 Prague Medical Report / Vol. 114 (2013) No. 3, p. 180–185

Painful Vaso-occlusive Crisis as a Prodromal Phase of Acute Chest Syndrome. Is Only One Chest X-ray Enough? A Case Report

Neocleous C.[1,2], Spanou C.[3], Adramerina A.[1], Spyrou G.[1], Tzanetis F.[1]
[1]Department of Pediatrics, General Hospital of Drama, Drama, Greece;
[2]Medical School, University of Thessaly, Larisa, Greece;
[3]School of Physical Education and Sports Science in Serres, Aristotle University of Thessaloniki, Serres, Greece

Received March 21, 2013; Accepted August 14, 2013.

Key words: Acute chest syndrome – Sickle cell anemia – Sickle cell disease – Vaso-occlusive crisis

Abstract: The predominant pathophysiological feature of homozygous sickle cell anemia (SCA) is the vaso-occlusion. Vaso-occlusion can be associated with painful crises, which are the primary reason for those patients to seek medical care. Vaso-occlusion is responsible for the acute chest syndrome (ACS) with large morbidity and mortality or more rarely (and especially in adults) for priapism and acute neurological events (strokes). A 10-year-old boy with homozygous SCA was admitted to the Pediatric Emergencies with painful vaso-occlusive crisis and fever. Initially he had normal chest X-ray but, after 24-hour-hospitalization, he developed ACS with new chest X-ray findings. He was treated with broad spectrum antibiotics, blood transfusions and bronchodilators and after a six-day treatment, he was significantly improved. The patient was discharged 13 days later with no other therapy at home. The possibility of ACS development should be still considered, even when a known patient with SCA presents a painful vaso-occlusive crisis with an initial normal chest X-ray. Therefore, repeated clinical examination is required and possible changes in the clinical status could indicate the necessity of a new radiographic examination. In this way, early ACS could be recognized and the catastrophic consequences due to this syndrome could be avoided.

Mailing Address: Charalambos Neocleous, MD., Department of Pediatrics, General Hospital of Drama, Drama, Greece; Phone: +306 955 099 935; e-mail: xneoc@yahoo.gr

Introduction

The predominant pathophysiological feature of homozygous sickle cell anemia (SCA) is the vaso-occlusion. Vaso-occlusion can be associated with tissue infract in the bones, causing acute episodes of severe pain (painful crises) (Mousa et al., 2010). Painful crises are the primary reason for these patients to seek medical care in hospital emergency departments (Yale et al., 2000). Acute chest syndrome (ACS) is another common complication of vaso-occlusion in patients with SCA, accounting for more than 90% of hospital admission and causing significant morbidity and mortality (Al-Dabbous, 2002). The term ACS was first suggested in 1979 by Charache et al. and was developed in order to reflect the unique nature of acute pulmonary illness in patients with SCA.

Case presentation

A 10-year-old boy with homozygous SCA was admitted to the Pediatric Emergencies of our secondary hospital, in North Greece, with an-eight-hour history of back and abdominal pain and fever (38.5 °C). The symptoms worsened on awakening the day of attendance. The pain was sufficiently severe to keep him awake at night prior to admission. The only medication received was hydroxyurea and folic acid daily. There was no history of recent illness, urinary tract symptoms or trauma. The past history revealed SCA, diagnosed at age of 9 months with hemoglobin electrophoresis. He has been followed at our hospital since the age of 3 years old and he has had recurrent vaso-occlusive crises in the course of his disease. In the last 3 years, he was frequently hospitalized in our department for severe bone pain. At those times, symptoms were resolved quickly with intravenous hydration and conservative treatment. Family history indicated that his brother also had SCA.

On physical examination, the patient's temperature was 38.2 °C, heart rate was 88 beats/min, respiratory rate was 20 breaths/min and blood pressure was 90/50 mm Hg. He complained about abdominal pain that he was not able to localize. Abdominal examination showed normal bowel sounds and no rebound tenderness. The liver was palpable at 2 cm and spleen tip was just palpable below the right and left costal margins respectively. Lungs were clear to auscultation. There was no lower extremity edema, leg pain, or palpation of the deep veins. No other findings were revealed from the rest systems examination. Abdominal and chest radiographs were normal, and an abdominal ultrasound demonstrated moderate splenomegaly and a normal pancreas, liver, and biliary tree. Basic blood tests were performed. Blood and urine cultures were also obtained (Table 1). Liver function tests, including gamma-glutamyl transaminase (γ-Gt), aspartate aminotransferase (AST) and alanine aminotransferase (ALT), serum electrolytes, serum amylase and serum glucose were normal on admission and remained normal throughout the patient's hospitalization. The most likely diagnosis was painful vaso-occlusive crisis and the initial management consisted

