

Hepatic Hematopoiesis In β -Thalassemia

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Citation

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Abstract

Tumor-like extramedullary hematopoiesis with liver localization in beta-thalassemia is an extremely rare clinical phenomenon and a prerequisite for serious differential diagnostic problems. We present a case of homozygous beta-thalassemia in a 23-year-old woman. The patient was examined by abdominal ultrasonography and CT scan because of biliary crisis and found to have microconcrements in the gallbladder and a tumor-like formation (34 x 30 mm) in the 7th liver segment. Conventional cholecystectomy was performed. The histological examination showed it focal extramedullary hematopoiesis with an underlying diagnosis of Cooley's anemia. Differential diagnostic difficulties and necessary diagnostic steps are discussed. Fine needle biopsy and/or immunohistochemical examination are the best methods for the precise diagnosis of extramedullary hematopoiesis.

INTRODUCTION

The complete or partial blockade of the synthesis of one or more polypeptide globin chains in cases of thalassemia results in a compensatory but defective erythropoiesis. In rare cases, this erythropoiesis goes out of the bone marrow and forms foci in different organs. Although it is quite rare such an extramedullary expansion in the liver is a serious diagnostic problem and is a prerequisite for unnecessary and even dangerous therapeutic interventions [1].

CASE PRESENTATION

We present a 23-year-old woman with major β -thalassemia, blood transfusion dependent, with a compensated anemia and optimal level of serum iron being at constant application of Desferal. A splenectomy was performed at the age of 8. A month before she was hospitalized she had fever up to 38°C, nausea, vomiting, pain and discomfort in the right hypochondrium. Concrements in the gall bladder were found by ultrasonographic examination, which also visualized a formation 3,0 cm in diameter in the right lobe of the liver. Eight months later she presented with symptoms of biliary crisis.

The clinical examination found a typical mongoloid face, subicterus of the skin, mucosa and sclera. Lungs examination proved normal, there was a moderate cardiomegally, liver was enlarged, and palpable 6 cm below the costal margin.

Blood tests showed ESR 40mm, hemoglobin 73 - 106 g/l, red blood cells $3.37 - 4.02 \times 10^6/\mu\text{L}$, white blood cells $53 - 35 \times 10^3/\mu\text{L}$, platelets $688-533 \times 10^3/\mu\text{L}$, reticulocytes 41/1000, normal differential blood count, erythroblasts in peripheral blood 85/100. Electrophoresis of hemoglobin found hemoglobin A 30.7%, hemoglobin A2 5.1%, hemoglobin F 64.2%. Iron in the serum was $21 \mu\text{mol/l}$, LDH 509, total bilirubin 33.3 mmol/l, direct fraction 13.1 mmol/l, coagulation status PT 12.3"; APTT 31.8", TT 18.2", fibrinogen 2.5g/l. Alkaline phosphatase, AST, ALT, GGTP, serum holinesterase, total protein and albumin were normal. Serology for echinococcosis was negative.

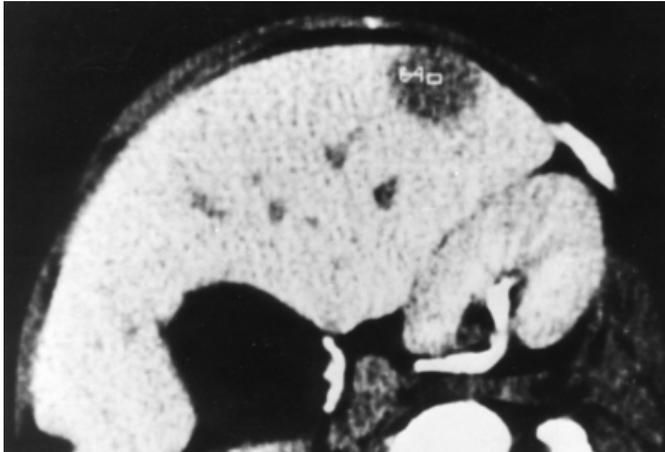
On abdominal ultrasonography the liver presented with smooth outlines, isoechogenic structure and enlarged in size. In the right hepatic lobe a tumor mass 34x30mm was found. The gall bladder was with smooth outlines, normal walls and about 10 concrements in it, 4-5mm in size. The choledoch duct and the portal vein were normal.

Abdominal CT scans with oral and intravenous contrast enhancement showed enlarged liver with preserved structure. There was an initial ectasia of the intrahepatic biliary ducts. Gall bladder was enlarged with small positive concrements in it.

A small tumor mass, 35mm in diameter, in the 7th hepatic segment was found near its wall, interpreted as a possible parasite cyst. Retroperitoneum was free. Kidneys and adrenal glands were normal (fig. 1).

