Presacral Extramedullary Hematopoiesis: A Diagnostic Confusion concerning a Rare Presentation

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Key Words

Thalassemia · Extramedullary hematopoiesis · Presacral mass · Pelvic mass

Abstract

Objective: To report a rare case of extramedullary hematopoiesis (EMH) with an asymptomatic intrapelvic mass in a patient with thalassemia major. **Clinical Presentation:** The patient presented with a pelvic mass discovered by ultrasonography before undertaking laparoscopic cholecystectomy for gallstones. Technetium-99m MDP bone scan failed to differentiate EMH from malignancy. A fine-needle aspiration smear was misdiagnosed when atypical megakaryocytes were interpreted as malignant cells. EMH was suggested by magnetic resonance imaging and confirmed by an ultrasound-guided Tru-Cut biopsy. **Conclusion:** This case report illustrates the need to consider EMH in the differential diagnosis of patients with chronic hematological disorders and mass lesions in extramedullary sites.

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Introduction

Extramedullary hematopoiesis (EMH), defined as the presence of hematopoietic elements outside bone marrow and peripheral blood, occurs as a compensatory phenomenon in several hematological diseases including thalassemia [1–3].

Although it tends to be microscopic, it may sometimes manifest as organomegaly or a tumor-like mass [4, 5]. Most of these tumor-like masses are intrathoracic. Extrathoracic locations are very rare and include the kidneys, adrenal glands, breasts, spinal cord and intracranial cavity [4].

Case Report

A 23-year-old Emarati female with thalassemia major had splenectomy 12 years prior to presentation to reduce the need for blood transfusion. Since then, she was maintained on folic acid and infrequent blood transfusion. She recently presented in India with a pelvic mass discovered by ultrasonography before undertaking laparoscopic cholecystectomy for gallstones. A computed tomography (CT) scan of the abdomen and pelvis at that time revealed a large, presacral soft tissue mass lesion 7 × 5 cm indistinguishable from the right ovary (fig. 1a) and expansion of the medullary cavity and periosteal elevation of the lower ribs (fig. 1b, c). Accordingly, fine-needle aspiration for cytology from the presacral mass was performed twice; one was diagnosed as possible adenocarcinoma, and the other was suggestive of EMH.

Fig. 1. Enhanced CT of the abdomen and pelvis. **a** Large presacral soft tissue mass with mild enhancement indistinguishable from the right ovary. Note the apparent sacral body erosion and mass effect against the adjacent adnexa. **b** Widening of the ribs by expansion of the medullary cavity and periosteal elevation with or without bony erosion are suggestive of EMH. **c** Chest X-ray demonstrating EMH in the ribs, most prominent in the anterolateral segment of the right 4th rib (compare with **b**).

Physical examination revealed pallor and mild jaundice. The liver was palpable 3 cm below the costal margin. Complete blood count revealed a hemoglobin of 7.8 g/dl, white cell count of 70.23×10^3 , platelet count of 871×10^3 , and a hematocrit of 25.7% with microcytic hypochromic anemia.

Follow-up ultrasonography in our hospital revealed a well-defined highly vascular mass at the right adnexa; the right ovary was separate from the mass (fig. 2).

Fig. 2. Pelvic ultrasonography revealed a well-defined hypoechoic mass displacing the uterus anteriorly. The mass was separate from the ovaries and hypervascular on color Doppler mapping. UB = Urinary bladder; UT = uterus.

Fig. 3. MRI of the pelvis. **a** Sagittal and axial T₁-weighted MR images of the pelvis showing a well-demarcated, lobulated mass that is isointense to the adjacent hypointense bone marrow. Note (1) the rarefaction of the anterior border of the sacrum seen in the sagittal section and (2) the extensively decreased signal intensity throughout the sacrum and vertebral bodies consistent with diffuse replacement of the bone marrow by extramedullary erythropoietic tissue. **b** Coronal T₂-weighted MR image of the pelvis shows that the mass is markedly hypointense. The adjacent bone marrow of the sacrum and pelvic bones visible within the field are also hypointense similar to the mass. The right ovary and uterus are displaced inferiorly.

Magnetic resonance imaging (MRI) of the pelvis revealed an oval mass $7.5 \times 5 \times 6$ cm, nearly homogeneous in echo texture and located in the presacral retroperitoneal area (fig. 3). The mass was well outlined apart from a small area posteriorly, which could not be identified separately from the sacrum. The sacrum, the pelvic bones as well as the mass were hypointense and showed enhancement in postcontrast injection films suggesting the diagnosis of EMH.

Technetium-99m MDP three-phase radioisotopic skeletal studies failed to show areas of increased radiotracer uptake in the pelvis on the postvoid scan. However, there was hyperactivity of bony ends, which indicated hyperfunctioning areas suggestive of EMH.

Tru-Cut biopsy under ultrasound guidance was performed and revealed a highly cellular smear, with polymorphic cellular infiltrates including many megakaryocytes with large multilobulated nuclei and erythroid cells with dense hyperchromic small nuclei. Some immature blasts with pale blastoid nuclei and granulocytes were also seen. These features were suggestive of extramedullary hematopoietic foci.

Since our patient was asymptomatic, she was advised to have regular blood transfusion to relieve chronic anemia and help suppress the EMH.

