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Acute Pulmonary Disease in a Young Woman with Sickle Cell Anemia and Moyamoya Disease

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Sickle cell disease is the most common inherited disorder among men and women of African ancestry. One of every 650 Africans is born with SCD and more than 8% are heterozygous for the sickle cell gene [1]. SCD is becoming more common in Israel in general, and in southern Israel in particular, owing to the presence of a community of African-Americans numbering about 3000 known as the "African Hebrews" that settled in several Negev towns. Also in the south are growing numbers of temporary foreign workers and refugees from the African continent.

As a result of these new populations more patients with SCD are expected to be encountered in Israel. We describe a young woman from the "African Hebrew" community with known SCD who was admitted with an acute chest syndrome; we also review the available literature on the management of acute complications associated with SCD.

PATIENT DESCRIPTION

A 23 year old woman of African-American origin was admitted to the internal medical department because of chest pain, shortness of breath and coughing. Six years previously she presented with microcytic anemia. Genetic testing revealed that she had SCD of SS phenotype. SCD was also diagnosed in her two younger brothers. So far there has been no need for blood transfusions.

In the year before admission she suffered from leg ulcers considered to be a vaso-occlusive complication of SCD and she was treated with local antibiotics. In the week before admission these ulcers had worsened. Also in the last year she suffered from recurrent seizures. The neurological workup, including magnetic resonance angiography, led to the diagnosis of Moyamoya syndrome, a rare neurological complication strongly associated with SCD. She was treated with levetiracetam 500 mg twice daily, which partially controlled her seizures; her last seizure occurred one week prior to admission. She does not smoke and had not received influenza or pneumococcal vaccines.

On admission her respiratory rate was 26 breaths/minute and oxygen saturation 92% on ambient air. Her temperature was 39°C. She was alert without any neurological deficit. Diffuse crackles and decreased lung sounds over the left hemothorax were heard. On the medial aspect of both legs above the ankles, ulcers with a diameter of 7 cm were present without signs of indurations or pus [Figure A]. The rest of the physical examination was normal.

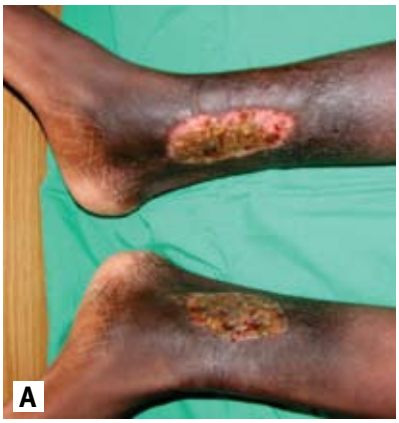
Her hemoglobin was 6.5 g/dl and hematocrit 18.7%, her white blood cell count was 21,800/μl with 61% polymorphonuclear cells, and platelets were in the normal range. The direct blood smear revealed a few target cells and many sickle cells. Her kidney function and electrolytes were normal with 1337 U/L lactate dehydrogenase. Blood gas analysis revealed respiratory alkalosis: pH 7.5, PCO_2 20, PO_2 68, HCO_3 20, and Sat 92.

Her chest X-ray demonstrated a left lower lobe infiltrate. Her oxygen saturation was much lower than expected from the radiological scan, and computed tomographic angiography revealed bilateral lower lobe consolidations in the lung with right minimal pleural effusion and areas of ground-glass opacities, without any evidence of a pulmonary embolism [Figure B].

Treatment comprised oxygen by nasal prongs, nebulized salbutamol and ipratropium bromide, intravenous

SCD = sickle cell disease

[A] Ulcers on the patient's legs



cefuroxime and oral roxithromycin, as well as a blood transfusion. Her blood cultures were sterile and serology for Mycoplasma was negative.

She was discharged one week later after her temperature had returned to normal and her complaints had resolved. After discharge she was seen in the hematology clinic with persistent anemia despite iron therapy. Thus, she continued to receive blood transfusions to keep her hemoglobin above 10 g/dl. She has had no further seizures but was rehospitalized due to leg pain, which was treated with analgesics and transfusions.

COMMENT

We report a young woman of African-American ethnicity who presented with acute chest syndrome related to sickle cell disease. Acute events associated with SCD include vaso-occlusive crisis and acute chest syndrome [1-3]. These events often result in admission to hospital, with considerable morbidity, sometimes leading to death [1,3].