Figure 1

Figure 1: Abdominal CT scan with intravenous contrast enhancement

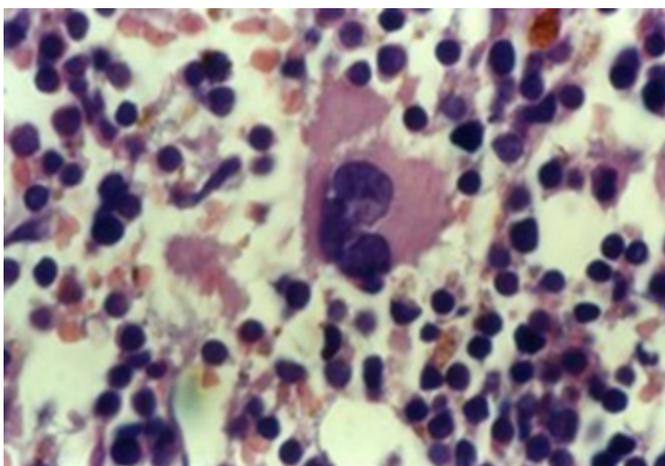


Intraoperatively a deep red, slightly elevated formation 3x3 cm in size with smooth surface and irregular outlines in the 7th hepatic segment was found. Lots of pigmented microcrements were present in the gallbladder. The choledoch duct and the pancreas were normal. A classic cholecystectomy and a puncture biopsy of the described mass were performed.

Histological examination of the tumor mass revealed a compact myeloid proliferation with the participation of the three hematopoietic lines and intense deposits of hemosiderin. Lots of megacariocytes (micro- and megaforms) were found, some of them with atypical nuclei (fig 2).

Figure 2

Figure 2: Histological preparation from the tumor mass



Seven years after the surgical intervention the patient is in satisfactory health, on treatment with regular blood transfusions and desferal. Follow-up ultrasonography at 3, 6,

9, 24 and 36 months after the operation showed no dynamics in the size of the tumor mass.

DISCUSSION

Tumor-like extramedullary hematopoiesis (EH) is a rare phenomenon in adults. It is a result of a compensatory hyperplasia in chronic congenital anemias like thalassemia and hemoglobinosis, myelodysplastic and myeloproliferative syndrome, secondary myelofibrosis, acquired H-hemoglobinopathies.

The most frequent sites of EH are in the thorax: costovertebral angle, retromediastinum and the parenchyma of the lungs [23]. Second most frequent is the intraabdominal EH - in the paraspinal region, in the retrocrustral areas, the presacral region, in the retroperitoneum, in the pelvis, near the kidneys, the spleen and the liver [456]. EH in cases of thalassemia is also described in the middle ear [7]. The sites of EH are mainly multiple, varying in size, from 1.2 to 17 cm. EH is rarely symptomatic. Mediastinal syndromes, spinal cord compression, renal insufficiency, focal engagement of the bones of the pelvis and slight organ dysfunctions have been reported in the literature [368]. In cases of progressive enlargement local radiotherapy, chemotherapy with Hydrea and surgical resection have been performed.

The hepatic localization of a focal EH is extremely rare [9]. In cases of α -thalassemia there are just a few reports [10112]. Dewar described a unique in size 12 cm focus of EH in the liver and in the same patient a smaller site in the retromediastinum. The symptoms depend on the size of the formation and its location in the liver, the possibility of compression on the biliary ducts and the big blood vessels. These formations are usually silent, do not have clinical manifestations and are found by chance by an ultrasonographic examination or a CT scan.

In all the described cases the findings were interpreted as hepatocellular carcinoma, metastatic tumors, hemangiomas, cysts, parasites, etc. For a precise definition of the findings various diagnostic methods were applied: abdominal ultrasonography, CT-scan, MRI, bone marrow colloid scintigraphy. Tamm and Rubin applied Tc 99 bearing RBC, a SPECT method with 89% sensitivity and 100% specificity [1314]. Sometimes diagnostic methods are not informative enough and this leads to the next obligatory diagnostic step - fine needle biopsy [1516]. The cytological verification is sufficient. The only difficulty comes from the giant

megacariocytes. If there is no information for the main disease, especially at the stage of the intraoperative histological examination, they can be thought to be malignant [17]. We also considered such an option. It is very useful to make a parallel examination of the myelogram and the phenotype of the proliferating cellular population.

CONCLUSION

The presented case and the literature review show that EH with liver localization may cause serious diagnostic difficulties. In patients with inherited hemolytic anemia and acquired states of hemolysis the finding of such formations must direct the diagnosis to EH. In the stages of the diagnostic process a CT-scan, MRI, bone marrow scintigraphy, fine needle biopsy and histological examination can be performed. When the result is uncertain the immunohistochemical examination has no alternative and finally proves the diagnosis.

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