Table 1 – Laboratory investigations

	Days of hospitalization					
Laboratory tests	1st (admission day)	Blood transfusion ↓ 2nd	Blood transfusion ↓ 3rd	4th	6th	10th
WBC k/μl (neut%/lymph%)	24.8 (80%/17%)	34.47 (85%/10%)	33.00 (85%/10%)		14.61 (63%/19%)	11.5 (54%/20%)
Hb g/dl	8.6	5.9	6.6		7.4	8.2
Ht	25	19	17		21.7	24.4
CRP mg/l (ref. range < 5)	4	139	175		85	41
Chest radiograph	normal findings	new infiltrate left lower lobe				
Blood culture	+[1]	+[2]			negative[1]	negative[2]
Urine culture	+	negative				
Arterial blood gases		pre transfusion		post transfusion		
pH		7.39		7.38		
PaO_2		68 mm Hg		85 mm Hg		
$PaCO_2$		33 mm Hg		37 mm Hg		
HCO_3^-		21 mm Hg		24 mm Hg		
SaO_2		91%		98%		

[1]first blood culture; [2]second blood culture; WBC – white blood cells; CRP – C-reactive protein

of intravenous fluids, oral painkillers, oral fluids as tolerated, oral clarithromycin and intravenous cefuroxime.

Twenty four hours later, the patient was suddenly cyanosed and developed nonproductive cough, dyspnea and pleuritic chest pain. Physical examination revealed that he was pyrexial (39.1 °C), with heart rate 110 beats/min, blood pressure 120/80 mm Hg, tachypnea (respiratory rate 40 breaths/min), accessory muscles use and widespread fine crackles and wheeze heard throughout the chest. He required supplemental oxygen therapy via nasal prongs to maintain oxygen saturation above 90%. A repeat chest X-ray was performed demonstrating a new left lower lobe infiltrate. New blood tests, arterial blood gases, and blood cultures were obtained (Table 1). The diagnosis of ACS was established and treatment with bronchodilators, intra-venous ceftriaxone and vancomycin initiated. Oral clarithromycin was continued and blood transfusion was performed immediately after the diagnosis of ACS had been established. A second blood transfusion followed 24 hours later (Table 1).

Six days after admission, the patient was significantly improved. He was apyrexial with normal physical examination and normal oxygen saturation. The haemoglobin (Hb) and haematocrit (Ht) values were also significantly improved (Table 1). The patient was completely recovered (normal physical examination and normal blood tests) (Table 1) ten days after the admission. He was discharged after a-thirteen-day-hospitalization with no other therapy at home.

Discussion

Patients with SCA frequently develop acute pulmonary complications due to their illness, including ACS. The diagnosis of ACS in sickle cell disease is an important challenge to the physician and especially to the pediatrician. Similar with our case, it may present insidiously and non-specifically, often complicating other conditions (Taylor et al., 2004).

ACS is currently defined as a new infiltrate on chest radiograph in conjunction with 1 other new symptom or sign: chest pain, cough, wheezing, tachypnea, and/or fever (>38.5 °C) (Bernard et al., 2007). Risk factors for ACS include homozygosity for the SS genotype, a low level of fetal hemoglobin, and higher steady state of leukocyte and erythrocyte counts (Atz and Wessel, 1997). Reviewing 671 episodes of ACS, the National Acute Chest Syndrome Study Group determined that infection appears to be a common cause of ACS in children, whereas fat embolism occurs more often in adults (Bernard et al., 2007). The management is still largely determined from the experience of individual practitioners, and there are no conclusive randomized controlled clinical trials to guide therapy (Miller, 2011). The most common therapy includes hydration, analgesia, supplemental oxygen, broad-spectrum antibiotics, bronchodilators, mechanical ventilation and early transfusion when it is indicated (Bernard et al., 2007).

Bernard et al. (2007) suggested that up to 50% of patients diagnosed with ACS, are initially admitted to the hospital for other reasons and subsequently develop the disease. The most common admission's reason in these cases, similar to our case, is a vaso-occlusive painful crisis (Taylor et al., 2004; Bernard et al., 2007). Therefore, the patients admitted to the hospital for painful crisis, should be considered to be in the prodromal phase of ACS and should be monitored closely in case they develop this syndrome. The average time of ACS development after hospitalization was suggested to be 2.5 days (Bernard et al., 2007). Our patient had developed ACS 24 hours after admission.

