g., a numeric self-report scale from 0 to 10, visual analog scale 0–10). Neither patient behavior nor other clinical variables (e.g., heart rate and blood pressure) should be used to determine the intensity of vaso-occlusive pain. Nurses should appreciate the severe and unpredictable nature of the pain and the urgent need for effective pain relief. Unrelieved acute pain is debilitating and dehumanizing and can lead to chronic pain, pseudo-addiction, and poor quality of life. Nurses should advocate for care that is based on evidence-based principles and not on negative anecdotal experiences. Development of an institutional SCD-specific pain treatment protocol should be a nursing service priority. Rapid triage, timely and adequate opioid dosing, and frequent pain reassessment should be components of the protocol (Yawn et al., 2014). Consistent use of the protocol may reduce provider bias and facilitate patient care during vaso-occlusive episodes.

Acute and chronic vaso-occlusive pain is often managed at home. Nurses should encourage patients to follow an individual pain treatment plan that may include opioid analgesics and nonpharmacological adjuvant measures (Yawn et al., 2014). Nonadherence to the individual pain treatment plan and hydroxyurea therapy may lead to poor pain control and frequent utilization of hospital services. Nurses should conduct medication reconciliation, provide parent/patient education, and reinforce medication adherence at all healthcare encounters (Loiselle et al, 2016). Multicomponent interventions may be needed to promote medication adherence and should include routine monitoring, support to prevent mistakes, assessment of side effects, and education to improve understanding of medication risks and benefits (Walsh et al., 2014). Poverty and vehicle access problems may also affect medication adherence (Hensley et al, 2018).

Home self-care is an important aspect of managing SCD. Self-care contributes to individual plan management and thus pain crises prevention (Matthie, Jenerette, & McMillan, 2015). Nurses should equip pa-

Table 2. Nursing Interventions for Patients With SCD With Bone, Joint, and Motor Complications

Musculoskeletal Complications	Nursing Interventions
Vaso-occlusive crisis (hospital care)	Provide a thorough and timely assessment of pain using standardized pain assessment tools
	Rapidly (within 30 minutes) initiate treatment with analgetics, including parenteral opioids if indicated
	Frequently monitor respirations, oxygen saturation, blood pressure, and heart rate for patients receiving opioids
	Reassess pain intensity frequently
	Provide adequate hydration (oral or intravenous) and monitor fluids input and output
	Upon discharge, develop an individual pain treatment plan
	Arrange outpatient follow-up at the time of discharge
	Reinforce seeking immediate emergency care for fever, shortness of breath, and chest pain
	Advocate for patients with SCD and help cultivate a positive climate in the healthcare setting
	Participate in the development of an institutional SCD-specific pain management protocol
Vaso-occlusive crisis (home care)	Encourage follow-up for individual pain treatment plan
	Encourage adequate hydration and avoidance of exertion, temperatures changes, and high altitude
	Recommend nonpharmacological adjuvant therapies to treat pain (heat applications, yoga, meditation, mindfulness)
	Recognize emotional and mental health complications of chronic pain and refer to psychological interventions as needed
	Encourage keeping appointment with healthcare providers
	Routinely monitor adherence to medications, address side effects, and educate about importance of medications
Growth retardation and mobility	Closely monitor development in infants, children, and adolescents
	Refer for developmental and other supportive services as needed
Osteomyelitis and septic arthritis	Recognize signs of osteomyelitis and septic arthritis and refer for medical care
	Administer antibiotics as soon as diagnosis has been established
	Encourage completion of full course of antibiotics
	Follow-up response to antibiotic therapy (improvement in pain and mobility)
Bone demineralization	Encourage vitamin D supplementation as prescribed
Avascular necrosis	Recognize signs of avascular necrosis and refer to the medical care
	Treat avascular necrosis with analgetics and refer to an orthopaedic surgeon for assessment and follow-up
	Educate about using assistive devices if indicated

Note. SCD = sickle cell disease. Data from Natrajan and Kutlar (2015); Vaishya et al. (2015); Yawn et al. (2014).

tients with resources necessary to participate in their disease management. Nurses should encourage maintaining regular checkups, receiving recommended vaccinations, staying hydrated, getting adequate rest and nutrition, and avoiding temperature extremes (Matthie et al., 2015). Sickle cell disease-specific strategies to improve self-care should be utilized and may include referring to social support and advocacy groups (e.g., Sickle Cell Disease Association of America), encouraging of journaling to develop self-awareness, providing SCD-related information, and coordinating care across healthcare settings (Matthie et al., 2015).

Impaired functional mobility and delayed growth and development should be a focus of nursing care of patients with orthopaedic complications. Nurses should use their knowledge to assess motor function and motor development and refer to physical/occupational therapy when needed. Home adaptations and use of assistive devices (canes, walkers) may improve level of independence and quality of life for individuals affected by musculoskeletal comorbidities.

Chronic and poorly controlled vaso-occlusive pain and the burden of SCD comorbidities can often affect psychological well-being of patients with SCD. Nurses should recognize that poor mental health can lead to medications nonadherence, more frequent pain episodes, and more healthcare visits. Nurses should initiate a discussion with patients about depressed mood, feelings of isolation, uselessness, and helplessness. They should proactively assess coping strategies and available sources of social support. Screening for depression and anxiety is warranted so that necessary referral for specialty care (e.g., mental health professionals) can be initiated.

Patients with SCD may have complex social needs that are often unmet. They may include challenges with transportation, clinic appointment scheduling, filling prescriptions, and insurance coverage (Smith, Johnston, Rutherford, Hollowell, & Tanabe, 2017). Disease-related complications reduce employment options, which, in turn, trigger economic stress and the loss of health insurance. These problems can affect a patient's ability to obtain necessary medical care and may lead to poor disease management. Nurses are ideally situated to have discussions with patients regarding difficulties they experience so that appropriate referrals (e.g., social services, case management) can be initiated. Nurses can successfully partner with community health workers, who can provide social support, navigation of health systems, and counseling. Nursing champions with the knowledge and interest in SCD can act as liaisons between providers, community, and patients.

Conclusion

Individuals with SCD experience multiple-system complications including those related to the musculoskeletal system. Orthopaedic nurses who understand these complications will be better equipped to provide evidence-informed care for this frequently undertreated population.

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