Extramedullary hematopoiesis in the axillary lymph node in a patient with an accelerated phase of chronic myeloid leukemia

Akselere faz kronik myeloid lösemili hastada aksiller lenf nodülünde ekstrameduller hematopoezis

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To the Editor,

Chronic myeloid leukemia (CML), the most common myeloproliferative disease, is characterized by a reciprocal translocation between chromosomes 9 and 22. CML has a triphasic clinical course, having chronic, accelerated and blast phases [1]. Although the blast phase is characterized by an increase in blasts in the bone marrow (BM) and blood, extramedullary accumulations of blasts can be seen in the skin, spleen, liver, body cavities, or lymph nodes, as a complication of the blast phase of CML [2]. Extramedullary involvement in CML presents as a tumoral mass, known as granulocytic sarcoma, which is characterized by the presence of blastic cells [2].

A 44-year-old man was diagnosed in a peripheral hospital as CML in 1995 with anemia, hepatosplenomegaly, Philadelphia (Ph) chromosome positivity, and increased white blood cell count. He was initially treated with hydroxyurea and interferon (5000 U/3 days per week). Two years later, his BM biopsy showed marked reticulin fibrosis without blastic infiltration. He began to use imatinib, 300 mg once a day, because of severe thrombocytopenia. Two years later, he was admitted with ascites, jaundice and edema, and was treated with cytosine arabinoside, diuretics, thalidomide and low-dose steroid due to myelofibrosis, massive splenomegaly and the presence of peripheral blastic cells. Three years later, he suffered from ascites and bilateral multiple axillary lymph nodes (3 cm in greatest dimension). Laboratory examination revealed anemia (Hb: 9.9 g/dl), increased white blood cell count (34.8×10^{12}/L), and thrombocytopenia (platelet count: 12×10^{9}/L). Abdominal ultrasound showed paraaortic and celiac multiple lymph nodes. Magnetic resonance portography findings were normal. A computed tomography scan of the thorax showed pleural effusion and atelectasis in the right lung. Cytologic examination of the peritoneal fluid was normal. Dasatinib (100 mg once daily) was started. Axillary lymph node biopsy and BM biopsy were performed. Microscopically, the sinuses were filled with factor VIIIRA-positive megakaryocytes, glycophorin A-positive erythroid precursors, myeloperoxidase (MPO)-positive granulocytic precursors, CD68- and lysozyme-positive histiocytes, and scattered mast cell looking - CD117-positive mononuclear cells in the axillary lymph node (Figure 1a-e, g-i). CD34 and Tdt were negative (Figure 1f). The diagnosis was determined as extramedullary hematopoiesis (EMH) in the lymph node. The hypocellular BM showed marked reticulin fibrosis and collagenization (Figure 2 a, b, e, f). There was no blastic infiltration within the lymph node or BM. Hypersegmented neutrophils were seen in aspiration smear (Figure 2c). Granulocytic and erythroid precursors were noted in the peripheral blood (Figure 2d). By immunohistochemistry, CD34 and Tdt were negative, and scattered interstitial CD117 strongly positive mononuclear cells, which were interpreted as

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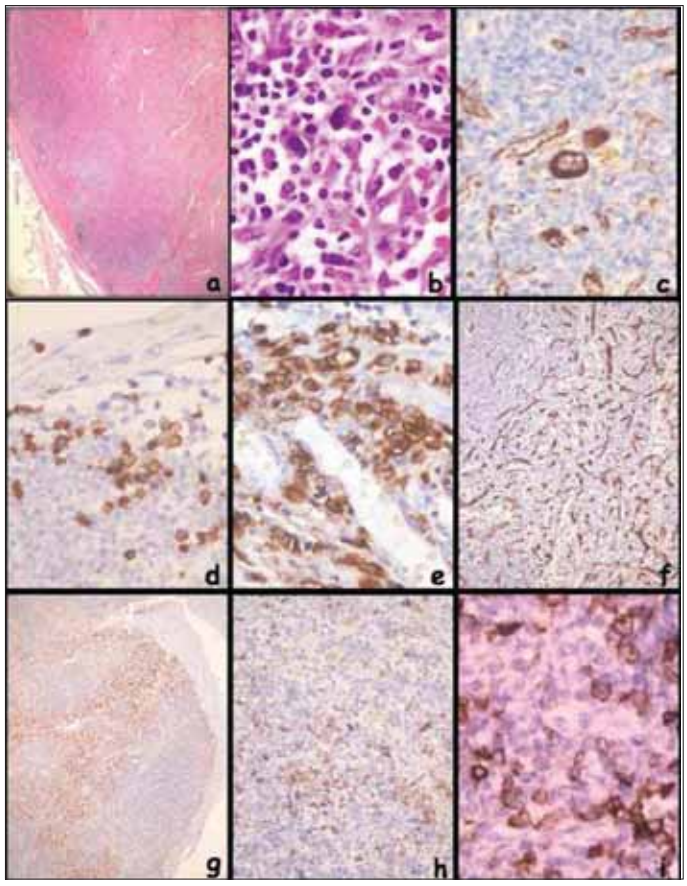

