Acute Chest Syndrome - A Case Report

Review of the literature

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ABSTRACT

Acute chest syndrome - A case report. Review of the literature.
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Acute Chest Syndrome (ACS) is a rare but often fatal complication in patients with micro-drepanocytic anemia as in those with beta Sickle Cell Disease (SCD). This case report refers to a female patient with known micro-drepanocytic anemia who was admitted to our ICU due to ACS. Treatment included RBC transfusions with WBC reduction, administration of FFP and plasmapheresis within 48 hours from the ICU admission. At the 3rd ICU day, HbA2 level was found elevated up to 77%. The following ICU days, the patient presented absence of the white series of the blood’s cellular components. After twelve days in the ICU the patient died due to hemodynamic shock and herniation of the brain stem. Given that sickle cell crises are potential precursors of this deadly syndrome, everyday practice should prioritize the prevention of sickle cell crises developing into ACS.

INTRODUCTION

The conditions that favour the polymerism of the HbS are related to the frequency of obstructive incidents in Sickle Cell Disease (SCD). During sickle cell crises, necrotic pieces of the marrow may be detached and cause fat embolisms in the base of the lungs resulting in the attachment of the sickle cells to the endothelium. That leads to new inflammation and new obstructions and finally to acute respiratory failure and the need of mechanical ventilation1-5. This case report refers to a patient with sickle cell anemic crisis and Acute Chest Syndrome (ACS), complicated with se-
vere respiratory failure and a need for mechanical ventilation support.

CASE REPORT

A 31-year-old female, with an acute bone ache crisis (in right knee and both hips), admitted to our ICU due to acute respiratory failure. The patient was intubated few hours earlier (PaO$_2$/FiO$_2$=57, Respiratory Rate=40 breaths/min). According to the patient’s medical history, she had micro-drepanocytic anemia, a splenectomy at the age of 4 and HCV(+) infection during the last two years. She usually ignored hematologist’s advices and she also avoided visiting the attending doctor.

From the clinical examination and lung auscultation she was found to have basal crackles bilaterally. The chest X-Ray revealed diffuse pulmonary infiltrations (Figure 1) and the thoracic CT-scan showed diffuse infiltrations bilaterally, as well as a presence of an air bronchogram.

**Figure 1. Patient’s chest X-Ray**

At ICU admission, the patient was hemodynamically stable, without the need of inotropic or vasopressor support. Her eye pupils were both of equal size (2mm) and responded normally to light. Patient management in the ICU stay included mechanical ventilation support (Pressure control mode, PEEP=10mmH$_2$O, Pressure level above PEEP=18 mmH$_2$O). The laboratory tests showed coagulation mechanism disorders (PT=18.7sec, aPTT=77.2sec, D-Dimers =34.98ng/ml), while blood tests revealed Hb=6.6g/dl, Hct=20.5% and PLT=10000/μL. Other laboratory testing showed, CRP=25.6mg/dl, LDH=3808U/L, Bil=9.3mg/dl (D-Bil=7.95mg/dl). An echocardiogram revealed a right heart deficiency and pulmonary hypertension: dilatation of the right atrium, severe tricuspid insufficiency, as well as interventricular septum with a deviation toward the left ventricle during systole. Bronchial secretions, blood and urine samples were taken on admission and empirical treatment was initiated with Ceftriaxone and Moxifloxacine.

Treatment included RBC transfusions with WBC reduction, administration of FFP, PLT and plasmapheresis within 48 hours from the ICU admission. At the 3rd ICU day, HbA$_2$ level was found elevated up to 77%. At that time there was no indication of exchange transfusion anymore, according to hematologists’ protocols. The same ICU day, despite an initial oxygenation improvement, patient developed a
fever (approximately 38.9°C) with haemodynamic instability. The next day, patient presented partial onset seizures and a oxygen desaturation (to a level of 62%), which were immediately dealt with an increase of FiO₂, an administration of midazolam 10mg IV and antiepileptic drug (phenytoin sodium). Following the aforementioned incident, mydriasis was observed in both eye pupils, with no response to light. A brain CT-scan took place (Figure 2) which indicated disappearance of the tanks bases (indicative of herniation), as well as cerebral edema and extensive subarachnoid hemorrhage.