The most commonly reported acute event is vaso-occlusive crisis associated with hemolysis resulting in microvascular entrapment of abnormal red blood cells followed by increasing viscosity and occlusion of the vascular bed [2]. This leads to tissue hypoxemia resulting in severe pain due to organ ischemia and infarction, and subsequent development of an inflammatory reaction [2]. Our patient had already suffered for more than one year from these ischemic leg ulcers that had worsened in the week before admission.

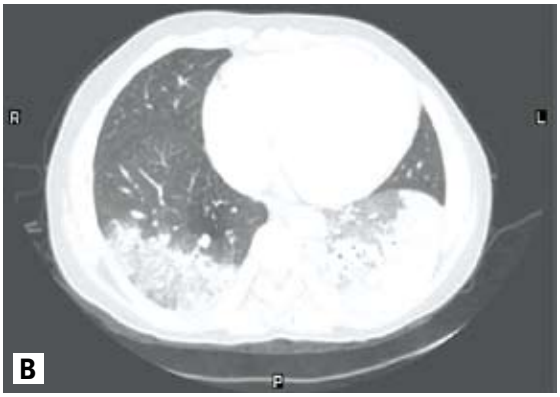
Another acute event complicating SCD is the acute chest syndrome, which is defined as the occurrence of fever and respiratory complaints (cough, chest pain, coughing and wheezing) along with a new pulmonary infiltrate [1,2]. A recent prospective multicenter study reported pneumonia and fat embolism as frequent causes of acute chest syndrome, although the etiology was unknown for about half the patients [1]. Fat embolism is the result of a vaso-occlusive crisis of the bone marrow of the long bones undergoing necrosis and is transported in the bloodstream to the pulmonary circulation where it induces a severe inflammatory response and subsequent endothelial dysfunction [2]. Acute chest syndrome may cause hypoxemic respiratory failure, even acute respiratory distress syndrome requiring mechanical ventilation. In such cases the mortality rate may reach 30%, which is similar to that seen in ARDS of other etiologies [2].

On admission our patient presented a differential diagnosis including community-acquired pneumonia and pulmonary embolism; the latter was not confirmed by the CT angiography, leading to the realization that she had suffered an acute chest syndrome event. It is not possible to unequivocally distinguish this syndrome from pneumonia based on radiological findings [1-3]. Our patient was hypoxemic with severe anemia and worsening of her neurological disorder (the seizure occurred one week prior to admission) and vaso-occlusive disease. The discrepancy between the severity of her clinical presentation and the radiological findings supported the diagnosis of an acute chest syndrome and not just a simple pneumonia. In both conditions the management is supportive and includes broad-spectrum antibiotics, oxygen and fluids. However, patients with acute chest syndrome may also need blood transfusion and control of pain that follows veno-occlusive events. It is noteworthy that due to a non-functioning spleen, patients with SCD are prone to infection, emphasizing the importance of vaccination against pneumococcal infections [1]. It was reported that 80% of patients who suffered an acute chest syndrome will have a subsequent recurrence [2].

Patients with SCD-related cerebrovascular complications are more likely to develop acute chest syndrome [1].

ARDS = acute respiratory distress syndrome

[B] Chest CT-angiography of the patient with acute chest syndrome, showing bilateral lower lobe consolidations with right minimal pleural effusion and areas of ground-glass opacities with no evidence of pulmonary emboli



Our patient had been diagnosed with Moyamoya syndrome, a neurological condition defined on magnetic resonance angiography as a telangioectatic network of collateral vessels that develops as a result of large cerebral vessel occlusion and is associated with recurrent stroke [4]. Moyamoya syndrome has been strongly associated with SCD. Recurrent and difficult to control seizures, as in our patient, have been reported as part of the Moyamoya syndrome.

Long-term follow-up for patients recuperating after an acute SCD-related event is warranted since hyper-reactive airways and chronic lung disease are not uncommon [5]. Patients with acute veno-occlusive events should also be followed for the development of pulmonary hypertension, which is associated with decreased survival [2].

In summary, we report a young woman of African-American ancestry known to suffer from SCD complicated with recurrent seizures (Moyamoya syndrome) and leg ulcers. She was admitted with an acute febrile respiratory illness consistent with acute chest syndrome, an event indistinguishable from other more common pulmonary conditions like pneumonia and pulmonary embolism. The latter was not confirmed by CT angiography. Moyamoya second-

ary to SCD is a neurological disease without clinical involvement of other organs or systems. Moreover, the lung CT did not show vascular occlusions or other features of vascular disease.. Our patient received supportive care with broad-spectrum antibiotics, fluids, oxygen, inhaled bronchodilators, and blood transfusion. We reviewed the available literature on the acute events associated with SCD, which we expect to become a less rare condition, considering the increase in predisposed populations in Israel.

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