BRIEF CLINICAL UPDATE

Primary Preventative Care for Patients with Sickle Cell Disease

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Introduction

Access to comprehensive quality care in patients with sickle cell disease (SCD) remains very challenging. The CDC states the average lifespan of an individual with sickle cell is more than 20 years shorter than the national average.[1] This is especially worrisome in Los Angeles where it has been reported that the average lifespan of sickle cell patients is 10 years shorter than national average.[2] Individuals with SCD face many difficulties navigating the health care system, frequently presenting to emergency departments for medical care that may be better suited in an established continuity outpatient setting. Sickle cell is a complex multisystem disease that affects multiple organ systems and places individuals at risk for serious morbidities and early mortality. Patients with SCD have better outcomes when cared for in a medical home that has expertise, knowledge, and resources such as a dedicated sickle cell center. [3] While access to specialist and comprehensive care remains challenging, this brief clinical update will review general screening illuminating specific goals and considerations following patients with SCD.

Phenotypes

Sickle Cell Disease (SCD) is an inherited group of disorders of the beta hemoglobin unit that have the structural variant of (Hb S); a single point mutation of (Glu à Val).[4] This can present as either the homozygous mutation (Hb SS) or compound heterozygosity with another beta globin variant such (sickle-beta thalassemia, Hb SC disease).[5] These mutations may lead to organ dysfunction due to vaso-occlusion episodes, as well as hemolytic anemia. Sickle cell trait is generally considered a benign carrier condition, however, can lead to sickling episodes with certain intense conditions such as hypoxia and very strenuous exercise.

Vaccinations

Individuals with SCD are considered immunocompromised due to repeated vaso-occlusive infarctions of the spleen that occurs during infancy.[6] Because of functional asplenia, compliance with immunization is important aspect of care as patients with SCD have increased risk for encapsulated systemic bacterial infections including: s. pneumoniae, n. Meningitidis, and HiB.[7] In addition to standard immunization practices for children and adults,[8] Men B is recommended with a booster dose 1 year after series completion and every 2-3 years thereafter.[9] Adults with SCD are recommended to receive updated meningococcal vaccination every 5 years.[7] Additionally, Pneumococcal vaccinations are recommended and specific serotype administration can be viewed using the tool PneumoRecs VaAdvisor.[10]

General Screening Considerations in Sickle Cell Care

As children are especially susceptible to encapsulated bacteria, prophylactic penicillin is recommended for all children with SCD from the age of 3 months to at least 5 years. Further antibiotic prophylaxis can be considered after 5 years of age on case-by-case basis. Abdominal examination with special attention to the spleen, can be helpful in counseling family regarding splenic sequestration.

Although there are newer and emerging therapies, Hydroxyurea is the first line medication that has been shown to reduce vaso-occlusive episodes, hospitalization, need for blood transfusions, acute chest syndrome and mortality.[11] Children at 9 months can start hydroxyurea[12] with frequent monitoring by Hematology or a provider familiar with sickle cell treatment. Three month follow up intervals are recommended for patients receiving disease modifying therapy.

One of the most common complications of SCD is silent cerebral infarction. Studies report 10% of children with sickle cell anemia experience strokes that have been associated with lifelong cognitive impairment. These may be precipitated by illness, acute chest syndrome or other vaso-occlusive crisis. Children with SCD are recommended to undergo annual screening, with transcranial doppler from age 2 to 16 years. If abnormal transcranial doppler findings are identified, referral for chronic transfusion therapy may be recommended for stroke prevention. A CDC study of children and adolescents found less than half of children and adolescents underwent stroke screening with approximately half on hydroxyurea.[1] Obtaining a baseline MRI/MRA of the brain may be indicated in adulthood.

Other sequalae of strokes include screening for neurocognitive delay. At least 38% of patients with SCD had positive screening suggestive of cognitive impairment.[4] However, there is no consensus regarding screening, modality. It is advisable to regularly screen for depression given the morbidities associated with sickle cell disease.[13]

Acute Ocular complications include SCD Proliferative Sickle Cell Retinopathy (PSR). Risk is increased in patients on iron chelators. Other ocular pathologies that may result in permanent vision loss include hyphemas and central retinal artery occlusion (CRAO).[12] Retinopathy screening is recommended beginning at age 10, with follow up evaluations every 1 to 2 years.

Acute kidney failure and kidney injury are prominent concerns for patients with sickle cell. Some estimates report 4-18% of all sickle cell patients have some degree of chronic kidney disease. A retrospective cohort study of nearly 3,000 Medicaid-enrolled adults with SCD in California reported a form of CKD in 26% of the population. Significant barriers of access were noted for both hematology and nephrology care. Of patients with CKD, only 48% met with a hematologist, and 61% were not evaluated by a nephrologist, documenting ongoing barriers accessing care.[14] In addition to routine lab work, it is important to screen for proteinuria, one of the earliest signs of renal damage. Annual screening for proteinuria is recommended starting at age of 10 or earlier if on nephrotoxic agents (such as chelators). If microalbuminuria is identified, a 24-hour protein collection is recommended. If abnormalities are found, a referral to Nephrology with consideration for ACEi can be considered.

Sickle Cell Specific Related Considerations

Routine screening includes monitoring for blood pressure goals.[11] Transthoracic echocardiograms and pulmonary function tests are not routinely recommended in the absence of symptoms, but are advised for patients with shortness of breath, acute chest syndrome, syncope or concerns for pulmonary hypertension. Patients with chronic blood transfusions or iron chelation therapy are at increased risk for end-organ iron deposition. Transthoracic echocardiogram and/or cardiac MRI may be warranted, especially if symptomatic. Additionally, if there is concern for iron deposition, Liver MRI with iron quantification may be indicated.

Pain is frequently why patients present to the Emergency Department. It is important to address chronic pain and create an individualized chronic pain plan. Conservative measures are recommended including NSAIDs, hydration, and physical therapy. Special considerations in patients with SCD include: low bone mineral density with increased risk of fracture due to inflammation, malabsorption or impaired blood flow.[15] Screening DEXA scan may be considered in adult patients especially with musculoskeletal concerns. Osteonecrosis is a common complication of SCD with impaired blood flow to susceptible joints and can lead to degenerative arthritis. Some report estimated prevalence of 10-30% which increases with age. Advanced disease may result in hip replacement surgery.[16] Monitoring for osteomyelitis and septic arthritis is needed given functional asplenia.

Patients with SCD are encouraged to have a reproductive life plan, including testing partners and referring to genetic counseling. Progestin-only OCPs, Levonorgestrel IUDs and barrier methods are preferred in patients with SCD. However, combined hormonal contraceptive pills may be used in patients with SCD if benefits outweigh risks. If Priapism is a concern, Urology consultation is suggested but increased hydration may be helpful.

Conclusion

Sickle cell is a complex multisystem disorder that requires equitable and comprehensive medical care. Patients with SCD in California and the Los Angeles area are especially vulnerable with a lower life expectancy than the national average for sickle cell patients. One study reported short term air pollution exposure in Los Angeles may trigger hospitalizations, given association with oxidative stress, vasoconstriction and inflammation.[17] While SCD remains a very challenging disease, new therapies show promising results. We need to reduce health disparities and improve access to care. We know that better patient outcomes are possible with comprehensive and equitable care.

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