Case Report

Pleural effusion as the main manifestation of intrathoracic extramedullary heamatopoietic masses in a patient with beta thalassemia minor

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Key words:
- Pleural effusion
- Extramedullary hematopoiesis
- Intrathoracic mass
- b-thalassemia

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ABSTRACT

We report a case of a patient who was admitted to the emergency Department with gradually worsening chest pain followed by shortness of breath. Chest X-ray showed right sided pleural effusion and a paravertebral lesion. Computed tomography of the chest showed sizable pleural effusion with atelectasis of the underlying lung and three intrathoracic paravertebral masses with sharp margins. Computed tomography guided fine needle biopsy was performed and established diagnosis of extramedullary haematopoiesis. The only therapeutic intervention applied was pleural fluid aspiration without relapse of the effusion during the period of ten months follow up.
Pneumon 2016, 29(2):156-160.

INTRODUCTION

Ineffective erythropoiesis (IE) occurring during chronic bone marrow failure (chronic haemolytic conditions or bone marrow infiltration by neoplastic or fibrotic tissue), results in a number of compensatory mechanisms, such as erythroid marrow expansion and extramedullary hematopoiesis (EMH). The erythroid bone marrow can expand to nearly 30 times, depending on the severity of IE.[5] This hematopoietic response is most often microscopic, but can also result in organomegaly or growth of tumor-like masses.[6-8] Almost any site of the body can be involved by EMH including the spleen, liver, lymph nodes, thymus, heart, breast, prostate, adrenal glands, kidneys, pleura, skin, retroperitoneal tissue, cranial nerves and peripheral nerves.[9,10,12,13]

CASE REPORT

A 48 year old woman, smoker (20 pack years), was admitted to the emer-

gency Department with worsening chest pain which had gradually started a month ago, followed by increasing shortness of breath for the last week and with a known medical history of beta thalassemia minor, who have never received blood transfusion.

On examination, she was tachypneic with a respiratory rate of 22- 24 breaths per minute, oxygen saturated hemoglobin 92% and absence of breath sound over the right hemithorax. Blood testing revealed hypohromic microcytic anemia (RBC: 4.83 M/μL, HGb: 9.0 g/dL, HCT: 30.0%, MCV: 62.1fL, MCH: 18.6 pg, MCHC: 30.0 g/dL) and elevated concentration of D- Dimer: 2.24μg/ml (normal: 0-0.3 μg/ml). Chest X- ray showed right sided sizable pleural effusion and a paravertebral mass (Figure 1). Electrocardiogram and echocardiogram were performed and the results revealed normal findings (EF= 70%, RVSP= 35mmHg, with a normal right heart size). Computed tomography of the chest and abdomen showed right sided pleural effusion with atelectasis of the underlying lung and three intrathoracic paravertebral masses with sharp margins (figures 2, 3).

Pleural fluid aspiration was performed draining gradually 3 liters of serous pleural fluid. Pleural fluid analysis revealed a lymphocytic exudate with 4600 cell/μL, Hct: 0.2%, PH: 7.36, ADA: 7 U/L, Glu: 85 mg/dl. Pleural fluid cultures and cytology were negative.

Computed tomography guided fine needle biopsy of the masses was performed. Histopathological and immunohistological analysis revealed features of extramedullary hematopoietic tissue (immunohistological analysis of Glucophorin, MPO, CD 61 revealed all hematopoietic cell lines and the epithelial marker expressed negatively).

As the patient was asymptomatic and in stable clinical condition, without pleural effusion, she referred to a Thalassemia Clinic for further treatment. Due to the absence of symptoms, no therapeutic intervention was performed. Only frequent chest X- rays and blood testing were carried out in order to intervene therapeutically in case of presenting symptoms. During a 10 month follow -up period, the patient continues to be asymptomatic without the need of blood transfusion, while the extent of pleural effusion after aspiration and the size of masses remained stable.

