MANAGEMENT OF ACUTE CHEST SYNDROME

OVERVIEW

In patients with sickle cell disease, acute chest syndrome is defined as a new pulmonary infiltrate on CXR consistent with alveolar consolidation but not atelectasis, involving at least one complete lung segment and in the presence of respiratory symptoms. In the Cooperative Study of Sickle Cell Disease, the rate of acute chest syndrome in HbSS patients was 12.8 cases per 100 patient years (1).

PATHOGENESIS

Acute chest syndrome refers to a clinical condition rather than a single underlying pathologic process. Three major pathophysiologic processes have been proposed: pulmonary infection, fat embolism, and pulmonary infarction from sequestration of sickled erythrocytes. Infection is the single most common cause – bacterial or viral agents were identified in 29% of 538 patients with acute chest syndrome analyzed by the National Acute Chest Syndrome Study Group (NACSG). Fat emoblism is the second most common cause of acute chest syndrome, and is thought to result from vaso-occlusion resulting in infarction and edema of the bone marrow, with release of contents into the bloodstream. As many as 46% of the cases in the NACSG had unknown etiology (2).

CLINICAL CHARACTERISTICS

Typically an acute chest syndrome develops 24-72 hours after the onset of severe pain in the arms, legs, and chest. Respiratory symptoms such as cough, wheezing, and new hypoxemia are often seen early on – chest x-ray findings often lag behind the clinical features. Fever, leukocytosis, and a drop in both Hb and Plts are typically seen. Mechanical ventilation is eventually required in 13% of patients with the syndrome, and overall mortality can reach 30% (2). See the following page for diagnostic grading criteria.

MANAGEMENT

Pain control – requires careful titration to avoid over-sedation and resulting decreased respiratory rate, poor inspiration, and hypoxemia.

Fluids – patients with acute chest syndrome typically have decreased oral intake due to pain and loss of appetite. Maintenance fluids with D5W-1/2 NS at 1.5x maintenance rate are typically initiated, though there is almost no data to support optimal fluid management strategy in these patients (3).

Transfusion – typically via simple transfusion vs. exchange transfusion. The latter offers the benefit of reducing HbS percentage without risk of iron overload or hyperviscosity. Exchange transfusion is typically indicated in moderate-severe disease as well as in patients with Hb ≥ 9 g/dL in order to avoid complications of hyperviscosity.

Oxygen Therapy – should be initiated when $SaO_2 < 92\%$ or $PaO_2 < 70$ mmHg. Typically low SaO_2 is responsive to low-flow O_2 administered by nasal cannula or face mask.

Antibiotics – infection, fat emboli, or infarction can all coexist, and it is impossible to distinguish between simple pneumonia and acute chest syndrome in a patient with sickle cell disease and active vaso-occlusive pain.

Treatment is generally empiric, using a third-generation cephalosporin + macrolide or monotherapy with a respiratory fluoroquinolone.

Bronchodilators/Incentive Spirometry – There have not been any trials showing benefit of bronchodilators or incentive spirometry in the treatment of acute chest syndrome – their use is mainly theoretical. In the National Acute Chest Syndrome study group, 1/5 of patients treated with bronchodilators showed "clinical improvement." Incentive spirometry has been shown to reduce the development of acute chest syndrome in patients admitted to the hospital for a vaso-occlusive pain crisis (ARR 36%) (4).

REFERENCES

1. *The acute chest syndrome in sickle cell disease: incidence and risk factors. The Cooperative Study of Sickle Cell Disease.* **Castro, O, et al.** 2, 1994, Blood, Vol. 84, pp. 643-649.

2. *Causes and Outcomes of the Acute Chest Syndrome in Sickle Cell Disease.* **Vichinsky, Elliott P, et al.** 25, 2000, New England Journal of Medicine, Vol. 342, pp. 1855-1865.

3. *Replacing fluids to treat acute episodes of pain in people with sickle cell disease.* **Okomo, U and Meremikwu, M M.** 7, July 2017, Cochrane Database of Systemic Reviews 2017.

4. *Incentive spirometry to prevent acute pulmonary complications in sickle cell diseases.* **Bellet, P S, et al.** 11, 1995, New England Journal of Medicine, Vol. 333, p. 699.

Box 2. Guidelines for transfusions in ACS

Simple transfusion
Single lobe involvement
Mild hypoxemia responsive to low-flow O_2
Worsening anemia
Moderate to severe ACS with Hb ≤5 g/dL

Exchange transfusion
Multilobar involvement
Refractory hypoxemia
Pao_2/Fio_2 ≤300
Rapidly progressive lung involvement
When clinical deterioration is eminent in the judgment of the physician

Mild	SaO2 > 90 on RA	Segmental/lobar consolidations in 1 lobe	Responsive to simple transfusion ≤ 2 units pRBCs
Moderate	SaO2 ≥ 85% on RA	Segmental/lobar consolidations ≤ 2 lobes	Responsive to transfusion of ≥ 3 units pRBCs
Severe	Respiratory failure (PaO2 < 60 mmHg) OR ventilator required	Segmental/lobar consolidations in 3+ lobes	Requiring simple/exchange transfusions to maintain HbA > 70%
Very Severe	Acute onset of bilateral infiltrates	PaO2:FiO2 ≤ 200 regardless of PEEP	ARDS is present by any definition

Scan the code or go to https://goo.gl/ao2qQQ to download this document