Ann Hematol (2001) 80:38–40

CASE REPORT

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Massive hemothorax due to intrathoracic extramedullary hematopoiesis in a patient with hereditary spherocytosis

Received: 23 December 1999 / Accepted: 31 May 2000

Abstract Extramedullary hematopoiesis (EMH) is a rare disorder, characterized by the appearance of hematopoietic elements outside of the bone marrow, which occurs in patients with chronic myeloproliferative disorders or congenital hemolytic anemias. We report on a 64-year-old man with hereditary spherocytosis, who presented with anemia, jaundice, intrathoracic EMH, and massive hemothorax. The diagnosis of EMH was established after computer tomography (CT)-guided punctuation of the paravertebral mass. The patient underwent splenectomy and thoracic drainage. After 1 year, the patient is in good health, with normal hemoglobin values, and hemothorax has not recurred.

Keywords Extramedullary hematopoiesis, · Hemothorax · Hereditary spherocytosis

Introduction

Hereditary spherocytosis (HS) is the most common of the red blood cell (RBC) membrane disorders, characterized by spherocytosis, increased osmotic fragility, and autosomal dominant or, less often, autosomal recessive patterns of inheritance. The clinical expression of the disease is highly variable, ranging from an asymptomatic condition to a severe, life-threatening hemolytic anemia.

Recent biochemical and molecular biologic studies have shown that this RBC phenotype is a consequence of deficiencies in a number of different membrane skeletal proteins involving spectrin, ankyrin, band 3, and protein 4.2 [7, 8].

Extramedullary hematopoiesis (EMH) is a rare disorder characterized by the appearance of hematopoietic elements outside of the bone marrow. It is usually associated with a neoplastic disease or with hematology disorders accompanied by peripheral cytopenias and inefficient hematopoiesis, including chronic myeloproliferative disorders [10], leukemias [2, 11], thalassemias [16], hemoglobinopathies [17], and hemolytic anemias, such as HS [6]. The heterotopic marrow is usually microscopic and most commonly involves the spleen, liver, and lymph nodes, but also can be seen in adipose tissue, adrenal gland, kidney, thymus, breast, mediastinum, pleura, pericard, retroperitoneum, epidural space, and epididymis [1]. Intrathoracic EMH tissue most commonly occurs in the posteroinferior mediastinum, but has been reported in the anterior mediastinum and pleura [12]. Pleural involvement is usually microscopic and asymptomatic and is noted only at autopsy [12]. Pleural effusion due to pleural involvement by EMH is rarely reported.

Case report

A 64-year-old man was admitted in September 1998 because of left upper abdominal pain, progressive dyspnea, fatigue, and jaundice for 1 week. His sister had been splenectomized because of symptomatic HS with splenomegaly. The patient was aware of his splenomegaly since childhood. He had been well up until 2 years before his initial presentation to our unit, when the patient was investigated in another hospital for anemia and an episode of left upper abdominal pain. A computed tomography (CT) scan performed at that time revealed two homogeneous left paravertebral masses in the lower mediastinum, 4 and 8.9 cm in diameter. One paravertebral mass was then punctuated and revealed abundant hematopoietic cells carrying the morphology of immature and mature erythroblasts, myeloid cells, and megakaryocytes. The patient was transfused with RBCs and discharged without further investigation or special treatment.

On admission to our hospital, he was pale, with moderate hepatomegaly, large splenomegaly (15 cm below the left costal margin), and left pleural effusion. The patient's hematological param-

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Table 1 Hematological parameters on admission. *WBC* White blood cells; *RBC* red blood cells; *Hb* hemoglobin; *Ht* hematocrit; *MCV* mean cell volume; *MCH* mean cell hemoglobin; *MCHC* mean cell hemoglobin concentration

