Review Article

Acute chest syndrome

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ABSTRACT

Acute chest syndrome is an acute pulmonary illness in patients with sickle cell disease. It is a common problem, causing significant morbidity and mortality. Many factors may cause this syndrome. Treatment is primarily supportive. Therapy includes hydration, analgesia, supplemental oxygen, antibiotics, blood transfusion and mechanical ventilation. Early detection and aggressive management may limit its severity and prevent its complications. This article reviews the current information for its definition, frequency, pathogenesis, clinical features, complications, investigations, management and prevention. Recent advances in management of acute and recurrent attacks will be discussed.

Keywords: Sickle cell disease, acute chest syndrome, pulmonary complication.

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Patients with sickle cell disease (SCD) are at risk of developing several rather distinctive acute or chronic pulmonary disorders.[1] Acutepulmonary complications include acute chest syndrome (ACS), pulmonary edema and bone marrow/fat embolism.[2] The chronic pulmonary complications include sickle cell chronic disease, pulmonary hypertension with cor-pulmonale and possibly thrombosis of large pulmonary arteries.[2] Of the acute complications, ACS is the most common.[2] It is estimated that at least one episode of ACS is experienced by 50% of sickle cell anemia patients and mortality rate after such an event can be as high as 10-12%.[3,4] It ranks 2nd as a cause for hospitalization and is responsible for 25% of deaths in SCD patients in some populations.[3,5] Such an important and common problem is rarely written about, even in those monographs on SCD. Therefore, this review article is presented hoping that it will help the physicians caring SCD patients in the management of this complication.

Definition. Acute chest syndrome is defined as an acute episode associated with clinical and radiologic evidence of new pulmonary abnormalities in patients with SCD and often accompanied by fever, bone pain, chest pain, cough, dyspnea, hypoxia, leukocytosis and decline in hemoglobin below the usual steady-state level.[2,6-8]

Frequency. It is estimated that ACS will occur in nearly one third of patients at risk.[7] It occurs in 5-45% of individuals with SCD.[2,4,8-12] It was found to be significantly more frequent among sickle cell anemia patients than in sickle cell Beta$^+$-thalassemia,[11,13] hemoglobin SC disease (HbSC) and sickle cell deletional hereditary persistence of fetal hemoglobin (SHPFH).[11] The frequency of ACS in Qatif (a medium-seize city in the Eastern Province of the Kingdom of Saudi Arabia (KSA), where the author is practicing) is 5-7.7%.[9,12] The low frequency of this syndrome in Qatif may be related to the type of SCD in this population which is relatively benign in comparison to SCD in other parts of KSA and the world.[12]

Pathogenesis. The pathogenesis of ACS remains poorly understood, which had led to the term "ACS".[14] Little is known regarding etiology.[7] Even the cause of the pulmonary infiltrate is uncertain.[7] It may reflect infection, infarction, pulmonary sequestration, in situ thrombosis, embolism of thrombus or bone marrow, pulmonary edema from

