BRIEF COMMUNICATION

Intraosseous myoepithelioma: A rare, distinct tumor entity

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ABSTRACT

Primary musculoskeletal myoepithelial tumors (METs) are distinctly rare tumors and are being increasingly recognized as a result of improved diagnostic criteria and objective confirmation with immunohistochemical markers, including epithelial markers. Recent studies have unraveled distinct molecular mechanisms underlying these tumors. Herein, we present our second diagnosed case of an intraosseous MET that occurred in the tibia of a 37-year-old lady. The case is discussed with regards to current clinicopathological perspectives on these rather uncommon tumors, including our personal experience.

KEY WORDS: Intraosseous myoepithelioma, musculoskeletal mixed tumors, rare bone tumors

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INTRODUCTION

Primary musculoskeletal myoepithelial tumors (METs) are rather uncommon, but are being increasingly recognized as a result of established histopathological criteria and their confirmation with immunohistochemical antibody markers such as epithelial membrane antigen (EMA), pan cytokeratin (AE1/AE3) with S100-P, glial fibrillary acidic protein (GFAP), and other myoepithelial markers such as p63, smooth muscle actin (SMA), and calponin.[1-4] Few recent studies have unraveled *EWSR1* gene rearrangements underlying these tumors.[1,4-6]

In a recent series of eight intraosseous METs, including review of other such previously documented cases, Kurzawa *et al.*[1] observed a relatively younger age of onset (range, 16-49, median, 33.5 years) with ilium as the most common site (three cases), followed by tibia in two cases, with tumor size ranging from 1.5 to 5.7 cm in the largest dimension. There have been two documented case reports of intraosseous METs involving the iliac bone, including one of our cases.[6,7] We intend to share our experience with musculoskeletal METs, especially with regards to another recently diagnosed case of an intraosseous MET from our Institution.[5,6]

MATERIALS AND METHODS

Immunohistochemistry (IHC), staining was performed by immunoperoxidase technique, using MACH2 Universal HRP-Polymer detection kit, Biocare, CA. 3'-3'-diaminobenzidine tetrahydrochloride was used as the chromogen. The details of various antibody markers utilized, including their respective dilutions are EMA, Monoclonal, E29, 1:200; AE1/AE3; GFAP, polyclonal, 1:800; S100-P, polyclonal, 1:600; SMA, Monoclonal, 1A4, 1:400; p63, Monoclonal, 4A4, 1:200; calponin, monoclonal, CALP, 1:50, Dako, Produkionsveg, Glostrup, Denmark.

CASE REPORT

A 37-year-old lady presented with pain in her left leg of 2 months duration. Radiograph imaging disclosed a well-defined lytic lesion in her proximal tibia [Figure 1a]. Positron emission tomography computed tomography scan showed the lesion as lytic, hypermetabolic with low fludeoxyglucose-uptake (SUV max 3.5). Initial biopsy and subsequent wide-excision revealed a fairly well-circumscribed, myxoid stroma-rich tumor comprising cells with polygonal to spindle-shaped nuclei, eosinophilic cytoplasm and mild atypia, arranged in lobules and reticular patterns. There were no mitotic figures or tumor necrosis. There were no osteoclast-like giant cells, epithelial differentiation, chondroid or osteoid differentiation. The tumor was confined to the bone, exhibiting focal cortical destruction and was seen bulging into the adjacent soft-tissues. By IHC, the tumor cells were positive for EMA; focally for p63 and SMA, whereas these were negative for S100-P, GFAP, CK/MNF116, CD34, and brachyury/T. Ki-67/MIB1 was 5-6%. Diagnosis of myoepithelioma was finally offered [Figures 1b and 2a-e].

DISCUSSION

A spectrum of histopathological features is observed in primary musculoskeletal METs, in terms of tumor cell type and interspersed stroma/matrix. The cells are polygonal, spindly or plasmacytoid with eosinophilic to the clear cytoplasm, embedded in a variable stroma that could

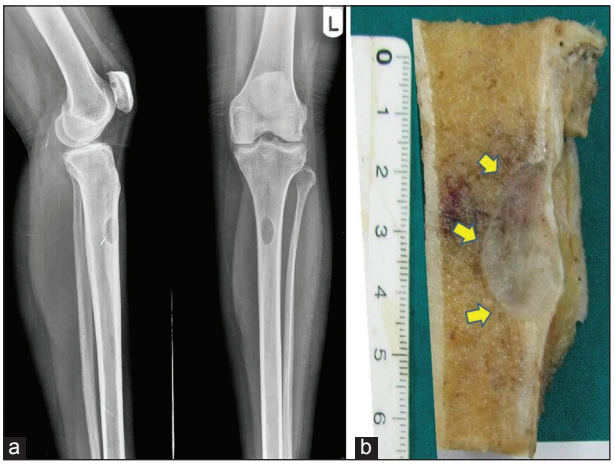

Figure 1: (a) Radiograph imaging showing a well-defined lytic lesion in the proximal tibia. (b) Resected specimen showing a distinct tumor (arrow heads) in the tibial diaphysis with a myxoid cut surface