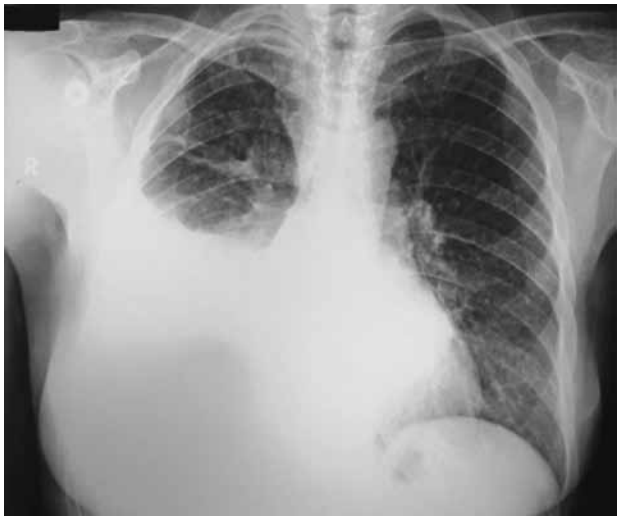
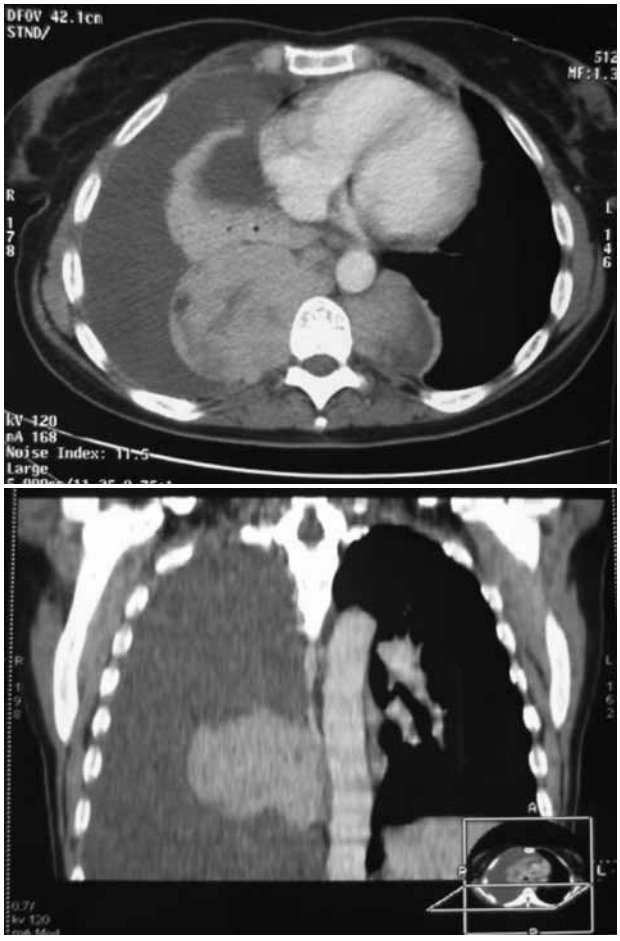


FIGURE 1. Chest X-ray reveals right sided sizeable pleural effusion and presence of paravertebral mass with sharp margins.



FIGURES 2 AND 3. Chest Computed Tomography reveals right sided pleural effusion with atelectasis of the underlying lung and three intrathoracic paravertebral masses with sharp margins.

DISCUSSION

The mediastinum is the anatomical space bounded laterally by the pleurae, superiorly by the thoracic inlet and inferiorly by the transverse thoracic plane. Based on anatomical landmarks on the lateral X-ray view, the mediastinum can be divided into three parts: anterior, middle and posterior.[1] The posterior mediastinum consists of the descending thoracic aorta, esophagus, azygous vein, autonomic ganglia and nerves, thoracic lymph nodes and fat.[2]

Mediastinal tumors can be caused by a wide range of diseases. The differential diagnosis for a posterior mediastinal mass includes: neurogenic tumors (neurofibroma, schwannoma, and malignant peripheral nerve sheath tumor), neuroblastic tumors (neuroblastoma, ganglioneuroma), non-neurogenic tumors (chordoma, pheochromocytoma), descending aortic aneurysm, paraspinal abscess, esophageal neoplasm, hernias (hiatus hernia, Bochdalek hernia), lymphoma, extramedullary hematopoiesis, thoracic meningocoelle, neurenteric cyst[3,4].