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over hydration and hypoventilation from narcotic analgesics administered to combat pain in the chest or elsewhere or hypoventilation from chest, back and abdominal pain.[7,15,16] In the early 1970s, Barret-Connor[17] suggested that most of the episodes of ACS (up to 80%) are due to bacterial infections especially in children. Subsequent studies in children and adults proved that bacterial infection occur in minority of these patients (<20%).[8,18-21] One possible exception to this is in the population <5 years of age in whom *Pneumococcal bacteremia* is most prevalent.[2] Another possible exception is that in certain area such as Ghana, in which infection may be more common than infarction.[11] The differentiation of the 2 conditions (infarction versus infection) is extremely difficult,[22] and may be only academic, since primarily infective lesions may develop areas of secondary infarction, and primarily infarctive lesions are likely to become secondarily infected.[10,11,22] Microvascular occlusion and abnormalities in host defense are the most widely studied areas that contribute to the pulmonary pathology.[2] There are several factors that are thought to contribute to the process of microvascular occlusion. Polymerization of hemoglobin S (HbS) is a key contributor to microvascular occlusion.[2,23,24] Other factors that may also contribute to microvascular occlusion include elevated blood viscosity due to (poorly deformable dense discocytes and irreversibly sickled cells), bone marrow/fat embolism, increased adhesion of the sickle erythrocyte to vascular endothelium, vascular intimal hyperplasia, thrombosis and altered vascular reactivity due to either vasospasm or failure of compensatory vasodilatation.[2,3,20,24,25] Several factors make the lung one of the most propensive sites for sickling.[13] It was suggested aggregates of sickle cells, intermingled with thrombocytes, leukocytes, cellular debris, hemoglobin crystals and fibrin escaping from dilated capillaries, sinusoids and venules in various parts of the body, lodge in the pulmonary arteries. It would also be expected that gross sickling of unsaturated blood in the pulmonary arteries would precipitate in situ vasoocclusion followed by the local addition of thrombosis after stasis has developed.[24] Pulmonary fat embolism secondary to bone marrow necrosis may be a common cause of ACS.[3,25] It was reported in both pediatric and adult autopsy series, with variable incidence ranging from 13-75% of SCD patients. It is likely that tissue infarction which can occur in the intramedullary cavity of a bone during vasoocclusive crisis, could generate an equivalent source of fat to that which accompanied a major fracture. Vigorous hydration and narcotic analgesics are possible risk factors for pulmonary edema and ACS.[26] An increase in pulmonary capillary permeability related to the use of narcotic analgesics and to underlying pulmonary vascular abnormalities may lead to the development of pulmonary edema. Vigorous fluid administration may potentiate edema formation by increasing pulmonary capillary pressure and by decreasing pulmonary colloid oncotic pressure. Furthermore, an increase in cardiac output in patients with sickle cell anemia may reduce their cardiovascular reserve to handle volume expansion from fluid administration or blood transfusion.[26] The basic immunological defects that increase susceptibility to infections, especially by encapsulated bacteria, are opsonization abnormalities, abnormality in phagocytosis and lack of specific circulating antibodies to encapsulated bacteria. Important infectious causes in ACS are[2,10,11,14,17,25,27-30] pneumococcal pneumonia, mycoplasma pneumonia, *Hemophillus influenza, Staphylococcus aureus, Klebsiella species, Escherichia coli*, *Salmonella species, Chlamydial pneumonia*, cytomegalovirus and parvovirus B19. Legionnaire's disease has also been reported in sickle cell anemia.[31] A more recent study suggested that ACS was commonly precipitated by fat embolism and infection, especially community-acquired pneumonia.[25] Mycoplasma pneumonia may be a common infectious cause of ACS.[8,20,25,28,32] Sickle cell anemia patients have more severe mycoplasma pneumonia than do normal host[8,30,31] and they may also have life-threatening anemia. Siblings with SCD would have concurrent infections.[30] Therefore these siblings should be closely observed for similar illness. In certain populations, chlamydia pneumonia can be a common cause of ACS.[21,25] Viral infection such as parvovirus B19,[14] and cytomegalovirus[29] may cause fatal ACS.

Clinical features. Onset. The onset of ACS is usually sudden but may be insidious. The symptoms and signs of pulmonary disease present either at admission, or hours to several days later.[2,13,19,20] The presenting complaints of patients admitted without pulmonary involvement are abdominal pain, back pain, limb pain and fever.[13,20] Acute chest syndrome may also develop after surgery (splenectomy, cholecystectomy, and so forth),[12,20] and during episodes of cholecystitis or trauma.[20]

Age and sex. The incidence of ACS in a Jamaican cohort study was similar in both children with sickle cell anemia and normal controls (with pneumonia) up to the age of 8 months, after which events were significantly ($P<0.001$) more frequent in sickle cell anemia. The relative risk being 4 times greater than in normal controls by the age of 4 years.[10] The age of patients with ACS ranged from infancy up to 45 years.[8,12,19,33] There may be a predominance of males.[12,33]

