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Myoepithelioma of Soft Tissue With Both Squamous and Adipocytic Metaplasia

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Abstract

Soft tissue, or cutaneous, myoepitheliomas are rare tumors arising solely from a myoepithelial origin. These neoplasms are typically associated with uncertain differentiation and can contain cellular morphologies that include spindle, plasmacytoid, epithelioid, or clear cell forms. Soft tissue myoepitheliomas are commonly found on the lower limbs and in the pelvic girdle but can occur throughout the body. A small minority display heterogenous differentiation, typically osseous or cartilaginous in nature. Squamous and adipocytic cell types are much rarer. We report the case of myoepithelioma of soft tissue with both squamous and adipocytic metaplasia. In the largest myoepithelioma series of 101 soft tissue myoepitheliomas, there were only 2 cases of squamous metaplasia and 1 case of adipocytic metaplasia. Our case displays the unique occurrence of 2 rare histologic findings occurring simultaneously within an already uncommon neoplasm.

Keywords

myoepithelioma; mixed tumor; soft tissue neoplasm

INTRODUCTION

Myoepitheliomas of soft tissue and cutaneous origin are a rare but increasingly recognized entity. They most often arise on the extremities or limb girdles, and tend to be slow growing and asymptomatic.[1,2] Like their salivary gland counterparts, myoepitheliomas demonstrate cytological and architectural diversity. Their malignant potential is determined by the degree of atypia rather than infiltrative growth. Interestingly, up to 15% of soft tissue myoepithelial neoplasms will exhibit heterogenous differentiation, most commonly osseous or cartilaginous, and much less commonly squamous or adipocytic metaplasia.[1–5] Here, we present a case of a subcutaneous myoepithelioma demonstrating both squamous and adipocytic metaplasia.

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CASE REPORT

A 72-year-old Asian woman presented to the dermatology clinic with a chronic, painless nodule on the right posterior lateral thigh. Clinically consistent with a lipoma, the lesion was electively excised with wide local excision. The excision specimen consisted of a 26 × 18 × 13-mm tan ellipse, which was submitted for paraffinembedded sections with routine hematoxylin and eosin staining. Immunohistochemical studies were performed using AE1/ AE3, CK5/6, p63, S100, glial fibrillary acidic protein (GFAP), and epithelial membrane antigen (EMA). Hematoxylin and eosin sections demonstrated a well-circumscribed, subcutaneous, nodular proliferation of small epithelioid cells with regular ovoid nuclei, fine chromatin, inconspicuous nucleoli, and eosinophilic cytoplasm. These were embedded in a reticular network of cords, nests, tubules, and formed ducts, disposed in a chondromyxoid and collagenous stroma. Squamous metaplasia, calcifications, and adipocytic differentiation were present. Occasional mitoses were also present, but no significant nuclear atypia was identified. Lesional cells were positive for AE1/ AE3, CK5/6, p63, S100, Smooth Muscle Actin (focal), and GFAP (focal), with EMA highlighting ductal structures (Fig. 1).

DISCUSSION

Salivary gland myoepitheliomas have been recognized for several decades, whereas the first published cases of myoepitheliomas of soft tissue origin only date back to the late 1990s.[2] Since then, several case series describing their clinical and histopathologic features have been published.[1–3,6,7] In the largest series to date, Hornick et al[1] reported only 2 cases of squamous metaplasia and 1 case of adipocytic differentiation of the 101 soft tissue myoepitheliomas. Our case presents 2 relatively rare histologic findings occurring simultaneously within an already uncommon entity. Of note, it is unlikely that our tumor's adipocytic component represented entrapped fat rather than differentiation. The tumor was encapsulated and contained islands of fat scattered throughout the tumor, including close to the capsule arguing for differentiation rather than entrapment. INI-1 staining retained in the entire tumor, as often in benign soft tissue myoepithelioma.

Clinically, soft tissue myoepitheliomas are slow growing and asymptomatic. They demonstrate no sex predilection and occur over a wide range of ages, 2–83 years, with a peak incidence in the third to fifth decades.[1,2] Approximately 20% of myoepithelial neoplasms occur in children, where more than half are malignant.[1,3] Myoepithelial neoplasms are currently felt to exist on spectrum and are classified as mixed tumors (pleomorphic adenomas), myoepitheliomas, or myoepithelial carcinomas. Resembling their salivary counterparts, mixed tumors possess both epithelial and myoepithelial features, whereas myoepitheliomas demonstrate minimal to no ductal differentiation. Malignant potential is primarily determined by the degree of cytological atypia. This is in contrast to salivary gland myoepithelial carcinomas, where the most significant predictor of malignancy is infiltrative and locally destructive growth.[4,5]

Myoepithelial neoplasms are well known for their cytological and architectural diversity. Myoepithelial cells may appear spindled, epithelioid, plasmacytoid, or ovoid, and grow in nested, trabecular, or reticular patterns. Furthermore, the surrounding stroma may be

myxoid, chondroid, or hyalinized. This remarkable range of phenotypes has historically resulted in underrecognition of this uncommon entity. The advent of immunohistochemistry has significantly aided in identification. Most myoepitheliomas coexpress epithelial antigens and S100. Broad-spectrum cytokeratin stains (pan-keratin, Cam5.2, and AE1/AE3) will be positive in 93%−100% of cases.[1–3,7] S100 is positive in 72%−100%, whereas GFAP positivity ranges from 27% to 54%.[1–3,7] Among myogenic markers, calponin is more likely to be positive than Smooth Muscle Actin (86%−100% vs. 36%−64%, respectively).[1,3,7] Desmin is positive in the minority of cases (0%−20%).[1–3,8] p63 expression is less common in soft tissue myoepitheliomas (7%−45%) than in mixed tumor myoepitheliomas of the salivary gland, where nearly all cases are p63 positive.[1,3,9–11] In summary, a panel including cytokeratin, EMA, S100 protein, and GFAP will identify myoepithelial differentiation in most cases.

