CASE FOR DIAGNOSIS

A patient with pancreatitis, anaemia and an intrathoracic tumour

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CASE HISTORY

A 62-yr-old white nonsmoking male, with no history of serious diseases, was referred to the emergency department due to increasing epigastric pain during the previous 2 days. Physical examination revealed clinical signs of peritonitis. Abdominal sonography demonstrated cholecystolithiasis and splenomegaly. Abdominal radiography showed pronounced air content of the intestinal loops. Based on these results, the diagnosis of acute biliary pancreatitis was suspected.

Laboratory investigations revealed moderate microcytic anaemia (haemoglobin $5.3 \text{ mmol}\cdot\text{L}^{-1}$ ($86 \text{ g}\cdot\text{L}^{-1}$); haematocrit $0.25 \text{ L}\cdot\text{L}^{-1}$; erythrocytes $2.9 \text{ million cells}\cdot\mu\text{L}^{-1}$; mean corpuscular volume 83.9 fL ; mean corpuscular haemoglobin concentration $23.1 \text{ mmol}\cdot\text{L}^{-1}$; reticulocyte count 0.8% of total erythrocyte count; fig. 1), a raised white blood cell count ($19.9 \text{ leukocytes}\cdot\mu\text{L}^{-1}$), elevation of C-reactive protein ($109 \text{ mg}\cdot\text{L}^{-1}$) and a special pattern of increased transaminases (aspartate aminotransferase (ASAT) $2.11 \mu\text{mol}\cdot\text{L}^{-1}\cdot\text{s}^{-1}$; alanine aminotransferase (ALAT) $5.57 \mu\text{mol}\cdot\text{L}^{-1}\cdot\text{s}^{-1}$; alkaline phosphatase $8.5 \mu\text{mol}\cdot\text{L}^{-1}$; total bilirubin $146 \mu\text{mol}\cdot\text{L}^{-1}$). The results of the investigations substantiated the diagnosis.

The chest radiograph confirmed an intrathoracic mass located at the right side of the spine (fig. 2) and abdominal computed tomography (CT) revealed massive peripancreatic exudation, cholecystolithiasis and splenomegaly. On examination of the chest CT, the intrathoracic mass was located close to the

FIGURE 1. Peripheral blood smear taken on admission of the patient.

thoracic spine. It was $40 \times 20 \text{ mm}$ in size, ovally shaped and even surfaced (fig. 3).

The patient was transferred to the intensive care unit for treatment of acute pancreatitis, and underwent an endoscopic retrograde cholangiography with papillotomy and extraction of numerous pigmentary gallstones. Laboratory signs of inflammation and cholestasis normalised during the following

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FIGURE 2. Posteroanterior (a) and lateral (b) chest radiograph at the day of admission.

BEFORE TURNING THE PAGE, INTERPRET THE RADIOGRAPHS, THE BLOOD SMEAR AND THE BIOPSY, AND SUGGEST A DIAGNOSIS.

FIGURE 3. Thoracic computed tomography section just below the bifurcation of the central pulmonary artery.

FIGURE 4. Haematoxylin and eosin-stained histological appearance of the paravertebral tumour. Scale bar=25 µm.

days. However, microcytic anaemia remained unchanged and the question of an association to the thoracic tumour was still unresolved. Finally, a CT-guided percutaneous biopsy from the thoracic tumour (fig. 4) was performed.

INTERPRETATION

Peripheral blood smear

The blood smear revealed anisocytosis, small spherocytes and some bigger polychromatic erythrocytes (fig. 1).

Chest radiography

In the posteroanterior view, the diameter of the heart is in the upper normal range with a tortuous aorta (fig. 2a). An unspecific pleural density can be seen at the left lateral chest wall. The lateral view reveals an opacity, ~2 cm diameter, of smooth surface, located dorsally at the level of the middle to upper thoracic spine (white arrow). There were no signs of inflammatory shadowing of the lungs.

CT of the thorax

In an area below the bifurcation of the pulmonary artery, a tumour with a density of 80 Hu was found along the right paravertebral side (fat tissue has a Hu ranging 40–50). No additional nodular opacities, no pathologically enlarged lymph nodes and no pulmonary infiltrations were found (fig. 3).

Histological examination of the soft tissue tumour

Histological examination revealed that the tumour was of haemopoietic origin (fig. 4). It was similar to bone marrow (figure not shown) but with markedly augmented cell content, especially due to increased erythropoiesis, a clear increase of siderosis and a relative decrease of the yellow bone marrow cells (fat marrow).

Diagnosis: Tumour-simulating asymptomatic intrathoracic extramedullary haematopoiesis (EMH) in a patient with hereditary spherocytosis.

CLINICAL COURSE

Once clinically stable, the patient underwent a cholecystectomy and splenectomy. Serum parameters of haemolysis improved following splenectomy. Follow-up radiographic controls showed no progression of the intrathoracic tumour and a stabilisation of the blood cell count. The peripheral blood smear post-splenectomy showed normalisation of anaemia, slight leukocytosis, elevated thrombocytes (1096 gigaparticles·L⁻¹), no reticulocytosis and some Howell-Jolly bodies within erythrocytes. A series of lung function tests revealed values within the normal range.

