Massive Hemothorax in a Beta-Thalassemic Patient Due to Spontaneous Rupture of Extramedullary Hematopoietic Masses: Diagnosis and Successful Treatment

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Intrathoracic extramedullary hematopoiesis is an unusual but well-described entity. The condition is typically found in patients who have chronic hemolytic anemias, especially thalassemia. We report a case of a 38-year-old man with underlying beta thalassemia/hemoglobin E who developed intrathoracic extramedullary hematopoiesis. The hematopoietic masses spontaneously ruptured, resulting in massive hemothorax. The condition was confirmed by video-assisted thoracoscopy and successfully treated with surgery, hydroxyurea, and radiation. *Key words: extramedullary hematopoiesis, spontaneous hemothorax, beta thalassemia.* [Respir Care 2006;51(3):272–276. © 2006 Daedalus Enterprises]

Introduction

Extramedullary hematopoiesis (EMH) is a common compensatory mechanism for chronic anemia found in patients with hemoglobinopathies such as thalassemia, sickle cell anemia, and hereditary spherocytosis. These patients are usually asymptomatic. EMH usually manifests in the thorax as multiple posterior mediastinal or paravertebral masses and masses along the lateral margins of the ribs.[1–3] Hemothorax associated with trauma in the patient with EMH has been described.[4] However, nontraumatic spontaneous hemothorax is a rare complication of EMH; our review of the literature found only 7 similar reports.[1–3,5–8] Herein, we report a patient with beta-thalassemia/hemoglobin E (HbE) disease who presented with massive hemothorax caused by spontaneous rupture of an EMH. The condition was confirmed via video-assisted thoracoscopy and was successfully treated with surgery, hydroxyurea, and low-dose radiation.

Case Report

A 38-year-old man with underlying beta-thalassemia/HbE disease presented to the emergency department because of sudden shortness of breath and chest pain on the right side. He denied chest trauma. He had undergone splenectomy at the age of 5, and cholecystectomy at the age of 31. The cholecystectomy preoperative chest radiograph had shown bilateral paravertebral soft-tissue masses. After that operation he had normal daily activities and was lost to follow-up for several years. However, he required frequent blood transfusion. His baseline hemoglobin was 6.5–8 g/dL. Hemoglobin typing study showed HbA_2 of 0% (normal 2.3–5.8%), HbA of 29% (normal 94.2–97.7%), HbF of 33% (normal $< 2\%$), and HbE of 38%.

On examination, blood pressure was 80/50 mm Hg, heart rate was 94 beats/min, and respiratory rate was 32 breaths/min. Chest auscultation revealed decreased breath sounds and decreased vocal resonance at the right lower lung. Cardiac examination revealed sinus tachycardia with prominent second heart sound and pulmonic component. Hep-

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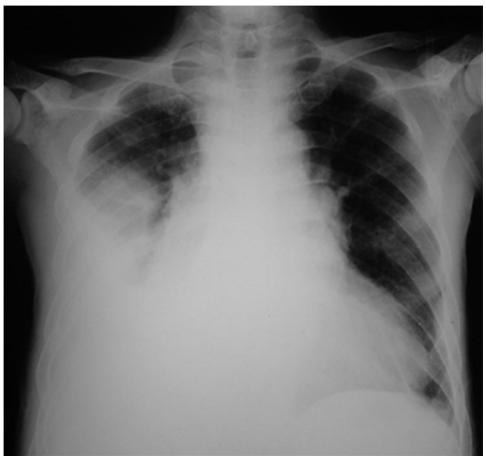

Fig. 1. Posteroanterior chest radiograph showing bilateral paravertebral soft-tissue masses and massive right pleural effusion. Note diffuse thalassemic bone changes.

