Myoepithelial Tumors of Bone

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KEYWORDS

• Myoepithelioma • Myoepithelial carcinoma • Bone • Pathology • Immunohistochemistry • EWSR1 • FUS • Fusion gene

ABSTRACT

Myoepithelial tumors (METs) of bone (BMETs) are a rare but distinct tumor entity. METs that are cytologically benign are termed myoepitheliomas; METs with malignant histologic features are called myoepithelial carcinomas. BMETs have a wide age range, may involve any part of the skeleton, and have a variable spindle cell and epithelioid morphology. Bone tumors to be considered in the differential diagnosis are discussed. Additional techniques are indispensable to correctly diagnose BMETs. By IHC, BMETs often express cytokeratins and/or EMA together with S100, GFAP, or calponin. Half of BMETs harbor EWSR1 (or rare FUS) gene rearrangements with different gene partners.

OVERVIEW, HISTORICAL PERSPECTIVE

To the novice in musculoskeletal pathology who was taught in medical school that the most common bone tumors differentiate along mesenchymal or neuroectodermal lines, it may come as a surprise that some bone tumors show myoepithelial differentiation.

Myoepithelial tumors (METs) of bone (BMETs) are rare. To date, up to 30 cases have been described in the literature.[1–12] BMETs were recognized as a distinct clinicopathological entity only after their initial description in soft tissue.

In 1997, Kilpatrick and colleagues[13] first proposed the unifying concept that METs morphologically resembling myoepithelial counterparts presenting as skin adnexal or salivary gland tumors, may also occur in soft tissue. Hornick and Fletcher[14] described a series of 101 soft tissue METs in 2003, after which Gleason and Fletcher[15] reported a series of 29 soft tissue METs presenting in childhood in 2007. Soft tissue METs represent a wide histologic spectrum with cases showing benign and malignant histomorphology and clinical behavior. In the 2013 World Health Organization (WHO) classification of tumors of soft tissue and bone,[16] the terms myoepithelioma and mixed tumor are used for the benign variants and myoepithelial carcinoma is the proper name for the malignant phenotypes. Myoepithelioma is mainly composed of myoepithelial cells, whereas mixed tumor also shows clear-cut ductal differentiation. The older term parachordoma, which was still used as a synonym for myoepithelioma in the 2002 WHO classification,[16] reflects the morphologic resemblance of some METs to chordoma, but clearly chordoma is a completely different tumor entity, as shown by nuclear immunostaining for the T-box transcription factor brachyury.[17]

Only in the past decade have molecular pathologic studies revealed that the molecular genetic pathogenesis of METs of soft tissue and bone is different from those occurring in skin and salivary glands.

EPIDEMIOLOGY, SITES OF INVOLVEMENT, AND GROSS FEATURES

BMETs have a wide age distribution and show an almost equal sex distribution. Most patients are adults and adolescents, but BMETs also arise in teenagers. The elderly are seldom affected.

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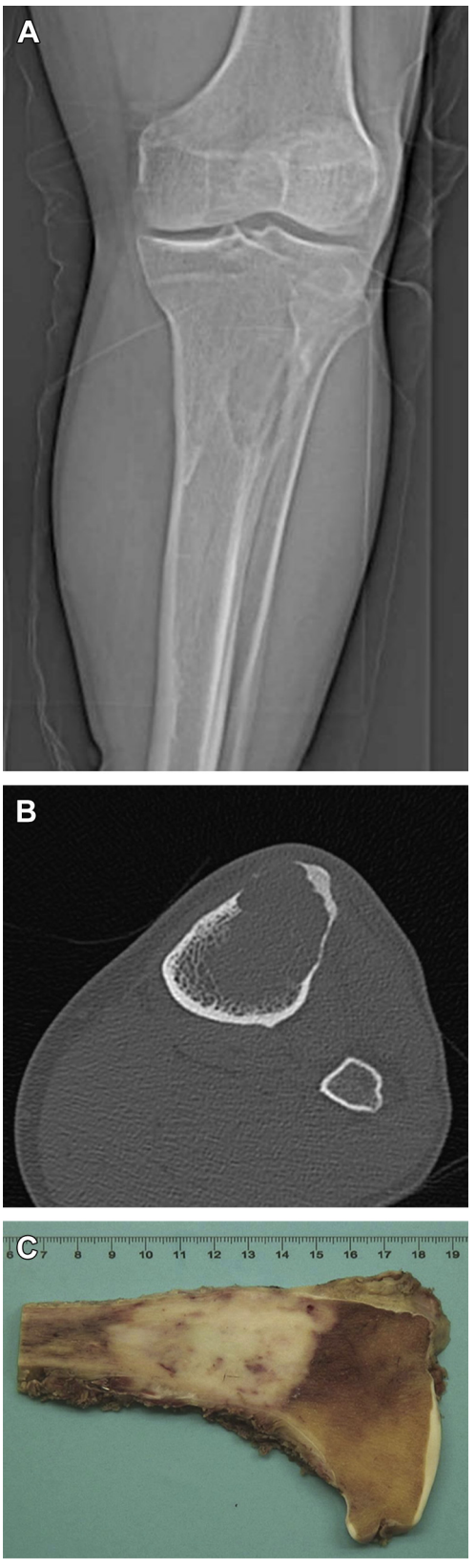

By location, BMETs have a variable distribution. The tumors most often present in long tubular bones (femur, tibia, fibula, humerus), but also occur in small tubular bones (phalanges), and axial skeleton (iliac bone, sacrum, vertebra, ribs, skull, and maxilla).

Although BMETs are usually intraosseous tumors, juxtacortical lesions also have been reported.[8]

By imaging studies (radiographs, computed tomography [CT], MRI) BMETs are well-demarcated, lytic tumors that may have aggressive features and show invasion of surrounding soft tissue (**Fig. 1**). By gross examination of surgical specimens, BMETs are solid, nodular tumors. Cortical destruction and extension in surrounding soft tissue may be present (see **Fig. 1**, **Fig. 2**).

Grossly, BMETs are well-demarcated, nodular, lobulated masses. On cut surface, color and consistency are proportionate to cellularity, collagenization, and myxoid change or hemorrhage. Commonly, BMETs are solid and gray-white, whereas myxochondroid areas are gelatinous and glistening.

MICROSCOPIC FEATURES AND DIAGNOSIS

The histology of benign BMETs (myoepitheliomas) is variable and resembles their salivary gland counterparts (**Fig. 3**). Microscopically, myoepithelial tumor cells can have different features,[18] with areas consisting of bland eosinophilic spindle cells, epithelioid cells, clear cells, squamous cells, or plasmacytoid cells (**Figs. 4–7**). Some tumors are predominantly composed of spindle cells arranged in bundles (**Fig. 8**), whereas other BMETs show foci with epithelioid cells and clear or vacuolated tumor cells that form cohesive cell nests and cords (**Figs. 9** and **10**). Myxoid areas with spindle or epithelioid cells can show a reticular architectural pattern (**Fig. 11**). These neoplastic myoepithelial cells are embedded in a variable amount of fibrous, hyaline fibrous, myxoid, or myxohyaline stroma (see **Figs. 9–11**, **Fig. 12**). Frank cartilaginous or osseous differentiation is rather rare.

Fig. 1. Myoepithelioma of the proximal tibia. (*A*) The plain radiograph and (*B*) MRI both show an intramedullary lytic lesion that is well demarcated, but destroys the cortical bone (*arrows*). (*C*) Gross examination of the cut surface of the resection specimen reveals a well-demarcated, solid, gray-white tumor that is located intramedullary but destroys cortical bone.