

# QUIZ

## CORRECT ANSWER TO THE QUIZ. CHECK YOUR DIAGNOSIS

### SUBCUTANEOUS MYOEPITHELIOMA OF SOFT TISSUE

JAROSLAW JEDRYCH, JOHN VU

Department of Dermatology, Dermatopathology Unit, University of Pittsburgh Medical Center, Pittsburgh, USA

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We present a case of a 75-year-old female with a subcutaneous back mass diagnosed as myoepithelioma of soft tissue. The diagnosis of this tumor may be challenging and familiarity with its broad morphological spectrum is important to distinguish it from a number of histologically similar soft tissue proliferations, in particular those displaying a prominent myxoid stroma. The correct diagnosis can be facilitated by the use of a panel of confirmatory immunohistochemical markers, including cytokeratins, neural, and muscular antigens, revealing the myoepithelial nature of the tumor cells.

**Key words:** myoepithelioma, mixed tumor, soft tissue.

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#### Introduction

Myoepithelioma of soft tissue (MST) is a rare under-reported mesenchymal proliferation involving various anatomical locations in patients over a broad age range and with no gender predilection. It is characterized by considerable architectural and cytomorphologic variability. MSTs predominantly follow a benign clinical course, although recurrences are seen in approximately 20% of tumors with overall low-grade morphology. Due to a significant histological variability associated with neoplastic cell proliferation, MST enters the differential diagnosis of a variety of soft tissue tumors.

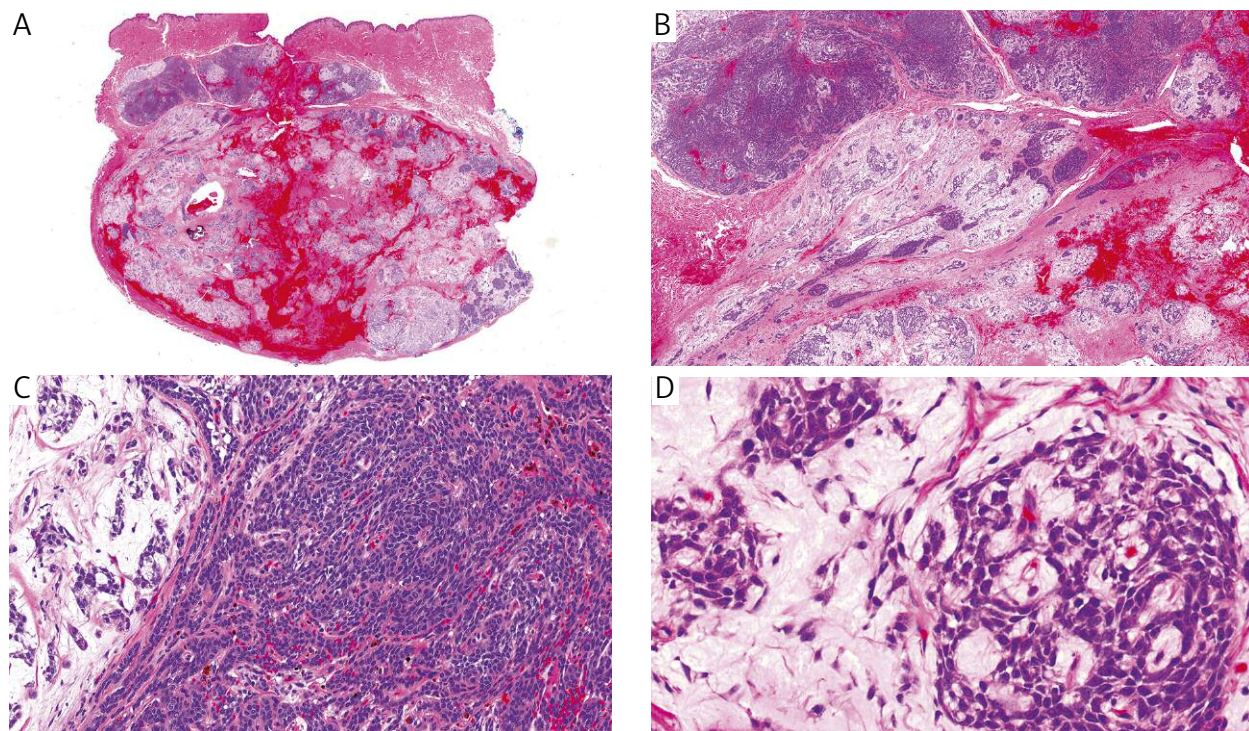
#### Case report

A 75-year-old Caucasian female presented with a subcutaneous lump, a few centimeters in size, located on her lower back and slowly enlarging for a few years. The overlying skin was unremarkable. On macroscopic inspection of a deep elliptical skin excision, there was a 3.7 cm × 2.9 cm × 1.7 cm subcutaneous well-circumscribed mass with hemorrhagic, tan-pink to gray, glistening cut sections. Histopathologic examination displayed a predominantly subcutaneous well-demarcated mass partially involving the deep reticular der-