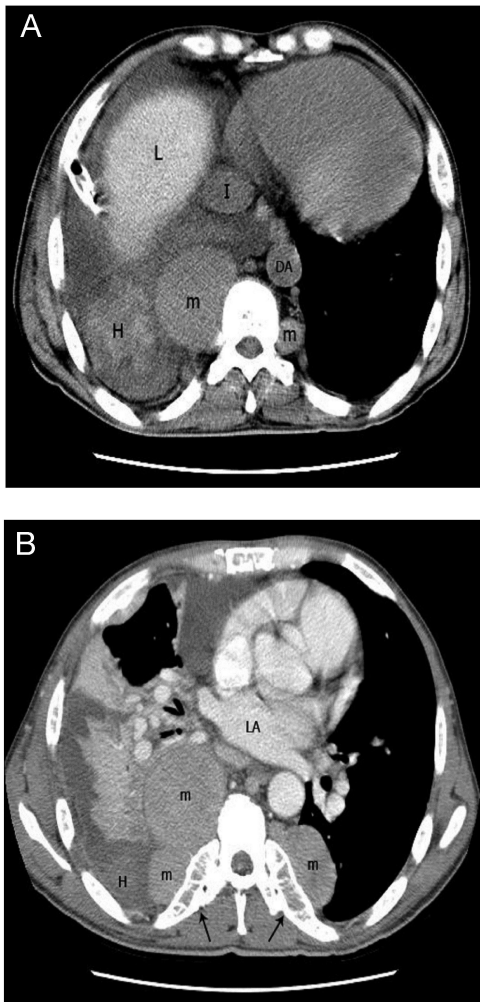

Fig. 2. A: Nonenhanced computed tomogram (CT) at the level of the ventricles, showing a mass of high attenuation (H) in the right pleural space, consistent with blood clot. There are also bilateral paravertebral soft-tissue masses (m). Note the right chest tube and relatively hyperdense liver (L). I = inferior vena cava. DA = descending aorta. B: Enhanced CT at the level of the left atrium (LA), showing enhanced bilateral paravertebral soft-tissue masses (m), consistent with extramedullary hematopoiesis. A right hemothorax (H) and partially collapsed right lung are visible. Note the thalassemic bone changes (arrows).

atomegaly was found on abdominal palpation. He had generalized hyperpigmentation of the skin. His serum ferritin was 3,200 ng/mL (normal 20–300 ng/mL in men and 10–130 ng/mL in women). Complete blood test in the emergency department revealed a white blood cell count of 49,000 cells/μL and nucleated red cells of 244 per 100 white blood cells. The hematocrit was 21% and hemoglobin was 6.5 g/dL. Serum electrolytes were within normal limits. The liver function test revealed total bilirubin of 2.6 mg/dL (normal 0.2–1.2 mg/dL), direct bilirubin of 0.4 mg/dL (normal 0.1–0.5 mg/dL), aspartate aminotransferase of 66 U/L (normal 5–40 U/L), alanine aminotransferase of 55 U/L (normal 5–40 U/L), and alkaline phosphatase of 97 U/L (normal 40–105 U/L).

He was admitted to the hospital and red-blood-cell transfusion was immediately instituted. The initial chest radiograph revealed bilateral paravertebral soft-tissue masses and massive right pleural effusion (Fig. 1). Thoracentesis yielded 1,600 mL of unclotted bloody fluid with the ratio of pleural fluid hematocrit (12%) to venous blood hematocrit (21%) greater than 50%. A chest tube was inserted into the right pleural cavity and red-blood-cell transfusion was continued.

Computed tomography (CT) of the chest showed multiple bilateral intrathoracic paravertebral soft-tissue masses of various sizes, extending from the fourth thoracic to the eleventh thoracic vertebral level, and bilateral paracostal masses. These masses showed homogeneous contrast enhancement (Fig. 2). Diffuse thalassemic bone changes were visible. There was a moderate amount of right pleural effusion, with evidence of blood clot in the right pleural cavity, causing partial collapse of the right lung. There was partial compression of the right intermediate and right lower-lobe bronchi by large paravertebral soft-tissue masses. There was enlargement of the right atrium, right ventricle, and central pulmonary arteries, which suggested pulmonary hypertension.

Six days after chest tube insertion, there was no bloody fluid from the chest tube. However, the chest radiograph revealed no lung expansion. His hematocrit dropped from 28% to 26%. Video-assisted thoracoscopy was performed to identify and stop an active bleeding point and to help expand the right lung. During the thoracoscopy, multiple lobulated reddish EMH masses along the paravertebral regions were noted. After removal of blood clots, an active bleeding point on the lower EMH mass was identified and repaired with 4–0 prolene and pledgets (Fig. 3). Thick

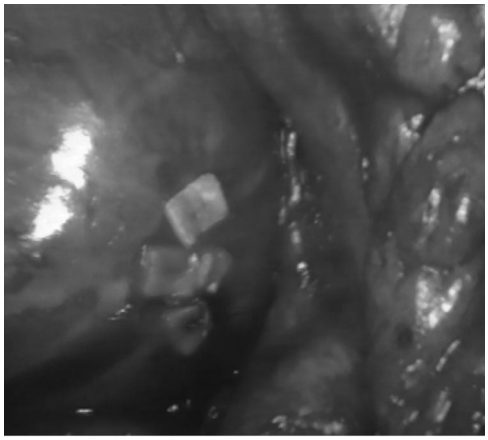

Fig. 3. Image taken during video-assisted thoracoscopy, showing highly vascularized lobulated mass along paravertebral regions, with a point of active bleeding.

fibrous adhesions around the right lung were completely removed by blunt dissection.