Symptoms and signs. Most patients with ACS present with history of fever.[12,13,20] Fever usually persists for a few days despite appropriate management.[8,13] Cough is a common symptom. It may be productive or non-productive. Sputum may be whitish, greenish, bloody or yellowish,[12] (**Figure**

1). Chest pain and dyspnea are common symptoms.[12,13,34] Physical examination in patients with ACS is variable.[12,20,34] Patients may be mildly affected with or without mild respiratory distress. On the other hand, they may be severely affected, ill looking, in severe respiratory distress and progressing rapidly to respiratory failure. They may be febrile (temperature >38^{o}C), tachypneic, with intercostal and subcostal retractions. There may be tenderness of ribs and sternum in the area of chest pain. Auscultation may reveal decreased breath sounds, rales (unilaterally or bilaterally) and pleural rub.

Degree of clinical severity. A simple scoring system to grade the clinical severity of the disease was developed on the basis of physical examination findings. Score "O" is made when there is no respiratory distress and will indicate mild disease. Score "1" is made when there is tachypnea (age adjusted) and will indicate moderate severity. Score "2" is made when there are tachypnea and retractions and will indicates severe disease.[35] These scores can be used to assess these patients and may help in giving the appropriate management.

Radiographic features (Table 1). Radiographic abnormalities in ACS are: patchy infiltrates, florid consolidation, linear atelectasis, pleural effusion and pulmonary edema.[19] These abnormalities nearly always involve the lower lobes.[2,13,19-21,35] Upper lobes, middle lobes and lingula may be involved. Bilateral involvement occurred in around one third of patients. Characteristic of the radiographic course is the rapid change (extension or resolution) that paralleled the variable clinical course[35] (**Figures 2 & 3**).

Hematological features. Hemoglobin level. The hemoglobin level in ACS frequently falls by 25% or more.[4,8,13,36] The fall in hemoglobin level occurred significantly in patients with thrombocytosis. The cause of anemia is uncertain, but may be in part due to increased hemolysis unrelated to glucose-6-phosphate dehydrogenase (G6PD) deficiency.[4] Life-threatening anemia associated with cold agglutinins of anti-I specificity may also occur in association with mycoplasm infection.[37]

White blood cell count. White blood cell count is usually elevated in ACS. This elevation may continue for a few days despite appropriate management.[4]

Platelet count. Platelet count may fall initially on admission. By the end of first week of illness, there may be an abrupt and significant increase in platelet count.[4] The thrombocytosis usually develops after the temperature returns to normal and the patient has been discharged from the hospital.

Blister cells. Blister cells were defined as red blood cells having a large vacuole at one end and resembling a round or conical basket and include cells with bilateral, thinned, hemoglobin free areas with intact cell membranes.[38] These cells were found to be suggestive of pulmonary embolism in patients with sickle cell anemia by some authors[39-41] but were unreliable to predict the cause of the pulmonary insult by others.[38] Whether this feature is diagnostic of pulmonary thromboembolism remains to be seen.[10]

Evaluation of anemia. As stated earlier, hemoglobin level frequently falls by 25% or more, which may be in part due to hemolysis. Reticulocytes, lactic dehydrogenase (LDH) and serum bilirubin may help in the diagnosis of hemolytic anemia and to role out other causes such as aplastic anemia.

Assessment of oxygenation status. Arterial blood gases should be obtained from all patients with ACS at the time of presentation.[2] Arterial blood gases should be monitored carefully even in those patients who appear to "look good", because cyanosis is not a useful physical finding in anemia.[42] Arterial oxygen/tension (PaO_2) has reportedly ranged from 46 to 73mm Hg in patients with ACS.[18] Pulse oximetry has become a popular means of assessing oxygenation. It is not affected by sickle hemoglobin.[43] A simple way to correlate saturation to oxygen tension is the "40-50-60/70-80-90" rule: a PaO_2 of 40mm Hg corresponds approximately to a saturation of 70%, a PaO_2 of 50mm Hg to a saturation of 80% and a PaO_2 of 60mm Hg to a saturation of 90%.[43]

