Ramonda Roberta (Orcid ID: 0000-0002-9683-8873)

A rare and misleading condition: isolated skeletal involvement of Erdheim-Chester Disease

Sara Bindoli[1,2] MD PhD, Stefania Vio[1,3] MD, Marta Sbaraglia[1,4] MD, Fabrizio Vianello[1,5] MD, Roberta Ramonda[1,2] MD PhD

1 Department of Medicine, DIMED, University of Padova, Padova, Italy

2 Rheumatology Unit, University Hospital of Padova, Padova, Italy

3 Radiology Unit, University Hospital of Padova, Padova, Italy

4 Surgical Pathology and Cytopathology Unit, University Hospital of Padova, Padova, Italy

5 Hematology Unit, University Hospital of Padova, Padova, Italy

Corresponding author:

Prof. Roberta Ramonda

Rheumatology Unit, Department of Medicine-DIMED

University of Padova, Padova, Italy

Address: via Giustiniani, 2

35128 Padova, Italy

Phone: +39 0498212199

Mail: roberta.ramonda@unipd.it

ORCiD:

SB: 0000-0002-9409-3329

RR: 0000-0002-9683-8873

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ABSTRACT

We are describing an unusual presentation of Erdheim-Chester Disease (ECD), a non -Langerhans histiocytosis provoked by abnormal aggregation of foamy histiocytes in several organs and systems. Our patient, already with osteoporosis, presented severe bilateral ankle pain with functional impairment, clinically mimicking “Complex Regional Pain Syndrome” (CRPS); the radiological images and subsequently the bone biopsy were fundamental for achieving the proper diagnosis. The diagnosis was challenging given the isolated bone localization which is uncommonly seen in ECD.

A 60-year-old patient with osteoporosis, complained of pain in the right ankle, which spread to the peri-malleolar region, and then the left ankle. No fractures were detected on the X-ray; magnetic resonance (MR) showed bone oedema in the cuboid-calcaneal bone heads and the left distal meta-diaphyseal tibia. The patient received non-steroidal anti-inflammatory drugs, analgesics, and bisphosphonates in the suspicion of Complex Regional Pain Syndrome (CRPS), without benefit. Given the persistent pain at the tibias bilaterally, computed tomography (CT) was performed showing sclerosis of the trabecular bone in the distal third of the tibial diaphysis (Figure 1A); sagittal T1-weighted and STIR MR showed extensive spongiosa oedema in the fourth and fifth segments of both tibial diaphyses, well-demarcated by the continuous trabecular bone, with a 7 cm craniocaudal extension (Figure 1 B-C); the skeletal scintigraphy confirmed the radiotracer uptake at the upper and lower tibial diaphysis (Figure 1 D). Given the atypical bone lesions and the unresponsiveness to the treatments administered, a bone biopsy was performed. The histology revealed inter-trabecular fibrosis and infiltrates of foamy histiocytes (Figure 1 E-G-H), diffusely positive for CD163 (Figure 1 F), aspects compatible with Erdheim-Chester disease, a non-Langerhans cell histiocytosis that provokes an abnormal aggregation of histocytes in several organs (cardiovascular and central nervous system, retroperitoneum), including long bones[1]. BRAF (V600E) mutation was detected (droplet-digital PCR, FA 0.06%), and histology supported the diagnosis by excluding other potential mimickers[2]. CT scan of the abdomen was negative for pathological findings; the patient was then advised to start the BRAF-inhibitor vemurafenib.

Figure 1. Radiological and histopathological aspects suggestive of Erdheim-Chester Disease. (A) CT scan of the ankle showing sclerosis of trabecular bone; (B,C) T-1 weighted and STIR MR images; (D) Lower limbs scintigraphy; (E) Bone biopsy shows atypical histiocytic aggregates (H&E,10x); (F) The atypical histiocytes are diffusely positive for CD163 (40x); (G,H) Atypical histiocytic aggregates present the aspect of foamy histiocytes (H&E, 40x).

References

1. Cives M, Simone V, Rizzo FM, Dicuonzo F, Cristallo Lacalamita M, Ingravallo G, Silvestris F, Dammacco F. Erdheim-Chester disease: a systematic review. Crit Rev Oncol Hematol. 2015 Jul;95(1):1-11.

2. Bindra J, Lam A, Lamba R, VanNess M, Boutin RD. Erdheim-Chester disease: an unusual presentation of an uncommon disease. Skeletal Radiol. 2014 Jun;43(6):835-40

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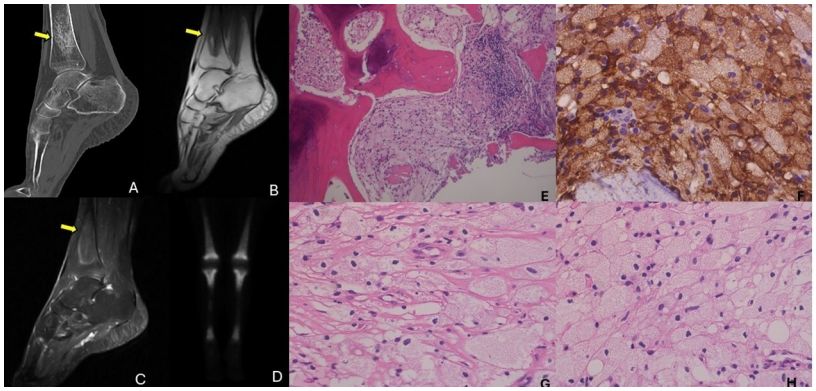

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