Hairy cell leukaemia mimicking multiple myeloma

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A 74-year-old female patient presented in November, 2017, with a 3-month history of pain in the upper left thigh. X-ray revealed three osteolytic lesions of the left femur, one of which was breaking the cortical bone. No organomegaly was noted on physical examination. Blood counts and biochemical tests were normal except for mild hypergammaglobulinemia (16·9%) with positive immunofixation for monoclonal immunoglobulin A (0·2 g/dL in the serum, but urine negative).

Multiple myeloma was suspected, and whole-body PET scan documented increased fluorodeoxyglucose uptake in several bone sites (SUV^{max} 4·9–10·9): at the head of humeri, sacrum, iliac wings, right acetabulum, and proximal femurs (figure, A), with extension into the soft tissues surrounding the broken cortex of the left femur.

A routine marrow biopsy from the iliac crest was unexpectedly normal on immunohistology for the plasma cell marker CD138 and the B-cell marker CD20. However, a core biopsy of the left femural neck documented a massive infiltration by mature lymphoid cells with ample cytoplasm and hairy projections positive for CD20, annexin-1 (figure, B), and $BRAF^{V600E}$, thereby establishing a diagnosis of hairy cell leukaemia.

Morphological and flow-cytometric analyses of peripheral blood did not show any hairy cells, and a sensitive allele-specific PCR assay for $BRAF^{V600E}$ was also negative in both the blood and iliac marrow aspirate.

The patient received chemotherapy with cladribine (0·14 mg/kg per day for 5 consecutive days subcutaneously) and her pain gradually subsided. A PET scan 8 weeks later showed substantially decreased uptake of fluorodeoxyglucose at multiple bone lesions.

Although skeletal involvement can occur in hairy cell leukaemia (in around 3% of cases), patients with hairy cell leukaemia, who are mostly males, usually also present with cytopenias, splenomegaly, circulating hairy cells, and diffuse leukaemic infiltration of the bone marrow. Focal bone lesions accompanied by none of these characteristic features, but rather by a monoclonal gammopathy of undetermined significance as occurred in this woman, represent a challenging differential diagnosis with more frequent neoplasms, especially multiple myeloma.

Contributors

LN and ET wrote the report. ET and BF evaluated and did the imaging of the critical annexin-A1 immunostaining, and evaluated the allele-specific PCR assay for $BRAF^{V600E}$. CM and EM did other immunohistochemical stains. FA, FRe, and FRu contributed to the writing of the text, and to data collection and analysis. This work was funded by a grant from the European Research Council (FP7/2007-2013 'Hairy Cell Leukemia,' 617471) and a grant (no. IG-19143) from Associazione Italiana Ricerca sul Cancro to ET. Written informed consent to publication was obtained.

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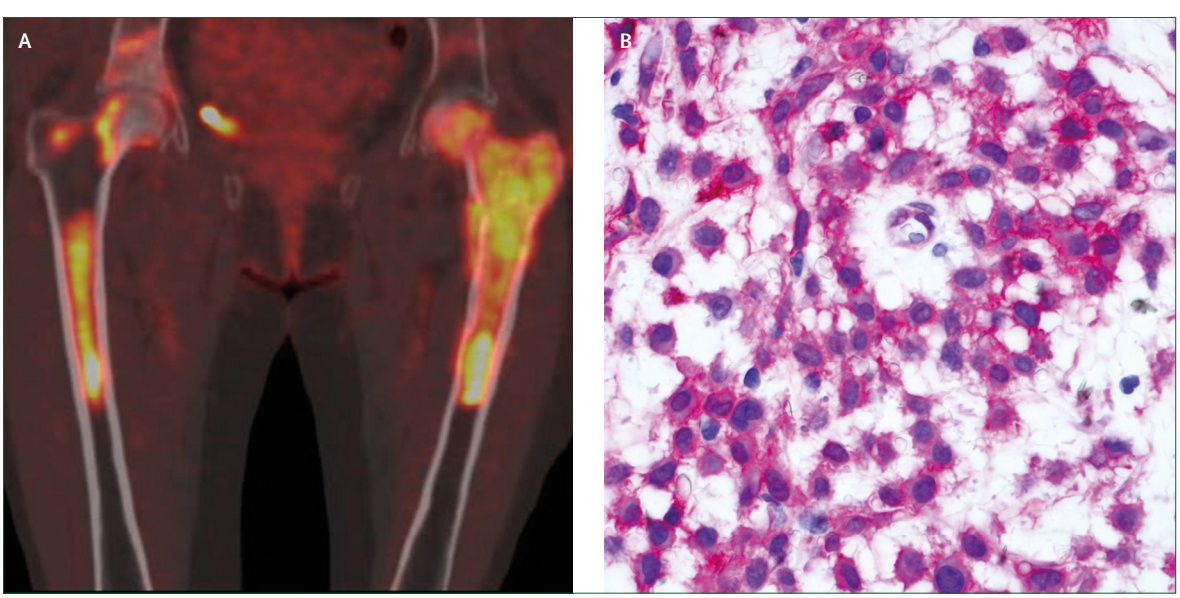

Figure: **Hairy cell leukemia mimicking multiple myeloma**
(A) Coronal PET scan of the thighs showing, in both proximal femurs, several hypermetabolic lesions, one of which extends outside the left femur. (B) Core biopsy of the left femural neck showing diffuse leukaemic infiltration by mature lymphoid cells with ample cytoplasm labelled in red by the annexin-1 immunostaining (nucleus counterstained in blue with haematoxylin; picture taken with a 40X microscopy objective).