Alveolar-arterial oxygen gradient. Alveolar-arterial oxygen gradient [(A-a) PO_2] can be calculated for patients whose arterial blood gas values were obtained while they were breathing room air at the time of diagnosis of ACS, using the following formula: (A-a) PO_2 = (7.13 x FIO_2) - ($PaCO_2$ x 1.2)-PaO_2,[35] where FIO_2 is the fraction of inspired oxygen, $PaCO_2$ is the partial pressure of carbon dioxide in arterial blood and PaO_2 is the partial pressure of oxygen in arterial blood. It was found that elevation of the (A-a) PO_2 is a predictor of an adverse clinical course, particularly in patients with homozygous sickle cell anemia. An elevated gradient is strongly associated with a higher clinical severity score.[35] Patients with an (A-a) PO_2 >30mm Hg are significantly more likely to undergo blood transfusion.

Search for infection. Blood, throat and sputum (if possible) cultures should be carried out for all patients with ACS. Patients with bacteremia are likely to have pneumonia in presence or absence of pulmonary infarction. The role of positive throat culture, particularly in those who did not respond to usual management, should be considered.[44] Culture of pleural fluid may be helpful if thoracentesis was carried out. Culture of endotracheal aspirates also may be helpful if the patient has been intubated.[21] Mycoplasma antibody titers or cold agglutinins titers should be carried out for all patients. Enzyme immunoassay to detect immunoglobulin M against

Table 1 - Investigations for patients with acute chest syndrome.

Routine investigations
Complete blood counts
Differential counts
Peripheral smear study
Reticulocyte counts
Lactate dehydrogenase
Serum bilirubin
Chest x-ray
Blood gases
Cultures (blood, throat and sputum)
Serology for mycoplasma, chlamydia
Special investigations
Viral study
Fungal study
Radio-isotope scanning of the lung
Computerized tomography scanning of the lungs
Serology for legionellosis

Table 2 - Risk factors for acute chest syndrome.

Young age
Rib infarction
Chest, abdominal and back pain
Severe lower limb's pain
Hematocrit, white blood cells, fetal hemoglobin
Bronchial asthma
Narcotics
Over-hydration
Smoking

Table 3 - Poor prognostic factors.

Bronchial asthma
Fall of hemoglobin by 25% or more
Thrombocytosis
Pleural effusion

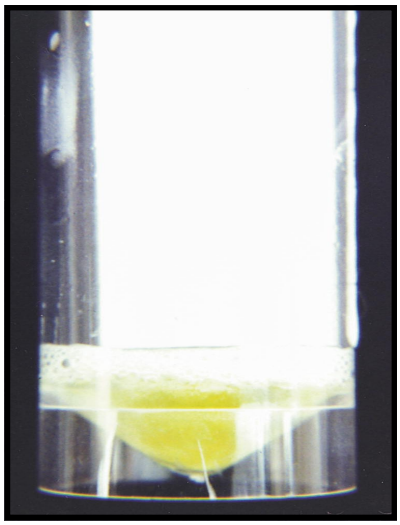

Figure 1 - Yellowish sputum from a patient with acute chest syndrome.

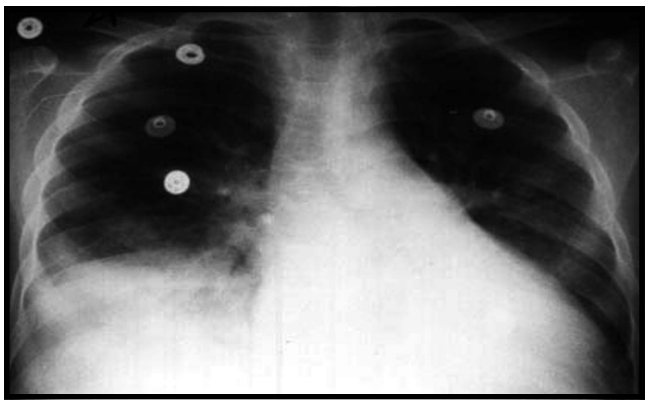

Figure 2 - A patient with moderate attack of acute chest syndrome.

