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Hematology Quiz – Case 63

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A 35-year-old male patient with history of β-thalassemia presented to the hospital for a prearranged orthopedic surgery. During preoperative evaluation, a radiograph and a computed tomography (CT) of the abdomen were conducted (figures 1, 2).

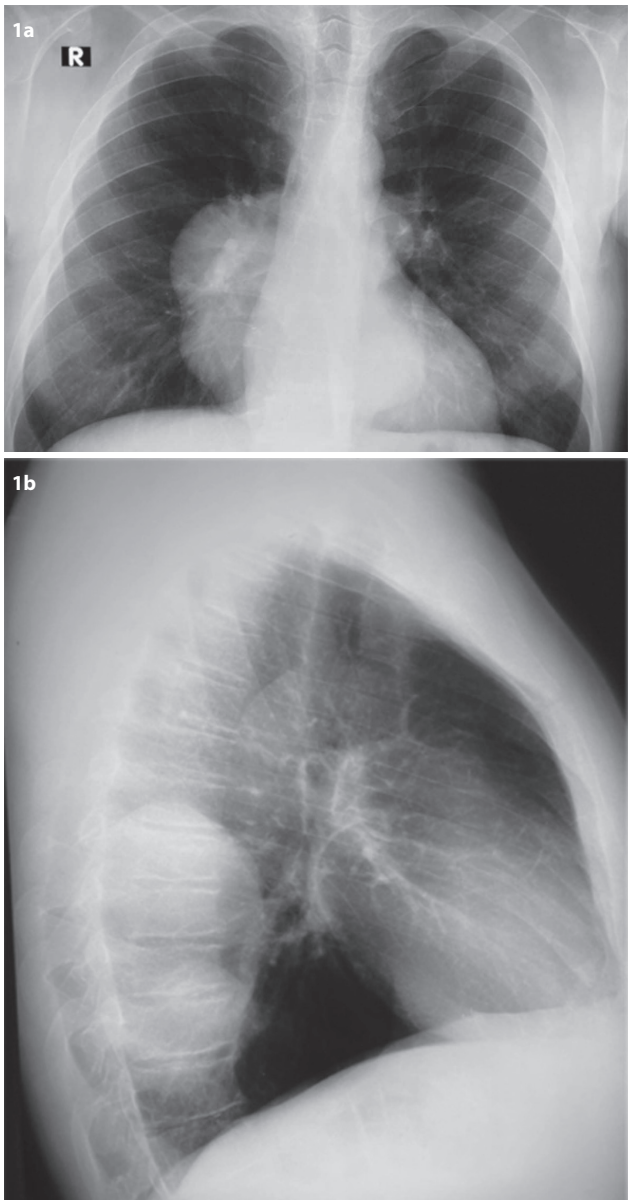

Figure 1. Chest X-ray, posteroanterior and lateral view, depicting opacities at thoracic levels T5–T8, adjacent to the vertebrae.

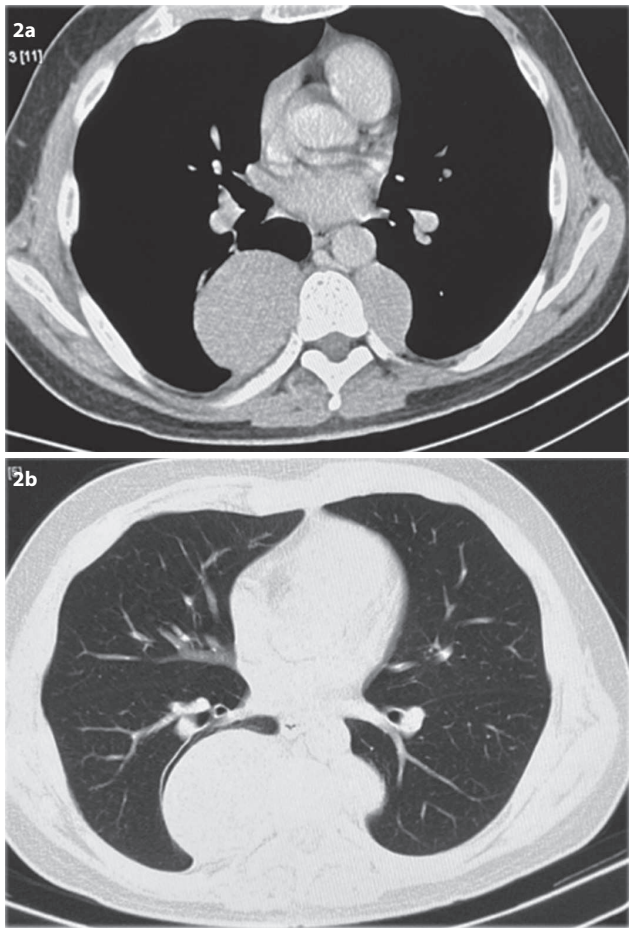

Figure 2. Chest computed tomography (CT), mediastinum and lung window, confirming the presence of hypodense lesions at both paravertebral sides.