Almost any site of the body can be involved by EMH including the spleen, liver, lymph nodes, thymus, heart, breast, prostate, adrenal glands, kidneys, pleura, skin, retroperitoneal tissue, cranial nerves and peripheral nerves. These sites are thought to be involved in the active haematopoiesis in the fetus. Although this sequence of reactions normally stops at birth, the extramedullary hematopoietic vascular connective tissues maintain the capacity to produce erythrocytes under conditions of long-lasting ineffective erythropoiesis.[9,10,12,13]

Intrathoracic EMH masses are usually found in the posterior mediastinum but they may also take the form of a pleural mass or/and interstitial pulmonary abnormality, can be single, multiple, unilaterally or bilaterally.[6] Paraspinal location for the EMH masses occurs in 11-15% of cases with extramedullary hematopoietic pseudotumors.[13-15]

Posterior mediastinal EMH masses essentially exert effects on the spinal cord owing to spinal compression (lower limb pain, paresthesia, back pain, Babinski response, exaggerated or fast deep tendon reflexes). The presence of neurologic symptoms depends on the chronicity of the disease, the size and location of lesions and the extent of spinal cord pathology.[10,13,16,20,21] More than 80% of cases may present no symptoms, while the lesions are usually detected accidentally by radiological methods.[10,13,17-19] On the other hand, posterior mediastinum EMH masses rarely cause airway obstructions and development of pleural effusion. The mechanism of developing pleural effusion is believed to be multifactorial. Mechanic lymphatic obstruction and liberation of inflammatory cytokines, which increase the capillary permeability during the friction between the pleura and the pseudotumors, seem to be the primary mechanism.[22] There have been only occasional literature reports of EMH-related pleural effusion. In these cases the underlying diseases identified were myelofibrosis, sickle cell disease, hereditary spherocytosis, and thalassemia major and intermedia. Pleural effusion was exudate in most cases and only a few cases of hemothorax were reported.[7,22,23,25-28] The most interesting aspect of our presentation is that according to our knowledge, there is no previous case reported in the literature regarding pleural effusion induced by EMH masses in patient with thalassemia minor.

Early diagnosis of intrathoracic EMH will affect the management and the incidence of irreparable neurologic damage and airway obstructions.[29] The medical history of hematological disease coupled with X-ray computed tomography helps in diagnosis. Magnetic resonance is regarded as the technique of choice for the diagnosis and follow-up evaluation of spinal cord compression.[30,31] Biopsy remains the best method for establishing a tissue diagnosis.[32] Fine needle biopsy (FNB) is a reliable, rapid, inexpensive and relatively painless technique.[11]

Treatment of EMH is unnecessary in the absence of complications[33,34] and generally depends on how severe symptoms are, on the size of the pseudotumor, the patient's clinical condition and previous regimen. Management options include blood transfusions, hydroxyurea therapy, surgical decompression, radiotherapy, or any combination of these procedures.[10,13] Surgical decompression or radiation therapy may be required in case of spinal cord compression or in case of fast growth, which may result in rupture and ensuing hemothorax.[35,36]

Treatment of pleural effusion associated with intrathoracic EMH masses depends on the underlying disease, the shrinking or inactivation of the ectopic heamatopoietic tissue, the production rate of pleural fluid, fluid 's characteristics and the patient's clinical status. In the most of the hemoglobinopathies and myelofibrosis cases reported in the literature, fluid aspirations could not control pleural effusion and pleurodesis and blood transfusion or/and hydroxyurea therapy or/and radiotherapy were applied to these patients.[22-24,26-28] The management of hemothorax caused by EMH should be individualized. Surgical intervention is the method of choice,[28,37-39] but in some myelofibrosis cases hemothorax can be controlled by low dose radiation.[7,28] In our case, only pleural fluid aspiration

was performed without relapse of the effusion during a period of ten months follow- up.

CONCLUSION

Pleural effusion caused by EMH masses in bone marrow dysfunction is a rare condition. Early diagnosis will affect the management and the incidence of irreversible neurologic damage or/and presence of airway problems. The management of these patients should be individualized.

This case report suggests that EMH related pleural effusion should be considered in the differential diagnosis in thalassemia minor patients with intrathoracic masses.

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