Acute Chest Syndrome

Description/Etiology
Acute chest syndrome (ACS) is a life-threatening pulmonary complication of sickle cell disease (SCD; for information about SCD, see Quick Lesson About … Sickle Cell Anemia and the series of related Quick Lessons and Evidence-Based Care Sheets) that can be triggered by many infectious and noninfectious conditions that are capable of producing hypoxia (i.e., oxygen saturation \( \leq 94\% \) or \( \geq 3\% \) below baseline) and lung injury. Pulmonary infection and fat emboli are among the most common identifiable causes. ACS is also caused by the release of inflammatory mediators, reduced levels of nitric oxide (NO), and increased expression of adhesion molecules on cell endothelium.

In ACS, regional hypoxia caused by an infection, fat embolus, or other condition prevents the reoxygenation of RBCs in the lungs, causing them to maintain their sickle shape. Less pliable sickle-shaped RBCs can obstruct blood vessels and cause vasoocclusive crises, tissue injury, and death of tissue in major organs, including the lungs. Potential complications of ACS include lung injury, respiratory failure, and death.

Diagnosis is made using X-ray imaging of the chest. Differential diagnoses include chest infection, opioid toxicity, hypoventilation secondary to pain, septic arthritis, and fluid overload. Diagnostic criteria for ACS include new infiltrate on chest X-ray in combination with one or more of the following: fever, tachypnea, wheezing, chest pain, or cough. The enzyme secretory phospholipase A\(_2\) (sPLA\(_2\)) is used as a marker in early ACS. sPLA\(_2\) is a catalyst for proinflammatory mediators that release free fatty acids, which increases risk for fat embolism of the lungs; elevation can indicate impending ACS 24–48 hours before clinical diagnosis is possible. Additional laboratory tests and imaging are performed to monitor the patient’s physiologic status and to exclude deep vein thrombosis (DVT) as an underlying cause of signs and symptoms.

Treatment of ACS is supportive and includes hydration therapy, incentive spirometry, bronchodilators, and oxygen therapy. Broad-spectrum antibiotics (e.g., macrolides, third- and fourth-generation cephalosporins) that cover Streptococcus pneumoniae, Haemophilus influenzae, Klebsiella pneumoniae, Mycoplasma pneumoniae, and Chlamydophila pneumoniae are typically prescribed. Blood transfusions are often indicated; automated RBC exchange can be indicated (e.g., if the patient’s condition is deteriorating, the patient is in respiratory distress, significant acute organ dysfunction is present). Vasoocclusive crises (VOCs) that commonly occur in SCD are painful and appropriate pain management is necessary. Prognosis is guarded; patients with severe and progressive ACS are at risk for respiratory failure and death, and each episode of ACS increases this risk.

Facts and Figures
SCD is one of the most common genetic diseases, affecting approximately 100 million persons worldwide. In the United States, 0.3% of Blacks have SCD and 8–13% are carriers of the causative mutation. In sub-Saharan Africa, 1–4% of babies are born with SCD. Up to one-third of patients with SCD develop ACS at some point in their lives. ACS is the leading cause of SCD-related mortality and the second most common cause of hospitalization in patients with SCD. ACS account for up to 25% of all SCD-related deaths. The overall ACS-related mortality rate is 1.8%; adults with ACS are four times more likely to die than children.
Risk Factors
All patients with SCD, regardless of age, are susceptible to ACS. Risk factors include hospitalization for VOC, general anesthesia, surgery (particularly abdominal surgery), asthma-related bronchospasm, smoking, and chronic hypoxia. In children, ACS is more common during the winter months, possibly because of a higher incidence of viral infections.

Signs and Symptoms/Clinical Presentation
Signs and symptoms include fever, tachypnea, tachycardia, wheezing, chest pain, cough, decreased fetal Hgb, and hypoxia. In children, fever and cough are the most common ACS manifestations.