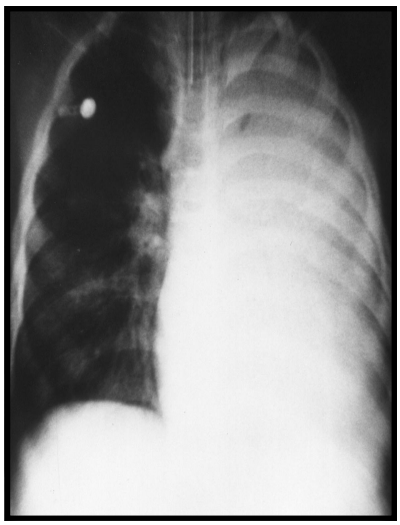

Figure 3 - A patient with severe attack of acute syndrome.

chlamydia pneumonia can be carried out if possible.[25] Serology for legionnaires' disease may be useful if a patient develops progressive pulmonary infiltrate while on therapy with a penicillin, cephalosporin or aminoglycoside.[31,45] Viral studies may be useful in severe cases.[14,29] Fungal cultures of bronchial aspirate may be helpful in a prolonged attack.[46]

Lung scans. Radioisotope lung scanning can be carried out (if available). It can show pulmonary infarction, but adds little to the chest x-ray with clear cut consolidation.[11] Early utilization of this scanning may help in the diagnosis of acute reversible pulmonary ischemia,[47] particularly in children, due to the interpretation of pulmonary scans carried out during an acute episode has been found to be difficult in adults with SCD due to the high prevalence of chronic lung changes.[47-49] It can be carried out on admission and then after a few days.

Computerized tomography scan of the chest. Computerized tomography scans of the chest can be carried out for selected patients with ACS, particularly those who had recurrent attacks, to determine the presence and extent of microvascular occlusion, and can help in the timely selection, planning and monitoring of an appropriate treatment regimen.[50]

Risk factors (Table 2). Young age. The risk of ACS in sickle cell anemia seems to be related to young age,[7] being highest in children 2-4 years old and lowest in adults.[34]

Rib infarction. Rib infarction may cause bone pain, followed by soft tissue reaction, pleuritis, and splinting. The resultant hypoventilation leads to atelectasis and subsequent development of the radiographic changes of the ACS.[51]

Chest, abdominal and back pain. Any chest, abdominal or back pain, whether due to painful crises or due to other causes such as postsplenectomy, postcholecystectomy, trauma, may cause hypoventilation and subsequent development of ACS.[20,51]

Severe lower limbs infarction. Severe infarction can occur in the intramedullary cavity of lower limbs during vasoocclusive crisis and generate fat equivalent to that accompanying a major fracture.[3]

High hemoglobin and white blood cells. High steady state hemoglobin levels and leukocyte counts are associated with a high ACS incidence.[7,34] This relationship is unexplained. The association of high hemoglobin levels and ACS may be due to increased blood viscosity.[34] On the other hand, the association of leukocytosis with ACS could reflect the fact that both high leukocytes counts and high ACS rate are more frequent in patients with severe disease.[34]

Decreased hemoglobin F. Increased hemoglobin F is a possible protective factor against many complications of SCD, including ACS.[7,52]

Bronchial asthma. Bronchial asthma has been known to precipitate or exaggerate sickle cell crises,[53,54] including ACS, and can make prognosis of SCD worse.[11]

Smoking. Cigarette smoking may increase the risk of ACS.

Differential diagnosis. Infection versus infarction. It has been suggested that upper lobe disease, age less than 5 years and positive sputum or blood cultures favor a diagnosis of pneumonia, while a diagnosis of pulmonary infarction is favored by painful bony crisis, lower lobe disease and a clear chest radiograph on presentation in adults,[2] but as mentioned above, the literature clearly support that there are no clinical, laboratory or radiographic features that distinguish pneumonia from pulmonary infarction.