	Patient	Control
WBC ($\times 10^9$/l)	7.6	
RBC ($\times 10^{12}$/l)	2.39	
Hb (g/l)	79	
Ht	0.221	
MCV (fl)	92	
MCH (pg)	33.2	
MCHC (g/l)	360	
Platelets ($\times 10^9$/l)	160	
Reticulocytes ($\times 10^9$/l)	401	
Neutrophils (%)	79	
Lymphocytes (%)	14	
Eosinophils (%)	1	
Monocytes (%)	4	
Myelocytes (%)	2	
Erythroblasts/100 white cells	2	
Osmotic fragility		
Initial hemolysis (%)	0.55	0.45
Final hemolysis (%)	0.45	0.40

eters on admission are given in Table 1. As is shown in the table, the mean cell volume (MCV), 90.3 fl, was within normal limits and the mean cell hemoglobin concentration (MCHC), 36 g/dl, was increased. Total bilirubin, 95.8 μmol/l, was elevated, the indirect bilirubin was 75.3 μmol/l, and the LDH was slightly elevated. No erythrocyte autoantibodies were detected by the direct and indirect Coombs test. The Ham test, as well as a test for sickling, were negative. On hemoglobin electrophoresis, the HbA_2 was 2.4% and HbF was $<2\%$. On a blood smear, a significant number of spherocytes were found. No other morphological changes were detected (Fig. 1). On the basis of the above data, the diagnosis of HS was confirmed. A bone marrow aspirate showed a hypercellular marrow with erythroblastic hyperplasia (M/E ratio: 1/5). The granulocytic and megakaryocytic series were normal.

The plain chest film on admission showed left-sided pleural effusion, extending almost to the lung apex. Thoracentesis yielded a hemorrhagic fluid. Pleural fluid analysis was negative for malignant cells and for microorganisms on smears and cultures. A thorax CT scan confirmed the presence of pleural effusion on the left hemithorax, as well as two non-homogeneous round masses with peripheral calcifications, symmetrically located in the paravertebral space at the level of the 8–11 thoracic vertebrae (Fig. 2).

During hospitalization, a fever and a compensated intravascular coagulation aggravated the patient's general condition. A chest tube for continuous drainage was inserted, and finally the patient underwent splenectomy without complications. The spleen weighed 1500 g immediately on removal. Microscopy showed hypertrophy of the red pulp, with no evidence of myeloid metaplasia. The enzyme activity of G6PD, 9.6 U/g of Hb, tested 2 months postoperatively, after normalization of the Hb value was within normal limits. The patient has been in close observation for 1 year now since the operation. He is in excellent condition, with normal Hb values. The chest X-ray showed that the paravertebral masses were unchanged and no more pleural effusion was evident.

Discussion

EMH is a well-recognized complication of diseases in which there is encroachment on marrow spaces or a chronic increase in the rate of production of RBCs [10]. It is generally assumed to be a compensatory bone marrow hyperplastic phenomenon, with seeding of circulating hematopoietic progenitors at various sites. It has been demonstrated that the compensated hemolytic state of HS is produced by an inappropriately high serum erythropoietin level, and that the pattern of erythropoietin overproduction is a biological characteristic of the disease [5].

The most common sites of EMH are the liver and spleen, but foci can occur in many other organs and tissues, including lymph nodes, pericardium, pleura, and the paraspinal area of the posterior mediastinum [9]. The preference of EMH tissue for the intrathoracic region is not clearly understood; a possible explanation is that negative pressure at that site could facilitate the extrusion of hyperplastic hematopoietic tissue from vertebral marrow [14]. In the case of mediastinal EMH, the mediastinal masses present on plain thorax X-ray as

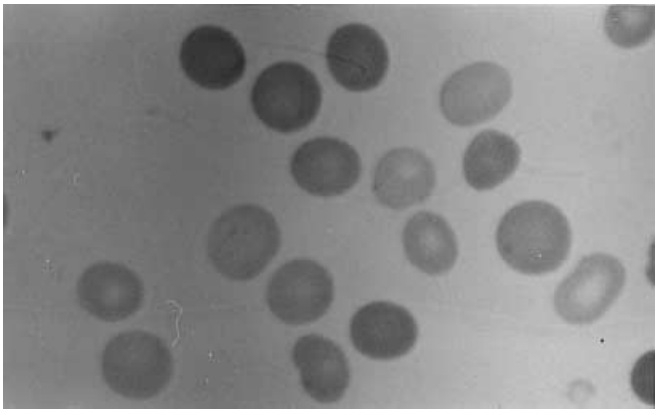

Fig. 1 Blood smear with spherocytes. No other morphlogical abnormalities of RBC were evident