**Figure 2.** Patient’s brain CT-scan.

The following days the patient presented absence of the white series of the blood’s cellular components. After twelve days in the ICU the patient died due to hemodynamic shock and herniation of the brain stem.

**DISCUSSION**

Nowadays, in the developed countries, patients with sickle cell anemia (SCD) survive to the 5th or 6th decade of their lives, mainly due to the improvement of the supportive care. The average age of death is 42 years old for men and 48 for women. The increase in survival rate is accompanied by an increase in the frequency of complications that results in chronic failure of various organs. Lung failure is considered the most common complication. The pulmonary complications of the SCD are related either to a chronic condition (Sickle Cell Chronic Lung Disease–SCCLD) or to an acute condition (Acute Chest Syndrome–ACS). The acute condition, also known as Acute Chest Syndrome, is the most common cause of death and the second most common reason for hospitalization of the adult population suffering from SCD.

According to the Co-operative Study of SCD (CSSCD) almost 50% of the SCD patients will suffer an ACS. Up to 78% of the ACS incidents suffer a vasoocclusive crisis, which usually occurs within the first 48h to 72h after hospital admission. In our patient this crisis occurred during the 4th day after the admission.
in ICU. There is a higher mortality rate in adults (up to 77%), mainly due to the higher incidence of fat and bone marrow emboli.\textsuperscript{9,10} While the treatment of ACS episodes is similar in adults and children suffering SCD, the higher rate of serious ACS incidents in adults should be treated with rapid red blood cell transfusion therapy. Our patient was treated with RBC transfusions with WBC reduction, administration of FFP, PLT and plasmapheresis within 48 hours from the ICU admission. In numerous case reports and series, fat emboli has been cited as a source of 44 to 77% of adult ACS episodes.\textsuperscript{1,9} Despite the difficulty in documenting fat emboli as the cause of instigating ACS, compelling data, which includes laboratory findings, post-mortem assessment, imaging studies of bone marrow biopsies, as well as bone marrow biopsy, support this etiology. Considering that the research for fat emboli requires bronchoscopy, the true frequency of fat emboli in patients with ACS remains unknown. Bone marrow aspiration which indicates bone marrow necrosis,\textsuperscript{2} support the causative role of fat emboli in ACS. In various studies which include bronchoalveolar lavage, the presence of fat in alveolar macrophages (using a cut-off point of >5% fat consistent alveolar macrophages), in 60% of the cases in ACS patients suffering SCD, are associated with fat emboli.\textsuperscript{14,11} In 92% of the above cases, bone marrow cases infarction data was recorded in MRI or radioisotope bone imaging. Retinal lipemia (lipemia retinalis) and petechiae are not commonly observed in cases of fat emboli due to SCD. As these findings are noted, they would be coherent to the clinical syndrome of fat emboli. Possible causes of ACS also include the potential concurrence with Parvovirus B19 infection, which is also associated with necrosis of the bone marrow and fat emboli. Vascular occlusion is either the cause triggered by some conditions (e.g. infection, asthma and hypoventilation) or the result (e.g. fat or marrow emboli).\textsuperscript{5} Once intrapulmonary vascular obstruction starts, hypoxia, inflammation and acidosis is also present. Oxygen desaturation was presented in our patient during the 4\textsuperscript{th} day of ICU stay. Bone marrow ischemia and necrosis, which are characteristics of vascular occlusive incidents in ACS, induce discharge of bone marrow and fat into the venous circulation. That, via a mechanical obstruction of the blood vessels and an advancement of pro-inflammatory condition,\textsuperscript{9} affects the functionality mainly of the lungs and the CNS. The presence of seizures in our patient supports the above statement. The inflammation associated with fat emboli is probably due to the presence of free fatty acids derived from the decomposition of neutral fat through the effect of secretory phospholipase A\textsubscript{2}.\textsuperscript{9} The free fatty acids have strong inflammatory properties and produce
greater tissue damage than neutral fats. Hypoxia and inflammation advance further vascular obstruction, creating a vicious cycle.