Pulmonary fat embolism. Pulmonary fat embolism should be considered in the differential diagnosis when severe painful episodes (bone) occurred before the onset of ACS.[3,55] Altered mental status in association with ACS strongly suggests that pulmonary fat embolism may be the underlying cause.[3] Lipemia retinalis and petechial lesions in conjunctiva and upper thorax may support the diagnosis.[55] Characteristic laboratory findings in ACS associated with pulmonary fat embolism are: thrombocytopenia, decrease in hemoglobin, increase in nucleated red blood count. Hypocalcemia and hyperuricemia may be found. Lipid droplet found in blood sample obtained by Swan-Ganz catheter, bronchoalveolar fluid, urine and sputum may confirm the diagnosis.

Acute chest pain. Other causes of acute chest pain may be considered in the differential diagnosis of ACS. Such causes may include painful crisis of the muscle of the chest wall or painful crisis of chest bones. Severe hypoximia secondary to acute sternal infarction in sickle cell anemia without ACS was reported.[56]

Management. The aim of treatment of ACS is to reverse the pulmonary pathology, to correct significant hypoxemia, to relieve the chest pain and to prevent the recurrent attacks.

Admission. All patients with ACS should be admitted.[6,28,55] In severe cases, intensive care units is required.[6,55]

Analgesia. Analgesia should be administered to patients with ACS, particularly those patients with chest pain.[2,6,55] Narcotic analgesia may be required, but large doses of narcotics should be avoided when possible, since they may cause hypoventilation and pulmonary edema.[2,26]

Hydration. Maintenance intravenous fluid should be given. Previous recommendations for aggressive intravenous hydration (1.5-2 times maintenance) have been revised.[26] Excessive hydration especially with hypotonic saline can cause pulmonary edema.[2,26,57]

Oxygen therapy. Oxygen therapy is indicated for hypoxemia, tachycardia and tachypnea.[55] The use of

supplemental oxygen is warranted when the PaO_2 is less than 60-70 torr.[2,25] The role of oxygen therapy is to improve arterial hypoxemia caused by a ventilation-perfusion imbalance, to increase oxygen transport to the tissues,[58] and to minimize microvascular occlusion and exaggeration of any underlying pulmonary hypertension.[2] The aim of oxygen therapy is to maintain PaO_2 within normal range.[58] Increasing PaO_2 above normal (100 torr) is not of proven benefit,[2,58] and may suppress erythropoiesis which may cause rebound elevations of irreversibly sickled cells after discontinuation of oxygen therapy.[58,59] When patients improve and oxygen therapy is no longer required, supplemental oxygen is preferably tapered to prevent any rebound effects.[58]

Antibiotics. Antibiotics should be started empirically in all patients with ACS. These antibiotics should cover organisms commonly causing community acquired pneumonia such as *Streptococcus pneumoniae* (*Strep. pneumoniae*) and *H. influenzae*.[2,25,57] Ampicillin may be the drug of choice for mild cases. If the patient does not improved or deteriorates, ampicillin should be substituted by 2nd or 3rd generation of cephalosporin. In moderate to severe cases, the 3rd generation of cephalosphorin (Cefuroxime, Cefotaxime, Ceftriaxone) may be the drug of choice. In very sick patients with life-threatening condition, Vancomycin and extended spectrum of Cephalosporin may be started due to increased frequency of drug-resistant *Strep. pneumoniae*.[60,61] Erythromycin can be given in addition to the other antibiotics to cover mycoplasma pneumonia, chlamydia pneumonia and legionella.[2,6,25,55,57]

Bronchodilators. Airway hyperactivity should be assumed to be present, even if the patients is not wheezing, and treatment with bronchodilators should be initiated.[25,62] It was found that one fifth of the patients who were treated with bronchodilators had clinical improvement.[25]

Intravenous dexamethasone. Preliminary results showed that intravenous dexamethasone (0.3mg/kg every 12 hours, for 4 doses) in children with mild to moderately severe ACS significantly reduced the length of hospitalization, the duration of supplemental oxygen therapy, duration of opioid analgesia, need for blood transfusion, occurrence of clinical deterioration, and persistence of fever.[63]

Simple blood transfusion. Simple blood transfusion may be beneficial in patients with ACS, in the form of shortening the clinical course and possible decreasing mortality.[16,28,64] The following can be used as indications for simple blood transfusion:[28] clinically sick patients with moderate to severe distress, consolidation involving one or more lobes, PaO_2 less than 75mm Hg despite oxygen therapy, alveolar-arterial oxygen gradient more than 30 mm Hg[35] and if the condition deteriorates despite other modes of therapy. Routine early transfusions are indicated for patients at high risk for complications.

