Management of Fever in Pediatric Sickle Cell Disease Patients

Background
Sickle cell disease (SCD) is a genetic blood disorder that results in the formation of abnormal hemoglobin S within the red blood cell. This abnormal hemoglobin results in stasis of flow in the spleen, resulting in hypoxic damage, fibrosis and eventual autosplenectomy, typically by age 5. Autosplenectomy results in compromised immune function and increased risk of serious bacterial infections, particularly with encapsulated organisms (S. pneumoniae, N. meningitides, H. influenzae type b, S. typhi). Serious bacterial infections carry the risk of progression to sepsis, shock and death. A rapid diagnostic workup and the rapid administration of empiric broad-spectrum antibiotics are critical to prevent serious infections in this patient population.

Definitions
- **Fever**: a temperature of > 38.5 C (>101 F). NOTE: A subjective (tactile) fever is acceptable for the definition of fever.
- **Sickle Cell Disease**: A group of inherited red blood cell disorders including HgSS, HgSC, HgSE and Hgb Sβ-thalassemia types that predispose patients to anemia, infection and other complications.

Target Population and Inclusion Criteria
This pathway should be used for patients > 6 months of age with SS, SC, SE or Sβ-thalassemia sickle cell disease who have a temperature ≥ 38.5°C.

Patients eligible for outpatient management:
- Non-toxic appearing
- < 40° C
- No history of sepsis
- No infiltrate on chest radiograph
- No hypoxia
- Labs at baseline
- WBC < 30,000
- No social concerns (reliable follow up, access to transportation, at least 1 functioning telephone number)
Evaluation

1. General: Assess stability
   a. Vital signs, mental status, respiratory and circulatory status
   b. Place on cardiorespiratory monitor with pulse oximetry

2. History
   a. Duration of fever
   b. Presence of other symptoms
   c. Hydration status
   d. Contact hematologist on call: Baseline hemoglobin
   e. Medical history: SCD complications, previous admits/ICU
      admits, splenic sequestration/splenectomy, last transfusion,
      last antibiotics
   f. Medications: Penicillin prophylaxis, hydroxyurea, immuni-
      zation status

3. Physical Exam
   a. Vital signs
   b. General appearance: jaundice
   c. Respiratory
   d. Circulatory
   e. Abdomen (spleen size)
   f. Neurologic
   g. Signs of focal infection

4. Diagnostic Evaluation:
   a. CBC with differential and reticulocyte count
   b. Blood culture
   c. Electrolytes
   d. Liver function tests
   e. Type and Screen
      i. If suspected splenic sequestration, acute chest
         syndrome pale, persistent tachycardia, ill appearing,
         aplastic crisis (reticulocyte count < 1%)
   f. Chest Radiograph
      i. A CXR is indicated if the patient has any of the following
         signs or symptoms to rule out acute chest syndrome
         (ACS). ACS syndrome is the leading cause of death in
         SCD. Diagnosing and treating quickly is imperative.
         1. Chest pain
         2. Shortness of breath
         3. Cough
         4. Hypoxia
   g. Respiratory Viral Panel
      i. If suspected viral illness
         1. Patients testing positive for influenza should be
            treated with Oseltamivir
   h. Urinalysis and Culture
      i. If clinical suspicion, history of urinary tract infection
         or renal anomaly or appropriate age range

Treatment Recommendations

Goal of antibiotic administration within 1 hour of presentation.
All sickle cell patients with fever should be discussed with the
pediatric hematology attending on call (617-636-5114).

1. Administer ceftriaxone (50 mg/kg, max 1 g) as soon as the
   blood cultures and labs are obtained. Do NOT wait for the lab
   results to administer the antibiotic.

2. In septic appearing patients, add Vancomycin (15 mg/kg/
   dose) to the empiric treatment.

3. In suspected ACS, add azithromycin 10 mg/kg to the empiric
   treatment.

4. Antibiotics are to be given to all SCD patients who present
   with fever even if they are “well appearing.”

5. Administer IV fluids and other supportive medications as
   indicated by the patient’s clinical presentation.

6. Use caution with IVF administration if suspected acute chest
   syndrome or splenic sequestration.

Admission Criteria

Consideration for admission should be a dynamic process taking
into account reassessment of patient over time and in response
to intervention. However, there are some instances in which
admission is necessary or strongly encouraged:

1. Toxic, ill appearing or clinically suspected ACS
2. Child is under 6 months old or not up to date on vaccinations
3. Hemoglobin and /or reticulocyte count well below baseline
   or WBC > 30,000
Follow Up

1. Follow up at 24 hours is necessary, even if patient has defervesced
   a. Follow up may be via telephone or in person
   b. Clinician to ensure reliable phone number on record prior to patient discharge

2. For patients with central venous access, next day follow up in person is necessary for antibiotic administration
   a. Ceftriaxone (50 mg/kg IV/IM, max 1g) to be administered every 24 hours until blood cultures are negative for 48 hours.
   b. Options for in-person follow up:
      i. Primary care physician with hematologist on-call contacted
      ii. Hematology-Oncology department at Floating Hospital for Children
      iii. Emergency room with hematologist on-call contacted (i.e. weekend, holiday)

References

3. National Institutes of Health; National Heart, Lung and Blood Institute Guidelines for the management of sickle cell disease; 2014.

Practice guidelines do not necessarily apply to every patient. A provider’s clinical judgment is essential. As always, clinicians are urged to document management strategies.

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Acute Chest Syndrome: New infiltrate on chest x-ray associated with >1 of the following: fever, cough, sputum production, dyspnea, hypoxia.

Eligibility for outpatient management criteria includes:
- Non toxic appearing, T< 40 C
- No history of sepsis
- No infiltrate on CXR
- No hypoxia
- Labwork at baseline
- WBC < 30,000
- No social concerns (i.e. reliable follow up, access to transportation, at least 1 functioning phone)

Patients with central venous catheters should receive two doses of ceftriaxone until their blood culture is negative for 48 hours; this can occur in outpatient setting.

* Rapidly administer empiric antibiotics. Do not wait for the results of the labs/diagnostic work up.