With the large diversity of morphologies found in myoepitheliomas and their difficulty in establishing differentiation state, genetic characterization has become an evolving way to classify and distinguish these tumors.[12] The most recent update of the World Health Organization classification of myoepitheliomas includes *EWSR1* gene rearrangements, as a new genetic finding after 1 study reported that almost half of the 66 myoepithelial tumors they sampled had this genetic change. These *EWSR1*-positive tumors more often showed cytological atypia which characterizes malignancy compared with the genetically negative counterparts.[13] In 2 other studies on *EWSR1*-negative myoepitheliomas, *PLAG1* gene rearrangements were common and had similar qualities to salivary gland adenomas. These genetic distinct groups aligned with different histological appearances: *PLAG1*-positive cells had positive nuclear staining and visible tubuloductal differentiation, whereas *EWSR1*-positive cells appeared clear and often epithelioid in appearance.[12,14,15]

Heterogenous metaplasia of a myoepithelioma containing both squamous and adipocytic differentiation is a notably rare discovery. Although this specific heterogenous metaplasia does not indicate clinical malignancy, it should be acknowledged as a factor in the differential diagnosis of myoepithelial neoplasms to correctly identify the type of tumor. The authors suggest that further investigations should be performed to comprehend the relationships between the histological appearance, genetic classification, and malignant potential of myoepithelial tumors.

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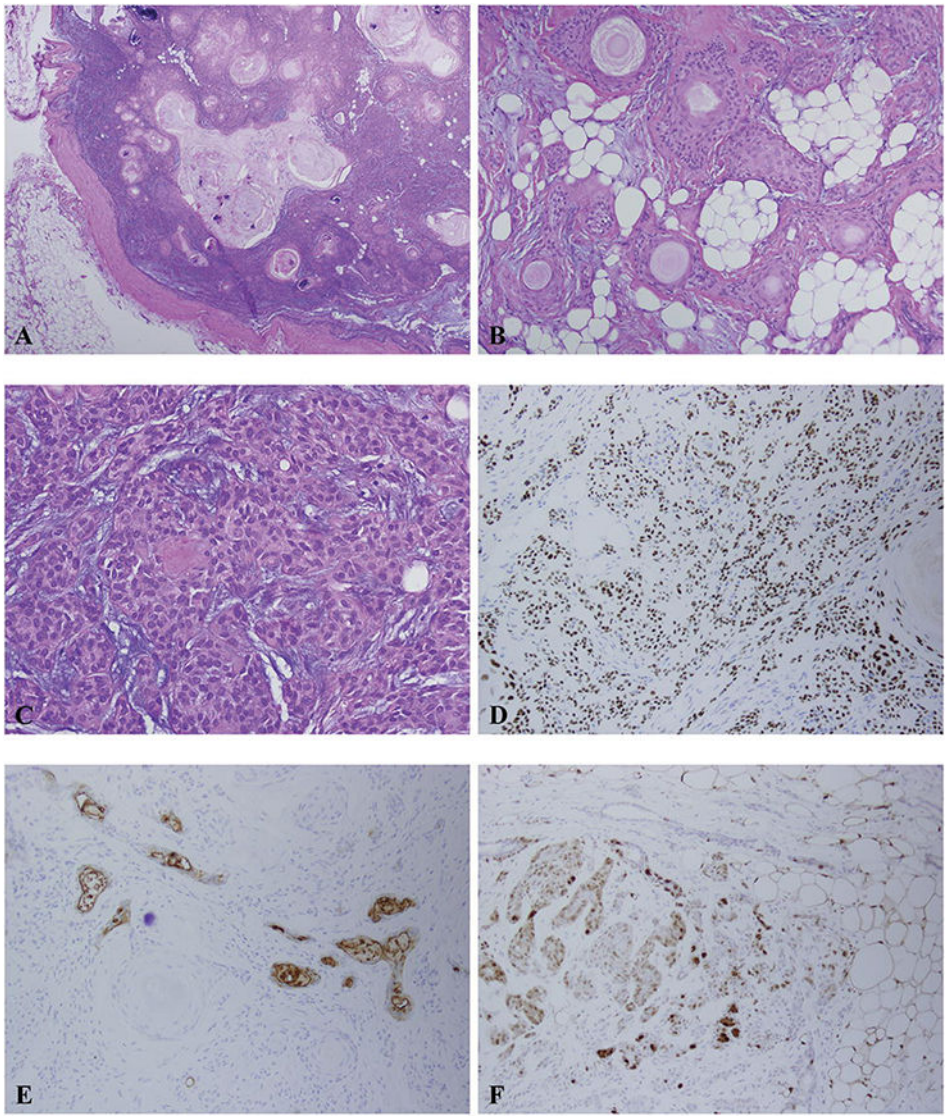

FIGURE 1.

Encapsulated myoepithelioma of soft tissue with squamous and adipocytic metaplasia. A, Hematoxylin and eosin (H&E) stain, ×40 magnification of the excised specimen shows an encapsulated and heterogenous myoepithelial tumor with wellformed ducts and calcifications. B, H&E, ×100 magnification with adipocytic differentiation adjacent to squamous metaplasia containing keratin whorls. C, H&E, ×200 magnification nests of small epithelioid cells with regular ovoid nuclei, fine chromatin, inconspicuous nucleoli, and eosinophilic cytoplasm, disposed in a chondromyxoid and collagenous stroma. D, p63 stain, lesional cells stain indicating a myoepithelial origin. E, EMA stain highlighting ductal structures. F, S100 stain further identifies the tumor as a myoepithelioma.