A common point between all current definitions is that ACS occurs in patients with SCD characterized by a new radiodensity on chest radiograph accompanied by fever and/or respiratory symptoms. The major disorders to be distinguished from ACS include pulmonary embolus, acute coronary syndrome, and pneumonia. The broncho pulmonary filtration and the fever in an adult with SCD may be classified as either an ACS or as pneumonia, so empiric antibiotic therapy for community acquired pneumonia, including coverage for atypical bacteria, should considered for ACS treatment. In our patient empirical treatment was initiated with Ceftriaxone and Moxifloxacin.

Although ACS can be manifested severely from the onset, some patients may develop it gradually within 48 to 72 hours. In these cases, with gradual evolution, initial signs may include chest pain with or without hypoxia and lungs infiltration. Therefore, there should be great wariness for the presence and development of ACS during an episode of pain and that should be immediately treated.

The supportive management of an episode of ACS, as in our patient, requires a number of active interventions, including adequate pain control and fluid management, use of bronchodilators when wheezing is present, incentive spirometry to prevent the development of pulmonary atelectasis and use of supplemental oxygen. Although, there are no randomized studies to determine the best anti-ACS therapy in adults with SCD, the basic treatment involves blood transfusion. The need for transfusion and transfusion medium (simple versus exchange transfusion) depends on the severity of the ACS incident. Mild incidents do not require transfusion, while moderate ones require a simple transfusion or an exchange transfusion; severe incidents require an exchange transfusion. Exchange transfusion is made with erythrocytapheresis which allows rapid transfusion of large amounts of blood (e.g., 6-8 units of thickened red blood cells for a typical adult). That effectively reduces the rate of hemoglobin S. Hyper viscosity may occur when hemoglobin levels are elevated > 11 g/dl. Moderate incidents that either involve more than one lung lobe or signs of clinical deterioration, require exchange transfusion. The performance of plasmapheresis depends on the capabilities and resources that every hospital has. In hospitals where exchange transfusion is not available, the patient has to be transferred to a hospital that has the ability for such treatment. The cases of moderate to severe ACS incidents are better to be treated in the ICU with supportive treatment, mechanical ventilation and specialized treatment techniques. In
mild forms of ACS the most frequent practice is simple blood transfusion in order to increase hemoglobin up to 10 mg/dL. If started promptly, data indicates that many episodes of moderate to severe ACS are avoidable\textsuperscript{15}. In regards to therapy target, when plasmapheresis is performed, the final percentage of hemoglobin S and hemoglobin A\textsubscript{2} should be 30 % and 10 g/dL, respectively\textsuperscript{13}. Red blood cell units used for transfusion should be negative for strain of sickled cells (Sickledex negative), and phenotypic simulated for C, E and Kell antigens\textsuperscript{14}. Such extensive simulation reduces the alloimmunization rate in patients with SCD from 3 to 0.5% per unit\textsuperscript{16}. Regardless of the severity of ACS, if the hemoglobin is <5 g/dL, simple transfusion should commence to increase hemoglobin to 10 g/dL.

The use of glucocorticoids is not the usual practice for the management of ACS in adults with SCD. Although hospitalization was reduced in children who received dexamethasone, a high rate of painful episodes recurred after stopping the treatment. The rebound phenomenon of vascular occlusion after steroid treatment has been confirmed in various studies\textsuperscript{17,18}. For prevention of ACS recurrence as well as overall reduction in mortality, hydroxyurea is recommended to all adults with a history of ACS unless otherwise contraindicated (i.e renal failure). It has been cited that hydroxyurea significantly reduces the frequency of vascular-occlusive crises and episodes of ACS\textsuperscript{19,20}. In patients who have two or more episodes of moderate to very severe ACS episodes, in a 24-month period, despite maximal hydroxyurea therapy, a chronic transfusion program to maintain a hemoglobin S percentage <50 % is suggested.

**CONCLUSION**

ACS is a leading cause of death in adults suffering from SCD. Everyday practice should prioritize the prevention of sickle cell crises developing into ACS.

**REFERENCES**


Key words: Acute Chest Syndrome, sickle cell crisis

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