Discussion

EMH normally occurs during fetal life [1]. It also occurs as a compensatory mechanism in hemolytic anemia such as thalassemia major and intermedia, congenital spherocytosis and sickle cell anemia. Bone marrow insufficiency seen in myelofibrosis, carcinomatosis, lympho-

ma and leukemia can also result in EMH. Rarely can it be seen in pernicious anemia, vitamin B₁₂ and folate deficiency [2–5]. Due to chronic anemia that stimulates erythropoietin production, erythropoiesis is massively increased (10–15 times normal) [6]. This may occur by direct extension from the bone marrow, stimulation of embryonic multipotent hematopoietic stem cells or via hematogenous emboli [7]. The extrusion of proliferating marrow through the weakened bone cortex into a subperiosteal location explains its presence in the epidural, para-vertebral and presacral areas [8, 9].

EMH usually forms a soft, red mass resembling a hematoma on its cut surface [7]. Histologically, all hematopoietic elements found consist of myeloid cells, and erythroid cells at various stages of maturation, megakaryocytes [1]. Expansion of the erythroid tissue results in skeletal abnormalities such as coarse trabeculation of the bone and cortical thinning. With severe involvement, there is expansion of the bony cortex as well [7] (fig. 1b).

The diagnosis of EMH was made on clinical and radiological grounds. Clinical suspicion may be raised by a history of chronic anemia, such as thalassemia and evidence of EMH elsewhere, such as hepatosplenomegaly or lymphadenopathy [2].

Symptomatic EMH is very rare in spite of dramatic and striking radiological pictures. Reported complications include: spinal cord and cauda equina compression, massive hemothorax, obstructive uropathy, ascites, pleu-

ral effusion, pericardial tamponade, optic and sciatic nerve compression, pulmonary thromboembolism and intestinal intussusception.

CT scan demonstrates EMH as a homogeneous, lobulated and well-circumscribed soft tissue mass that is often adjacent to involved bone [4, 7] (fig. 1a). The absence of calcification and the presence of adipose tissue within the mass with widening of the ribs by expansion of the medullary cavity or periosteal elevation without bony erosion are suggestive of EMH [4, 5] (fig. 1b).

MRI is the technique of choice in evaluating this condition through its multiplanar capabilities and soft tissue resolution [8]. Thus, it helps differentiate EMH from other soft tissue lesions, such as abscesses or metastatic depositions [2]. It can also be of additional value by demonstrating the presence of adipose tissue within the mass and by confirming that the bony cortex is intact [4]. In our case, MRI confirmed the integrity of the anterior border of the sacrum by demonstrating the presence of bone rarefaction rather than the apparent bone erosion seen on CT (fig. 1a, 3a).

Radionuclide bone marrow scanning using ^{99m}Tc sulfur colloid, ^{99m}Tc dextran, ^{99m}Tc nanocolloid, ^{111}In chloride and ^{52}Fe citrate are helpful in establishing the diagnosis by demonstrating activity in the mass [3, 4, 10]. However, caution should be exercised in the use of these modalities as the sole method of investigation because of the occasionally reported failure of these investigations to detect [10] and differentiate EMH from lymphoma [11]. Therefore, the exclusion of malignancy obviates the need for tissue biopsy, preferably by a wide-bore (18 G) needle or Tru-Cut biopsy, as in our case.

Fine-needle aspiration cytology may be a useful method for diagnosing EMH. However, there is a pitfall of misdiagnosing atypical megakaryocytes as malignant cells on fine-needle aspiration smears, as was seen in our case, especially when the proper history and clinical data are not available to the cytologist [12]. This is why we switched to a Tru-Cut biopsy rather than a third fine-needle aspiration biopsy.

Treatment of EMH is usually unnecessary except when complications occur [3]. Hematopoietic tissue is highly sensitive to irradiation, and radiotherapy is the treatment of choice for patients with spinal cord compression. Neurological improvement has been achieved in 3–7 days after initiation of treatment [2].

Surgery confers the immediate relief of cord compression and provides tissue for histological diagnosis. It has the disadvantages of incomplete excision, operating on anemic individuals who are poor surgical candidates,

and it has the potential risk of profuse bleeding from the surgical site [2, 7]. Therefore, surgery is only indicated where immediate relief of spinal cord or nerve root compression is required to prevent permanent neurological damage.

Blood transfusion and iron chelation with desferrioxamine is the ideal treatment for asymptomatic individuals. It relieves anemia and suppresses EMH, and is most effective when used as an adjunct to surgery or radiotherapy [2, 7]. In certain clinical situations, in which both surgery and radiotherapy present special risks (such as pregnancy), transfusion therapy has been successfully used to cause regression of hematopoietic tissue by relieving the anemic stress and lowering serum erythropoietin [8].

More recently, the use of drugs such as hydroxyurea, which enhances fetal hemoglobin production, has been used with some success. Patients with paraparesis and cauda equina syndrome secondary to EMH have been successfully treated with hydroxyurea alone or in conjunction with transfusion therapy [2].

Conclusion

This case report illustrates the need to consider EMH in the differential diagnosis of patients with chronic hematological disorders presenting with extramedullary mass lesions. Fine-needle aspiration may be misleading. Exclusion of malignancy obviates the need for invasive diagnostic measures.

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