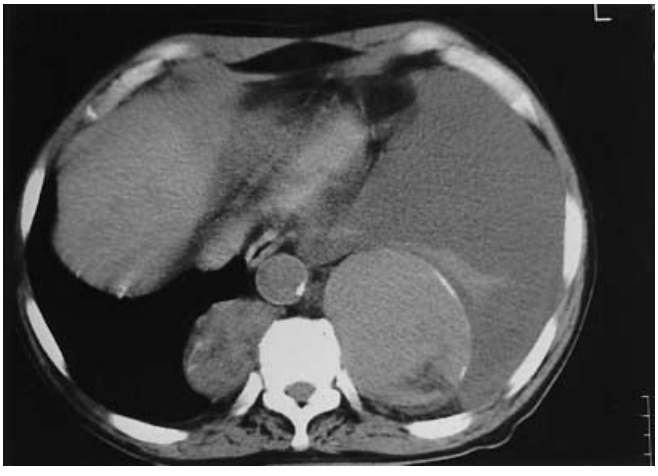

Fig. 2 CT scan of chest showing bilateral paravertebral masses of hematopoietic tissue. They are non-homogeneous with peripheral calcification. The grater mass on the left side is surrounded by hemothorax

well-demarcated or lobulated masses in the posterior mediastinum, below the level of T6. They may be unilateral or bilateral, do not contain calcification, and are not associated with bone destruction [10]. CT studies of EMH have described homogeneous, well-demarcated soft-tissue masses usually in the paravertebral region, confirming the absence of calcification and bone destruction [3]. In our patient, the paravertebral masses on a CT scan showed a clearly defined peripheral calcification. The absence of bone destruction and the frequent finding of lobulation are the main radiological features to distinguish EMH from neurogenic tumors commonly located in the posterior mediastinum [16]. EMH may also be detected by radionuclide imaging with $^{99}Tc^{m}$ sulfur colloid or ^{111}In chloride [10]. Whatever radiological technique is used to demonstrate the disease, biopsy confirmation is essential. Although invasive diagnostic procedures have been used, including thoracotomy and needle aspiration biopsy, they are potentially hazardous because of the highly vascular nature of the thoracic masses, and hence an increased risk of bleeding [16]. The occurrence of EMH in the pleura with effusion is rare. Among the 20,793 pleural, pericardial, and peritoneal effusions studied by Garcia-Riego [4], there were seven pleural and one peritoneal effusions from five patients with EMH. In any case of bloody effusion or hemothorax when EMH is suspected, thoracic surgery should be avoided because of the increased risk of bleeding. In these cases, the treatment of choice is radiotherapy [12].

Treatment of patients with EMH is only required in the presence of complications. Regression of asymptomatic EMH has been referred to in a patient with homozygous β thalassemia treated with hydroxyurea [17]. EMH tissue is highly radiosensitive and relatively small doses of radiotherapy are effective [1, 16]. Extradural EMH, which can otherwise lead to serious neurological sequelae or death, responds well to radiotherapy [10]. In some cases, treatment with radiotherapy may be proven disadvantageous for the patient, due to the removal of a compensatory source of hematopoiesis and the exacerbation of the underlying anemia [16]. In cases of plural effusion due to EMH, the use of pleural sclerosing agents is contradicted because these agents can worsen bleeding [12]. Splenectomy, by eliminating the main site of RBC destruction, is considered the treatment of choice for patients with EMH due to HS [6, 15]. It has been reported that EMH in patients with HS can be prevented by early diagnosis and subsequent splenectomy [15]. Nevertheless, EMH has been described [18] following splenectomy in a case of HS.

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