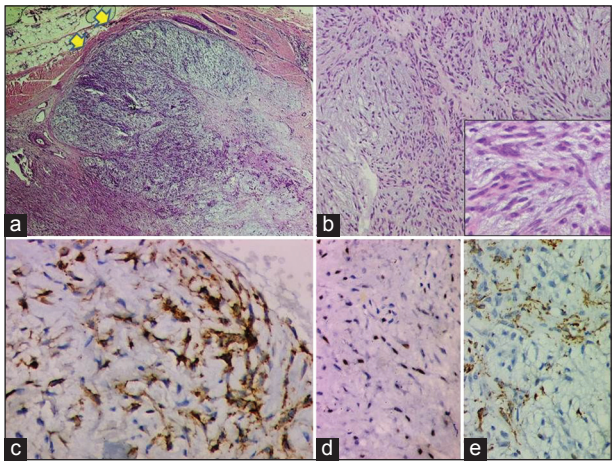

Figure 2: Microscopic findings. (a) Circumscribed, nodular, myxoid-rich tumor bulging into adjacent soft-tissues (arrow heads towards tumor) (H and E, ×40). (b) Cellular tumor composed of the oval to spindle cells in an abundant myxoid-rich stroma (H and E, ×100). Inset: Tumor cells arranged in cords and singly within a myxoid stroma and exhibiting mild nuclear atypia (H and E, ×200). Immunohistochemical results. (c) Diffuse epithelial membrane antigen positivity (Diaminobenzidine, ×200). (d) Focal p63 positivity (Diaminobenzidine ×400). (e) Focal smooth muscle actin positivity (Diaminobenzidine ×400)

be myxoid, myxochondroid, chondroid, and/or osteoid. METs form the histopathological continuum with mixed tumors and parachordomas, all which are distinct from extra-axial chordomas.[1-3,5,6] By IHC, these tumors display positive expression with epithelial markers such as EMA, AE/AE3, along with variable S100-P, GFAP, p63, calponin, and SMA positivity.[1-9] Kurzawa *et al.*[1] observed EMA and S100-P positivity in all METs. At the same time, S100-P negativity has been noted in other reported musculoskeletal METs.[5,8,10] While positive immunoexpression of one of the epithelial markers is necessary for diagnosis, lack of S100-P and GFAP in does not refute a diagnosis of an intraosseous MET. In such cases, other myoepithelial IHC markers such as p63, calponin, and SMA are supportive.[5,10] Brachyury/T negativity militated against a soft-tissue/extra-axial chordoma that displays overlapping histopathological and IHC profile with a MET.[11] Lack of significant atypia, mitotic figures and tumor necrosis ruled out a malignancy in the present case. Possibility of metastasis, especially from the head and neck region was ruled out with whole body imaging. Unlike soft-tissue METs, criteria for malignancy in intraosseous myoepitheliomas are not well-defined.[3] Presently, moderate nuclear atypia is the acceptable criteria for soft-tissue myoepithelial carcinomas.[3] Extensive cortical destruction, tumor necrosis with adjacent tissue infiltration are suggestive of malignancy.[8]

Kurzawa *et al.*[1] observed *EWSR1* rearrangement in five out of eight METs (71%), including two out of three pelvic tumors. Antonescu *et al.*[4] observed *EWSR1-POU5F1* fusion transcript in METs with clear cell morphology. Earlier, we observed *EWSR1* rearrangement 50% soft-tissue METs and in a case of an eccrine porocarcinoma.[5] *EWSR1* rearrangement was lacking in our earlier reported case of pelvic intraosseous MET.[6] Nonetheless, *EWSR1* rearrangement is a significant genetic mechanism underlying musculoskeletal METs.[1,4,5,10]

Almost all such cases are invariably treated with surgery in the form of curettage or resection.[1-4] In view of lack of malignant features, but a single positive resection margin; our earlier case underwent adjuvant radiotherapy. Until date, he has been free-of-disease over 29 months.[6] The present case underwent a wide-excision, is disease-free since 8 months and is on follow-up. Distinction between musculoskeletal myoepitheliomas and malignant myoepitheliomas/carcinomas is vital. Occurrence of a primary intraosseous MET has been attributed to intraosseous displacement of myoepithelial elements during embryogenesis.[9]

To conclude, primary intraosseous METs are extremely uncommon, but relatively less innocuous, unlike their diagnostic mimics, such as metastatic carcinomas, chondrosarcoma (skeletal and extraskeletal myxoid type) and other sarcomas exhibiting myxoid change. A wide panel of IHC markers is essential for their diagnosis. Differentiation of a myoepithelioma from a myoepithelial carcinoma is vital. Although both these tumor entities are optimally treated with surgical resection, unlike metastatic carcinomas that would require upfront chemotherapy; myoepithelial carcinomas have a more tendency for metastasis. Documentation of more such cases with molecular analysis and follow-up will enhance our understanding regarding their clinical course. Identification of *EWSR1* gene rearrangement in certain salivary gland and skin adnexal tumors indicates a certain level of genetic proximity between these tumors and the musculoskeletal METs.[5,12]

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