Exchange blood transfusion. Exchange transfusion is the only therapeutic modality demonstrated to reverse the acute respiratory failure seen in this syndrome independent of its etiology.[2] The goal of exchange transfusion is to reduce the HbS concentration to 20-30% while not exceeding a hematocrit of 30%.[2] The following can be used as indication of exchange transfusion: very sick patients, or patients with rapidly progressing disease, or signs of respiratory failure especially if hemoglobin is equal to or more than 8gm/dl,[6,28] or hypoxemia (with oxygen saturation below 90% by pulse oximetry or arterial blood sampling) despite supplemental oxygen.[16]

Mechanical ventilation. Some patients with ACS may deteriorate despite oxygen therapy and partial exchange transfusion. These patients may benefit from mechanical ventilation.[6,16]

Extracorporeal membrane oxygenation. If extracorporeal membrane oxygenation is available, it should be considered for severe ACS when conventional methods of mechanical ventilation fail.[16,65,66]

Nitric oxide. Nitric oxide may be beneficial in severe cases that have not responded to other treatments.[67] It may cause acute improvement in oxygenation in patients with acute hypoxic respiratory failure.[68]

Bronchoscopy. Bronchoscopy can be considered in severe ACS not responding to conventional management.[69]

Complications. Complications of ACS can be divided into acute and chronic complications. Acute complications include respiratory failure, pleural effusion, lung abscess and plastic bronchitis. These complications are poor prognostic factors (**Table 3**). Patients with these complications usually required prolonged treatment and hospitalization and are prone to chronic complications. Progression of pulmonary infiltrates, a rapidly falling hemoglobin and worsening hypoxemia may herald the development of acute respiratory failure.[2] Pleural effusion occurs in up to 38%[2,13,20,36] and can be unilateral or bilateral.[13] Patients may appear acutely ill with fever, non productive cough and chest pain.[2] Infarction is a well-recognized predisposition to pulmonary abscess formation in patients who have other conditions which cause tissue necrosis or vascular stasis.[70] Plastic bronchitis[69] is a rare complication, reported in association with ACS. It is characterized by the formation of branching mucoid bronchial casts. They may become firmly wedged and occlude the tracheobronchial tree at many levels. This possibility can be considered in severe cases not responding to conventional management.

Bronchoscopy may be required. Chronic complications include recurrent ACS, chronic lung disease, pulmonary hypertension, exercise intolerance and pulmonary tuberculosis.[11,22,71]

Recurrent acute chest syndrome. Recurrent ACS may occur in 20-80%.[2] Risk factors for recurrent attacks may include cystic fibrosis and bronchial asthma. Treatment may include chronic blood transfusion[72] at least for 6 months. Longer periods may be required. Hydroxyurea therapy[73,74] and transplantation[73,75] reduce the recurrent attacks significantly. Hydroxyurea should be considered for patients who had a severe attack, or two or more mild to moderate attacks of ACS. Transplantation should be considered for patients who had a life threatening condition. It should be performed only in the context of a clinical trail.[73]

Prevention. Patients and their physicians play an important role in the prevention of ACS. Regular follow-up of SCD patients in the sickle cell clinic will provide a good chance for education regarding this complication, vaccination (influenza, H. influenza and pneumococcal vaccines) and penicillin prophylaxis. These measures may play a role in prevention of infection which is an important factor in the etiology of ACS. Behavioral modification of the smoking habit in patients with sickle cell anemia may prevent ACS.[76] Careful use of intravenous fluid and opioid analgesia during management of acute painful crisis may also prevent ACS. Use of incentive spirometry during acute painful crisis (particularly acute chest, back and abdominal pain) and postoperatively may play a role in prevention of ACS.[77]

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