mis (Fig. 1). The tumor showed smooth outlines and somewhat lobular architecture. It was composed of small to medium sized spindle, stellate, plasmacytoid, and focally epithelioid cells arranged in strands, trabeculae, and cribriform nests set in an abundant myxoid stroma. No significant cytologic atypia, necrosis or increased mitotic activity was seen. On immunohistochemical studies, the tumor were showed strong and diffuse expression of cytokeratin AE1/AE3, S100, glial fibrillary acid protein (GFAP), patchy expression of calponin, and focal expression of epithelial membrane antigen (Fig. 2). P63 stain was negative. Based on morphological features coupled with the immunoprofile, the tumor was classified as myoepithelioma of soft tissue.

#### Discussion

Tumors of myoepithelial differentiation, common in the salivary glands, have also been documented in soft tissue [1, 2]. Although initially considered to be a part of the mixed tumor spectrum, a separation from the latter has been postulated to avoid misdiagnosis of a malignancy due to the variability of architectural and cytologic appearances of tumor composed of neoplastic myoepithelial cells [3]. Currently, tumors composed entirely or almost entirely of myoepithelial cell are clas-



**Fig. 1.** Subcutaneous myoepithelioma of soft tissue: (A) Low power view demonstrates well-demarcated predominantly subcutaneous tumor with partial involvement of the deep dermis (HE, 10 $\times$ ). (B) The tumor is variably cellular and shows lobular architecture. A prominent myxoid stroma is evident (HE, 20 $\times$ ). (C) Higher power displays intertumoral morphologic heterogeneity (HE, 100 $\times$ ). (D) High power magnification reveals overall bland but diverse cytomorphology of the tumor cells (HE, 400 $\times$ )

sified as myoepitheliomas [2]. However, a tumor with a minimal epithelial/ductal component is also allowed to be categorized as such [1, 3].

Myoepitheliomas of soft tissue occur equally in both sexes with a peak between the third and fifth decades of life. The extremities and limb girdles are most commonly affected [1]. The typical anatomic locations include subcutis and deep soft tissue [2]. Clinical presentation is of a localized asymptomatic nodule or mass growing for prolonged periods of time [4]. Phenotypic plasticity of myoepithelial cells and their capacity of both epithelial and muscular differentiation result in significant morphologic variability of MSTs [3]. Typically, tumors are well-demarcated with a lobular outline and trabecular to reticular arrangement of neoplastic myoepithelial cells set in a myxoid to chondroid stroma [1, 2]. Tumor cytomorphology is diverse including epithelioid, spindled, plasmacytoid, vacuolated and clear cell forms [2, 3]. Myoepitheliomas of soft tissue usually show intratumoral heterogeneity with areas of variable cellularity, architecture and cytologic features [1].