Another important aspect in these patients is that the radiographic findings of ACS can lag behind the clinical findings. So, if ACS is clinically suspected, a positive chest radiograph defines the disease, but a single negative radiograph cannot exclude it. On the other hand, it was suggested, that in many cases the clinical assessment of these patients was inadequate to identify ACS. Therefore, it has been demonstrated that every patient with sickle cell disease and fever who is presented to the emergency department, would be benefited from

a chest radiograph. For this reason, in patients with sickle cell anemia, a chest X-ray is indicated for diagnostic purposes also in different cases from an obvious respiratory illness (Bernard et al., 2007). It is also important for the physicians to keep in mind that radiographic findings for ACS often progress over the time (Vichinsky et al., 1997; Bernard et al., 2007). Vichinsky et al. (1997) supported that children are more likely to have no findings in chest X-ray at presentation. Likewise, our patient had negative chest X-ray on admission but 24 hours later he developed new infiltrates in a new chest X-ray. Kararmaz et al. (2006) suggested that since ACS may manifest in hours, physicians should have a low threshold for ordering chest X-rays for patients admitted with painful vaso-occlusive crisis.

Considering the above mentioned opinions and also the fact that serial radiographic examination is questionable in children with respect to radiation exposure, we strongly suggest repeated clinical examination in pediatric patients with SCA and painful crisis. A clinical status' deterioration should be the indicator for a new radiographic examination. In this way, early ACS can be recognized and the proper therapy applied during hospitalization, in order to avoid catastrophic consequences due to this syndrome.

Conclusion

This report serves as an example of a common diagnosis in patients with SCA admitted in hospital where vigilance for the development of ACS must be maintained, despite the lack of any initial chest X-ray abnormality. Therefore, in patients with SCA and painful crisis, ACS should be highly suspected. For this reason, repeated clinical examination is required and at the time the clinical status worsens, a new radiographic examination should be considered. In this way, early ACS can be recognized and catastrophic consequences due to this syndrome could be avoided.

References

Al-Dabbous, I. A. (2002) Acute chest syndrome in sickle cell disease in Saudi Arab Children in the Eastern Province. *Ann. Saudi Med.* **22**, 167–171.

Atz, A. M., Wessel, D. L. (1997) Inhaled nitric oxide in sickle cell disease with acute chest syndrome. *Anesthesiology* **87**, 988–990.

Bernard, A. W., Yasin, Z., Venkat, A. (2007) Acute chest syndrome of sickle cell disease. *Hospital Physician* **44**, 5–23.

Charache, S., Scott, J. C., Charache, P. (1979) "Acute chest syndrome" in adults with sickle cell anemia. Microbiology, treatment and prevention. *Arch. Intern. Med.* **139**, 67–69.

Kararmaz, A., Ayyildiz, O., Kaya, S., Turhanoglu, S. (2006) Acute chest syndrome in a patient with sickle cell anemia successfully treated with erythrocytapheresis. *Internet J. Emerg. Intensive Care Med.* **9**, 3.

Miller, S. T. (2011) How I treat acute chest syndrome in children with sickle cell disease. *Blood* **117**, 5297–5305.

Mousa, S. A., Al Momen, A., Al Sayegh, F., Al Jaouni, S., Nasrullah, Z., Al Saeed, H., Alabdullatif, A., Al Sayegh, M., Al Zahrani, H., Hegazi, M., Al Mohamadi, A., Alsulaiman, A., Omer, A., Al Kindi, S., Tarawa, A., Al

Othman, F., Qari, M. (2010) Management of painful vaso-occlusive crisis of sickle-cell anemia: consensus opinion. *Clin. Appl. Thromb. Hemost.* **16**, 365–376.

Taylor, C., Carter, F., Poulose, J., Rolle, S., Babu, S., Crichlow, S. (2004) Clinical presentation of acute chest syndrome in sickle cell disease. *Postgrad. Med. J.* **80**, 346–349.

Vichinsky, E. P., Styles, L. A., Colangelo, L. H., Wright, E. C., Castro, O., Nickerson, B. (1997) Acute chest syndrome in sickle cell disease: clinical presentation and course. Cooperative Study of Sickle Cell Disease. *Blood* **89**, 1787–1792.

Yale, S. H., Nagib, N., Guthrie, T. (2000) Approach to the vaso-occlusive crisis in adults with sickle cell disease. *Am. Fam. Physician* **61**, 1349–1356, 1363–1364.