After the operation his hematocrit increased to 40% and remained stable without red-blood-cell transfusion. The chest tube was removed 6 days thereafter. Hydroxyurea was given at 500 mg/d for treatment of EMH. Desferoxamine infusion was given at 3,000 μg/d for treatment of hemochromatosis. He was discharged from the hospital 10 days after the operation. Three weeks after discharge, external irradiation was started at a dose of 200 cGy/d, for 10 fractions, with a total dose of 20 Gy. The follow-up chest radiograph obtained 6 months later showed substantial decrease in the size of bilateral paravertebral soft-tissue masses. The follow-up chest CT revealed complete resolution of right hemothorax and pre-existing bilateral intrathoracic paravertebral soft-tissue masses. Residual right pleural thickening was seen (Fig. 4). The patient remained well and has had no recurrence of bleeding to date.

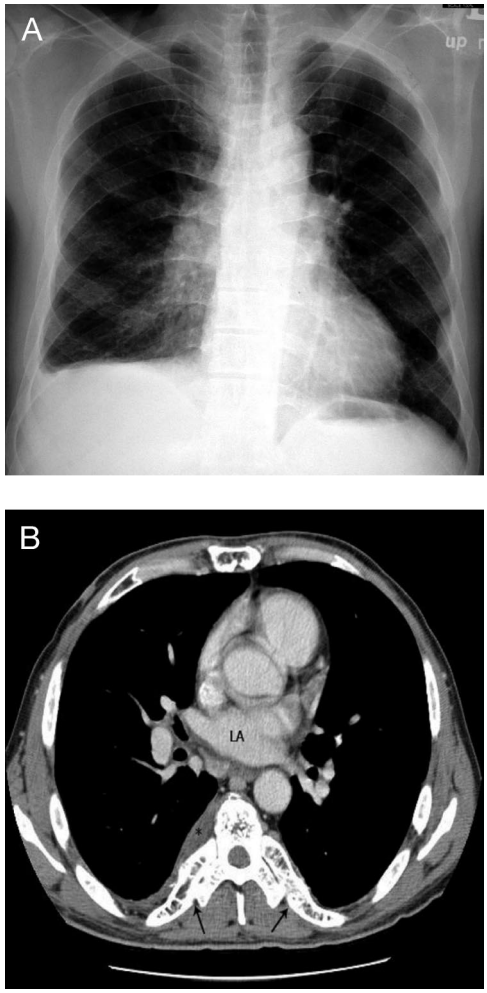

Fig. 4. Posteroanterior chest radiograph (A) and computed tomogram (B) obtained after radiation therapy, showing near resolution of bilateral paravertebral soft-tissue masses and right pleural effusion. Residual right basal pleural thickening is visible (around the asterisk). Note the thalassemic bone changes (arrows). LA = left atrium.

Discussion

EMH usually develops as a compensatory response in patients with anemia, particularly thalassemia, which is common in southeast Asia. This condition is rarely manifested as a mass-like lesion within the thorax in patients who have history of frequent blood transfusion and in whom hemoglobin level is kept above 7 g/dL.[2] However, EMH is commonly found in thalassemia-intermedia patients, who usually reach adult life without the need for frequent blood transfusion, because their erythropoiesis is not suppressed.[2] Intrathoracic EMH masses are usually located in the lower paravertebral areas and are usually multiple and bilateral.[1–3] Pathologically they may appear as lobulated dark red-purple fleshy paravertebral masses, without destruction of adjacent ribs and vertebrae, which helps distinguish them from other conditions, such as neurogenic tumors.[3] Other sites of intrathoracic EMH include the anterior mediastinum[1] and pleura.[5]

The pathogenesis of intrathoracic EMH includes the extrusion of bone-marrow stem cells through the thin cortex of the vertebral bodies and ribs, abetted by negative pressure; proliferation of the stem cells, which transform into a nodule of hematopoietic tissue upon demand; and proliferation of the embolized hematopoietic tissues from other areas to the intrathoracic region, such as the spleen.[1] In this patient, despite his hemoglobin being kept above 7 g/dL, he still developed EMH. This could be explained by a constant hypoxia and defective hemoglobin unloading in the periphery (elevated fetal hemoglobin) which may enhance erythropoiesis.