Assessment
› Patient History
  • Inquire about family and personal history of SCD, and ask about history of DVT
  • Assess onset, duration, and severity of the following:
    – Fever and chills
    – Shortness of breath, hemoptysis, productive cough, and wheezing
    – Chest pain
    – Vague pain in the extremities, particularly in older patients
› Physical Findings of Particular Interest
  • Fever > 101.3 °F/38.5 °C might be present; high fever is more common in younger patients
  • Patients with ACS and SCD will have golden colored sputum; this is not due to the presence of bilirubin but is instead the result of an intensive exudative process
  • Tachypnea, elevated pulse, and wheezing can be present, particularly in younger patients
  • Lung crackles might be heard on auscultation and hypoxia is often present
› Laboratory Tests That Might Be Ordered
  • CBC with differential will show elevated WBCs and reticulocytes
  • Hgb usually drops 0.7 g/dL below baseline; patients with Hgb < 10 g/dL are candidates for blood transfusion, and type and cross match will likely be ordered
  • ABGs are ordered to monitor for ventilation-perfusion mismatch
  • Serum metabolic panel is serially performed to monitor electrolyte imbalances secondary to dehydration
  • sPLA2 will be elevated; serial measurement is performed to assess for impending ACS
  • Culture of bronchoalveolar lavage samples can identify a microbial cause of infection
› Other Diagnostic Tests/Studies
  • Chest X-ray will show new infiltrate; children usually have upper-lobe infiltrate and adults have a multifocal presentation. Bilateral alveolar infiltrates correlate with severe ACS and increased risk for respiratory failure
  • Lower-extremity ultrasound is performed to evaluate for DVT
  • CT angiogram can be ordered to assess for pulmonary embolism

Treatment Goals
› Promote Optimum Health Status and Reduce Risk for Complications
  • Assess patient status and assist with resuscitation as appropriate. Monitor vital signs, I & O, pain level, and all physiologic systems (especially respiratory and cardiovascular); review results of laboratory tests (e.g., ABGs); report abnormal findings to the treating clinician; and provide prescribed treatment
    – Verify whether the patient has an advance healthcare directive and confirm availability of resuscitative equipment, as appropriate
  • Administer prescribed medications, which can include analgesics (e.g., morphine), antibiotics (e.g., azithromycin, cefTRIAXone), and/or bronchodilators (e.g., albuterol, levalbuterol); monitor treatment efficacy (e.g., for reduced pain, reduced leukocytosis, normalized respiration) and for adverse effects
  • Maintain optimum gas exchange and adequate hydration
    – Monitor airway patency, breath sounds, respiratory rate, and oxygen saturation with continuous pulse oximetry, as appropriate, and monitor for signs of hypoxia (e.g., dysrhythmias, reduced oxygen saturation); administer prescribed oxygen therapy to maintain adequate oxygen saturation of ≥ 96%
    – Initiate incentive spirometry, as ordered
Food for Thought

Hydroxyurea is the only U.S. FDA-approved medication for SCD. Hydroxyurea increases total Hgb and fetal Hgb, delays RBC sickling, reduces levels of circulating leukocytes, and reduces neutrophil adherence to the vascular endothelium; this results in decreased episodes of ACS and decreased incidences of pain and is associated with improved quality of life.

A decrease in WBC count, which confers an increased risk for infection, is a potential side effect of hydroxyurea administration.

In adults with ACS, the need for mechanical ventilation is an independent predictor of death (Allareddy et al., 2014).

Children with SCD have an average of 27 chest X-rays by age 18 years, potentially exposing them to significant cumulative doses of ionizing radiation. In a study of 91 children with SCD, lung ultrasonography demonstrated 87% sensitivity and 94% specificity for diagnosis of ACS in children with SCD and fever. The use of lung ultrasonography has the potential to reduce the routine use of chest X-rays in this patient population (Daswani et al., 2016).

Red Flags

Signs and symptoms can precede chest X-ray confirmation of ACS. A single chest X-ray that shows no infiltrate does not exclude ACS and repeat X-rays can be needed.

Patients with baseline leukocytes > 15,000/μL are at higher risk for death.

Overhydration can predispose to pulmonary infiltrates and exacerbate hypoxia.

Chest pain is less common in children with ACS than in adults.

What Do I Need to Tell the Patient/Patient’s Family?

Stay well-hydrated and use incentive spirometry at home to reduce risk for ACS.

Avoid smoking, alcohol use, and substance use.

Report the development of shortness of breath, chest pain, and fever to the treating clinician.

Adhere to bronchodilator treatment as ordered by the treating clinician.

Prevent infection by maintaining current vaccinations (e.g., pneumococcal, meningococcal, influenza).

Avoid exposure to low oxygen levels (e.g., mountain climbing, extreme exercising).

Promote Emotional Well-Being and Educate

Assess patient/family anxiety level, for knowledge deficits, and learning readiness; provide emotional support and educate about ACS pathophysiology, potential adverse drug effects, treatment risks and benefits, and the importance of following the prescribed treatment regimen and continued medical surveillance.

Refer patient/family members to the Sickle Cell Foundation Support Group at http://www.sicklecellsupportgroup.org/.

References


