MORPHOLOGY UPDATE

Erdheim–Chester Disease in Bone Marrow

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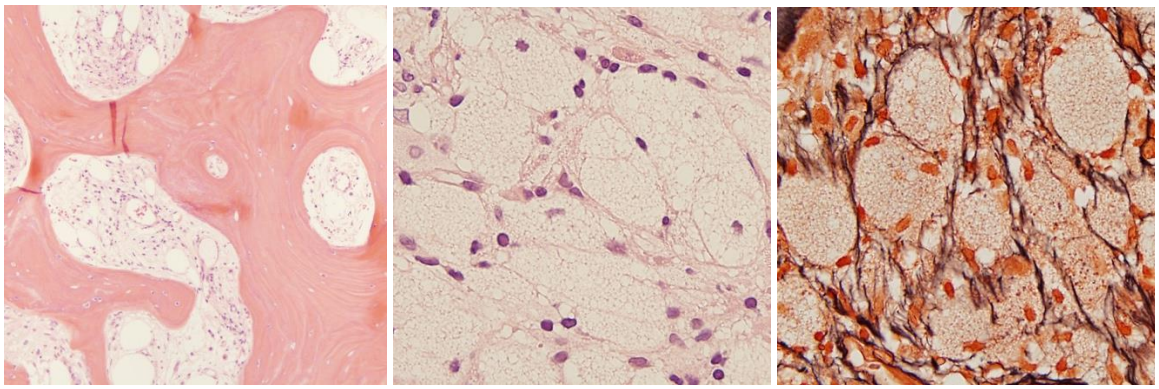

A 67-year-old man presented with bone pain, fatigue, weight loss, and dyspnea. A blood count showed mild normocytic anemia (hemoglobin concentration 114 g/L) with normal leukocyte and platelet counts. The erythrocyte sedimentation rate was elevated at 136 mm/hour as was C-reactive protein at 40 mg/L. Biochemical studies showed normal calcium and phosphate but minor elevation in alkaline phosphatase (156 U/L). Long bone radiographs demonstrated diffuse cortical thickening and sclerosis of the distal femora. A Positron Emission Tomography/Computed Tomography scan showed intense ^{18}F-fluorodeoxyglucose uptake in the distal femora and proximal tibiae (bottom, left and centre). Bone sclerosis was apparent in the distal femora (bottom, right). A core biopsy of

the left distal femur demonstrated marked expansion and irregularity of the bone trabeculae (top left). Normal hematopoiesis was virtually absent with a significant infiltrate of foamy histiocytes evident on hematoxylin and eosin staining (top centre). Reticulin staining demonstrated focal fibrosis surrounding the abnormal histiocytes (top right). Further immunohistochemical staining showed the histiocytes to be positive for CD68R and factor XIIIA but negative for S100 and CD1a. Next generation sequencing performed on bone marrow material detected a sequence variant c.1799T>A p.(Val600Glu) in codon 600 of the *BRAF* gene. The radiological and histopathological features, along with the presence of a *BRAF*^{V600E} mutation, were diagnostic of Erdheim–Chester disease (ECD).

ECD is a rare neoplastic disorder characterized by infiltration of multiple tissues by foamy CD68+CD1a− histiocytes. The disease can have protean manifestations but, most characteristically, long-bone pain and osteosclerosis. Recently, mutations activating the MAPK pathway have been found in more than 80% of patients with ECD, mainly *BRAF*^{V600E}. This condition is related to Langerhans cell histiocytosis, which is characterized by the same mutation. Treatment traditionally involved interferon-alpha, corticosteroids, and sometimes cytotoxic chemotherapy but more recently BRAF inhibitors, such as vemurafenib, have been shown to induce frequent durable responses.

CONFLICT OF INTEREST: nil

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