DISCUSSION

Hereditary spherocytosis (HS; also known as Minkowski Chauffard, spherocytic anaemia) belongs to the congenital haemolytic anaemias and is characterised by spheroid erythrocytes (fig. 1), resulting from an autosomal dominant protein defect of the erythrocyte membrane, which can be confirmed by the osmotic fragility test. Typically, patients with HS are almost asymptomatic. Symptoms may arise from haemolytic anaemia, such as icterus and splenomegaly. A widespread complication is cholelithiasis as a result of overpigmented bile. Haemolytic crises, mainly triggered by infections or potentially toxic materials (e.g. medicines), are frequent. Sometimes, such events are accompanied by a depression of the bone marrow, especially if the crisis is due to Parvovirus infection. During pregnancy, megaloblastic crises may be triggered by folate deficiency.

The decomposition of the spherocytes in the spleen and the resulting anaemia stimulate erythropoiesis, sometimes followed by megaloblastic transformation of the bone marrow. In cases with repeated and severe haemolytic episodes, the treatment of choice is splenectomy with consecutive elongation of the erythrocyte lifespan.

EMH is a rare disorder, which is characterised by the appearance of haemopoietic tissue outside the bone marrow. It was first recognised by ASK-UPMARK [1] in 1945. Theoretically, EMH can develop at any site of the body, but the most common sites are the spleen and liver. Less usual locations include the lymph nodes, kidneys, pleura, mediastinum or presacral region [2]. Solitary localisations have been described in the pelvis [3], the retroperitoneum [4] and the suprarenal gland [5], as well as in other parenchymatous intra-abdominal organs [6].

It must be emphasised that EMH is mainly observed in combination with chronic anaemia resulting from conditions such as thalassaemia [7], sickle-cell anaemia or, as in the current case, spherocytosis. It can also be associated with myeloproliferative syndromes (e.g. chronic myeloid leukaemia, osteomyelosclerosis or polycythaemia vera) and advanced stages of neoplasias with bone marrow infiltration or destruction by irradiation [2, 8]. Stimulating factors for EMH include increased production and/or excessive dismantling of blood cells, or a failure of normal bone marrow function [8].

Since 1990, some case reports about intrathoracic, predominantly mediastinal, EMH have been published. The incidence of EMH is low among patients with hereditary spherocytosis. The median (range) age of reported patients is 57 yrs (28–74), which is higher than expected in patients with spherocytosis. This is explained by the necessity of a protracted period of haematopoietic stimulation. There is also a strong male predominance [9, 10]. The current 62-yr-old patient had been symptom free from spherocytosis until presenting with abdominal complications of HS. The EMH tumour was only detected by chance.

The differential diagnosis of an intrathoracic paravertebral tumour includes all kinds of soft tissue, neurological or pleural tumours or metastasising extrathoracic malignomas, with a special emphasis on (non-Hodgkin's) lymphomas.

EMH is not associated with bone destruction. The density of the tumours revealed by CT may give some indication about the nature of the tumour. For EMH tissue, a density of -15 to +60 HE is indicated in the literature [11, 12]. This does not correspond with the current result of approximately +80 HE. The varying relationship between fat (lower HE values) and myelopoietic tissue and some content of contrast medium might account for this variability [11–13]. Therefore, for an exact diagnosis, histological examination is indispensable.

The pathogenesis of EMH is still not fully understood. It might originate from lymphonodular tissue, from reticulo-endothelial system cells, embryonal or foetal cell remainders or from embolic or metastatic displacement of bone marrow *via* the intercostal veins [1, 3, 10, 11]. Another hypothesis is that EMH devolves from primitive embryonic haematopoietic tissue resuming its function under the persistent stimulus of

anaemia [8]. Otherwise, such foci could develop from extrusion or herniation of hyperplastic marrow through thinned trabeculae of ribs and vertebral bodies [11, 12, 14], especially in mediastinal and paravertebral localisation of EMH. Indeed, the histological image of the tumour in the present case strongly resembled the patient's bone marrow probe.

Asymptomatic foci of intrathoracic EMH normally require no treatment. In case of complications, such as symptoms from displacement or impression of organs or vessels (cardiac decompensation, venous congestion, distressed lung function) [10], and/or recurrent pleural effusions [15, 16], haematothorax [17] or neurological symptoms [18, 19], irradiation of the abnormal tissue formation could be the method of choice favoured by the high radiosensitivity of the myelopoietic tissue [20].

It is most important to bear in mind that surgical interventions carry a risk of unexpected massive bleeding. Therefore, the clarification of the diagnosis by acquisition of histological material using percutaneous puncture, bronchoscopy, mediastinoscopy or video-assisted thoracoscopy is indispensable. Urgent surgery should be restricted to massive haematothorax or acute spinal cord compression syndrome.

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