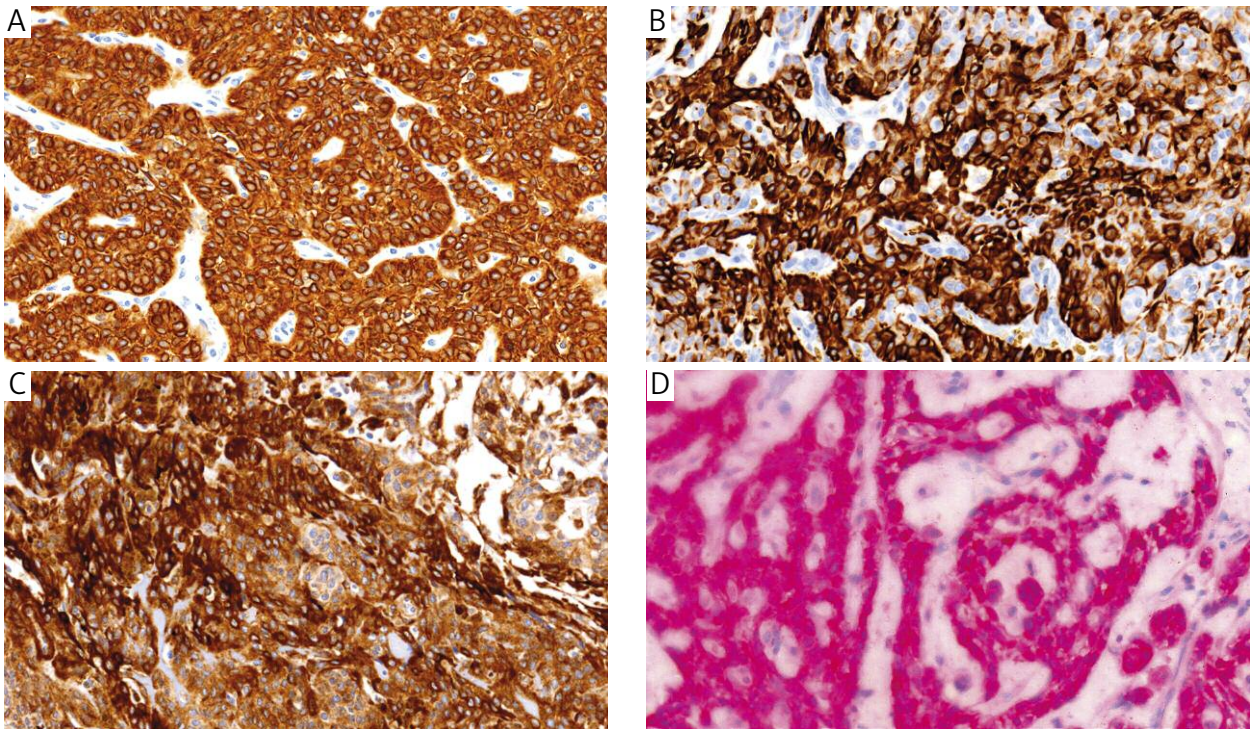
The antigens most commonly expressed and therefore most sensitive for MST include broad range cytokeratins (expressed in nearly 100% of cases), S100 (87%), and calponin (86%). GFAP, smooth muscle actin, and p63 expression is reported in approximately one-half, one-third, and one-fourth of the tumors, respectively. Desmin is usually negative [1].

Myoepitheliomas of soft tissue follow a benign clinical course in the majority of cases [5]; however, close to 20% of tumors with overall low-grade morphology recur [1]. Besides high-grade cytological atypia, accurate criteria for malignancy have not been established yet for myoepithelial malignancies [1, 3]. The clinical behavior of tumors with low-grade morphology is largely unpredictable based on histological features. There is no correlation between the tumor size, cellularity, mitotic activity, infiltrative tumor edge, and risk of recurrence or metastasis [1, 2].

Recent studies demonstrate frequent EWSR1 gene rearrangement detectable in 45% of myoepithelial tumors outside the salivary glands. The common fusion partner genes include PBX1, POU5F1, and ZNF444 [6]. The progress in molecular characterization of myoepitheliomas offers a possibility of more accurate classification of these tumors into genetically distinct groups, overcoming limitations of morphologic analysis of these histologically variable proliferations. Interestingly, chromosomal translocations in MSTs differs from translocations involving PLAG1 and HMGA2 genes reported in myoepithelial tumors of the salivary glands, [7] providing support for a different pathogenesis of these tumors.

The differential diagnosis of MST includes mixed tumor, extraskeletal myxoid chondrosarcoma (EMC), and ossifying fibromyxoid tumor (OFT), among others. Al-





**Fig. 2.** Subcutaneous myoepithelioma of soft tissue. Immunohistochemical studies demonstrate that the tumor cells express (A) cytokeratin AE1/AE3, (B) GFAP, (C) calponin, (D) and S100

though a histological spectrum exists and separation of MST from mixed tumor is controversial, the presence of a prominent epithelial component with duct formation favors the latter [1]. Extraskeletal myxoid chondrosarcoma is typically a larger and deeper seated tumor, although these clinical features cannot reliably distinguish it from MST [2]. Histologically, EMC demonstrates greater cytomorphologic uniformity and is usually negative for S100, cytokeratins, and muscular markers [2, 5]. Ossifying fibromyxoid tumor demonstrates a characteristic lobular architecture and consists of pale round cells associated with myxoid stroma and peripheral ossifications. It shows no expression of keratins and GFAP [1, 5].

In summary, the diagnosis of MST may be challenging and familiarity with a broad morphological spectrum of this tumor is important to distinguish it from a number of histologically similar soft tissue proliferations, in particular those displaying a prominent myxoid stroma. The correct diagnosis can be facilitated by the use of a panel of confirmatory immunohistochemical markers, including cytokeratins, as well as neural and muscular antigens, revealing the myoepithelial nature of the tumor cells. The risk of MST recurrence is largely unpredictable based on morphological features. However, recent progress in molecular characterization of these tumors may help to segregate them into genetically and clinically meaningful categories.

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## Address for correspondence

Jaroslav Jedrych  
200 Lothrop Street, Suite 3725  
Pittsburgh, PA 15213 United States  
e-mail: jaroslav.jedrych@gmail.com