Table 1. Summary of Previous Reports of 8 Patients Who Presented With Hemothorax Secondary to Ruptured Extramedullary Hematopoiesis

First Author, Year	Disease(s)	Sex	Age	Symptoms	Diagnosis	Treatment	Outcome
Chu et al, 1999[1]	Alpha thalassemia	M	44	Chest pain, dyspnea	Thoracotomy with biopsy	Decortication	No recurrent bleeding
Chute et al, 2004[2]	Sickle cell trait/ beta thalassemia	M	26	Acute shortness of breath, chest pain, productive cough	Autopsy	Intercostal drainage	Death
Smith et al, 1988[3]	Thalassemia intermedia (splenectomy)	F	46	Sudden onset of chest pain and dyspnea	Thoracotomy with biopsy	Local radiation	No recurrent bleeding
Xiros et al, 2001[4]*	Hereditary spherocytosis	M	64	Upper abdominal pain, progressive dyspnea	Computed tomography scan	Intercostal drainage, splenectomy	Unchanged mass Resolved effusion
Kupferschmid et al, 1993[5]	Myelofibrosis	F	73	Dyspnea, serosanguinous pleural effusion, clinical deterioration after tetracycline pleurodesis	Thoracotomy	Decortication, radiation	No recurrent hemothorax
Muthuswamy et al, 1989[6]	Hereditary spherocytosis	M	54	Post-traumatic hypotension	Thoracotomy	No data available	No data available
Tassiopoulos et al, 2004[7]	Beta thalassemia intermedia, (splenectomy)	M	27	Chest pain and dyspnea	Computed tomography scan	Serial thoracentesis, hydroxyurea	No residual pleural adhesion Marked regression of extramedullary hematopoiesis at 1 year
Bartlett et al, 1995[8]	Agnogenic myeloid metaplasia	F	61	Progressive dyspnea	Technetium^{99} bone marrow scan	Radiation	No recurrent effusion Decreased size of mass at 7 months

*hemothorax associated with trauma

Hemothorax is a rare complication of intrathoracic EMH. Our literature review found only 7 similar reports of hemothorax secondary to spontaneous rupture of an intrathoracic EMH.[1–3,5–8] The clinical presentations, diagnostic strategies, treatments, and outcomes from those previous reports are summarized in Table 1.

The chest radiographic appearance of EMH includes bilateral paravertebral or posterior mediastinal masses, as seen in this case.[1–3] CT with intravenous contrast enhancement is a useful imaging method for identifying EMH. The typical CT appearance of EMH is smoothly marginated, soft-tissue masses with homogeneous enhancement along the paravertebral regions.[4,6,7] The masses may extend into the epidural space and cause spinal-cord compression.[9,10]

On magnetic resonance imaging, EMH may appear as isointense paravertebral masses on both T1- and T2-weighted images, with intermediate enhancement after administration of a paramagnetic agent.[10] Technetium^{99} sulfur colloid radionuclide bone marrow scan may show increased tracer activity in the lung and intrathoracic cavity.[8] Cytological study of the pleural fluid may reveal enlarged megakaryocytes, along with factor-VIII-related antigen immunoreactivity.[11]

Because fine-needle aspiration of EMH increases the risk of bleeding complications, it was not performed on this patient. Instead, video-assisted thoracoscopy was done. Smith et al[3] suggested that hematopoietic nodules/masses lacerated and covered by blood and fresh blood clots along the paravertebral areas help confirm the diagnosis. Surgical intervention may not be necessary if there is no complication, such as compression symptoms. If EMH is suspected in a patient who presents with hemothorax, thoracic surgery should be avoided because of the increased risk of bleeding.[3] Medical pleurodesis using a sclerosing agent may be contraindicated because the sclerosing agent can worsen the bleeding.[5] In the present case, however, video-assisted thoracoscopy and surgical decortication were performed to enhance lung expansion.

Low-dose radiation should be the treatment of choice, because EMH tissues are highly radiosensitive.[5] Radiation therapy in conjunction with transfusion can inhibit hematopoiesis and decrease the risk of recurrence.[12] Saxon et al[13] demonstrated that hydroxyurea can induce regression of EMH and reduce ineffective erythropoiesis in beta-thalassemic patients with bony and spinal complications. In the present case, multiple fractions of low-dose irradiation and hydroxyurea were given postoperatively. On follow-up, there was almost complete resolution of the remaining intrathoracic EMH after 6 months.

In some cases, however, radiation may be disadvantageous and worsen anemia because of the destruction of the sources of compensatory hematopoiesis.[3] A conservative approach with serial thoracentesis and blood transfusion should be considered if there is progressive reduction in hematocrit level of pleural fluid.[7] Splenectomy may help eliminate the main site of red-blood-cell destruction, as previously reported in patients with hereditary spherocytosis.[3,14]

ACKNOWLEDGMENTS

The authors thank Amnuay Thithapandha for constructive suggestions and editing. The artwork provided by Adul Tohme and Pitsanuk Detakarat is also gratefully acknowledged.

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