Figure 1. a,b. Different lineages of hematopoietic cells within the sinuses in the lymph node (hematoxylin and eosin, x100, ×400); **c.** Factor VIIIRA-positive megakaryocytes (x400); **d.** Glycophorin A-positive erythroid cells (x400); **e.** MPO-positive granulocytes (x400); **f.** CD34-labelled vascular endothelial cells (x200); **g,h.** CD68- and lysozyme-positive histiocytes, respectively (x100, x200); i Mast cell looking - CD117-positive mononuclear cells (x400)

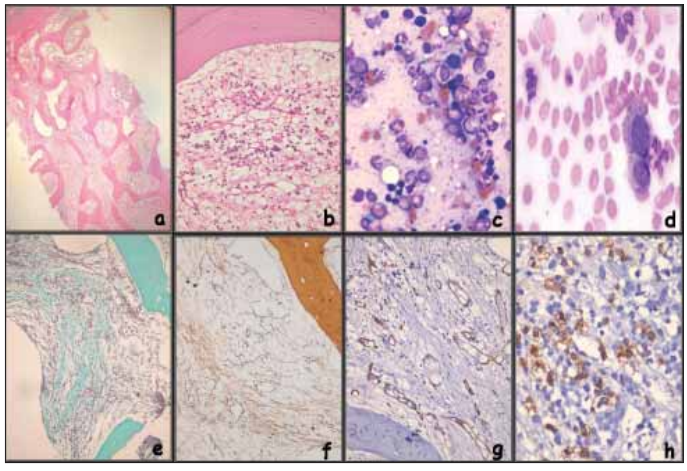

Figure 2. a,b. Hypocellular bone marrow (hematoxylin and eosin, x40, x200); **c,d.** Granulocytic precursors in the marrow aspirate and peripheral blood, respectively (x200, x400). **e,f.** Collagenization and reticulin fibrosis in the bone marrow, respectively (x200, x400); **g.** CD34 labelled vascular endothelial cells (x400); h. CD117-positive mononuclear cells (x400)

reactive mast cells, were present in the BM, as in the lymph node (Figure 2 g, h). Flow cytometric analysis of the BM was not informative because of myelofibrosis, but no blast was seen in the peripheral blood. Real-time polymerase chain reaction (PCR) analysis of the peripheral blood showed residual clonal disease. The patient died within two months due to hepatic failure.

EMH is a very rare complication of chronic myeloproliferative and myelodysplastic disorders, most commonly seen in idiopathic myelofibrosis. It is caused by the metastatic growth of abnormal clonal hematopoietic cells originating from the BM. EMH is often seen in the liver and spleen, but may also occur infrequently at other sites. To date, only five cases of CML with EMH have been reported [3-7]. In 1988, Shih et al. [3] reported a 48-year-old patient with Ph (+) CML developing skin and pericardial EMH. In 1995, three cases of CML with EMH in the atrium, endometrium, and pericardium, respectively, were reported [4-6]. The prognostic significance of EMH with CML is unclear due to the lack of a large series of such patients.

In summary, it is important to stress that although EMH is not a malignant process histologically, the patient should be examined for underlying hematological disorders clinically, when it is noted elsewhere.

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