Comment

Extramedullary hematopoiesis (EH) is characterized by production and accumulation of blood cells outside the medullary spaces of the bone marrow, which is abnormal in adults. It includes all the activities from early lineage commitment to late maturation of both

erythroid and myeloid hematopoietic cells. EH prevalence exhibits 5:1 male predominance. This procedure normally occurs during fetal development, when marrow is not sufficient to act as the main hematopoietic center yet, whereas healthy adults normally exhibit no EH. Spleen and liver maintain their hematopoietic capability and normally exhibit transient active EH during infections and consequent immune response, in order to produce antigen-presenting cells and phagocytes.

On the other hand, EH may passively complicate bone marrow insufficiency or ineffective hematopoiesis. In such occasions, EH either supports marrow hematopoiesis or becomes the main hematopoietic component. Hemolytic anemia, particularly sickle cell anemia, thalassemia intermediate, under-transfused thalassemia major, hereditary spherocytosis, congenital dyserythroblastic anemia and idiopathic thrombocytopenic purpura can be accompanied by EH. Various additional hematologic disorders including myelofibrosis, myelodysplastic syndromes, leukemia, lymphoma and irradiation of bone marrow can lead to EH. Stromal disorders of the bone can render bone marrow unable to support hematopoiesis and eventually promote EH. Such disorders are osteopetrosis, severe renal osteodystrophy, Paget's disease, bone marrow fibrosis due to inflammation, Gaucher and Niemann-Pick disease and metastatic tumors.

Tissue sites with specialized structure, appropriate signaling and preferably hypoxic conditions are required for hematopoietic stem and progenitor cell maintenance and differentiation. EH requires counterpart conditions to occur. Osteoblasts, CXC chemokine ligand 12 (CXCL12)-expressing reticular cells, and endothelial cells are the main cells which regulate normal hematopoiesis, whereas osteoclasts and sympathetic nervous system also contribute to the success of hematopoiesis. Important molecular pathways include Wnt, calcium-sensing receptors, angiopoietin 1, Tie-2 and extracellular components. Furthermore, external signaling towards hematopoietic cells may be mediated by Toll-like receptor ligands, metabolic/physiological products, inflammatory mediators and hormones. EH development presupposes conditions of bone marrow failure, excessive hematopoietic stimulation, abnormal cytokine production and tissue inflammation, injury and repair. Chemokine (C-X-C motif) ligand 12 (CXCL12)-positive cells trap circulating hematopoietic stem cells at the margin of sinuses near CXCL12-positive endothelial cells during the initial steps of EH. Therefore, CXCL12 expression is suggested to be significant for hematopoietic cell maintenance, colonization and migration during initial formation of marrow-like regions of EH.

EH can involve any mesenchymal tissue, whereas it is most often traced in liver, spleen and lymph nodes. Hepatic EH rarely occurs during hepatic disorders, sepsis, transplantation and hepatic tumors. Less frequent EH sites are adrenal glands, kidneys, adipose tissue, skin, heart, periosteum, pleural cavity, nasopharyngeal regions, para-nasal sinuses, mediastinal, retroperitoneal, epidural, intra-spinal, pre-sacral and paravertebral regions. In our aforementioned case, biopsy and pathological examination of the lesion confirmed EH in the paravertebral region of thoracic spinal region. EH serves as an additional contributor in the production of hematopoietic cells, but it might provoke complications as well. If it occurs inadequately, it will produce insufficient or immature blood cells. On the contrary, excessive EH may lead to inflammatory diseases. EH can even become life-threatening due to potential squeezing of adjacent structures, especially if it creates spinal cord compression.

Treatment is implemented if EH becomes complicated. Hypertransfusion or recurrent transfusions and nutritional support may temporarily reduce the innate need for EH if hemoglobin levels higher than 9 mg/dL are achieved. Nevertheless, in case of emergency, patients will eventually need some additional kind of treatment in order to control EH development, such as radiotherapy, decompressive surgery or hydroxyurea.

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Diagnosis: *β-thalassemia and extramedullary hematopoiesis*