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Case Report

Soft Tissue Myoepithelioma of the Shoulder

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Soft tissue myoepitheliomas are often misdiagnosed due to their rarity. Herein, we describe a case of soft tissue myoepithelioma of the shoulder. A 72-year-old woman had a suspected sarcoma on her shoulder and underwent open biopsy. She was referred to our hospital, where the tumor was widely resected and the diagnosis of myoepithelioma was histologically confirmed. No recurrence has been observed in the 3 years since the surgery. Careful and prompt planning is necessary for the effective treatment of myoepithelioma.

Key words: soft tissue myoepithelioma, unplanned resection, shoulder

Myoepitheliomas of the skin or soft tissue arising solely from the myoepithelium are rare [1]. Myoepitheliomas of the soft tissue are morphologically and immunophenotypically comparable to their counterparts of the salivary gland [2]. Most myoepitheliomas of the soft tissue (75%) appear on the limbs and limb girdles (lower > upper); the trunk, head, and neck are less often affected [2]. To the best of our knowledge, only 2 cases of myoepithelioma of the shoulder have been reported [3, 4]. Herein, we describe the first case of deep soft tissue myoepithelioma of the shoulder.

Case Presentation

A 72-year-old woman presented to a nearby hospital in August 2014 with a 6-month history of a progressively enlarging shoulder mass. Magnetic resonance imaging (MRI) performed at that hospital revealed a tumor mass in the muscle between the trapezius and the supraspinatus. A general surgeon performed an open biopsy in November 2014. Histopathological results indicated fibrosarcoma. The patient was then referred to our hospital in January 2015. Physical examination revealed a firm nodule measuring 8.3 × 6.5 cm, with a surgical wound on the nodule surface. The patient had no pain or tenderness, and Tinel's sign was negative. She had full range of motion in her shoulder. A plain radiograph showed enhancing soft tissue shadows. No calcification was observed. The MRI performed at the nearby hospital in October 2014 indicated that the mass was situated between the trapezius and supraspinatus with a low signal on T1-weighted images (Fig. 1A) and a high signal on T2-weighted images (Fig. 1B). Gadolinium (Gd)-enhanced T1-weighted MRI performed at our hospital in January 2015 revealed no contrast effect at the center of the tumor (Fig. 1C). Although the tumor was close to the scapula, Gd-enhanced T1-weighted MRI findings did not suggest that the tumor had infiltrated the scapula (Fig. 1D). ^{18}F-fluorodeoxyglucose-positron emission tomography (^{18}FDG-PET) imaging showed an accumulation of ^{18}F-FDG in the mass, with a maximum standardized uptake value (SUV_{max}) of 6.61 (Fig. 1E, F). On reviewing the pathological specimens resected at the nearby hospital, we detected spindle-shaped cells arranged in an interlacing fascicular pattern. We also noted that the

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nucleus was slightly swollen, and collagen fibers were observed. Immunohistochemical findings were positive for CD99 and vimentin. We also noted focal cytokeratin (CK), AE1/AE3, and epithelial membrane antigen (EMA) positivity, however, the specimen tested negative for CD34, S-100, desmin, and α-smooth muscle actin (αSMA). Based on these histological findings, we diagnosed the patient with synovial sarcoma. We planned and performed a wide resection of the tumor together with the surrounding muscles and the surface of the scapular spine *en bloc*. The resected specimen was red and white in color and had a hard yet yielding consistency. Hematoxylin-eosin (H-E) staining showed proliferation of the tumor cells, with round, ovoid, or spindle-shaped nuclei and clear acidophilic cytoplasm (Fig. 2A). Heterogeneous nuclear staining was observed, with differences in the size and shape of the nucleus (Fig. 2B). Necrosis was also seen (Fig. 2C). A predominantly reticular or trabecular growth pattern with prominent myxoid stroma, which is typically found in myoepitheliomas, was noted (Fig. 2D), and mitosis was observed in 6/10 high power fields (HPFs). However, there was no invasion into the adipose tissue or muscle. Immunohistochemical examination showed positive staining focally for AE1/AE3 (Fig. 2E), CAM5.2 (Fig. 2F), αSMA (Fig. 3A), calponin (Fig. 3B), h-caldesmon (Fig. 3C), desmin (Fig. 3D), and vimentin (Fig. 3E). Staining was negative for EMA, S-100, glial fibrillary acidic protein (GFAP), CD31, CD34, bcl-2, and CD10. Positive MIB-1 staining was observed, with an index of 9.8% (Fig. 3F). We also analyzed SYT-SSX gene fusion and EWSR1 gene translocation or rearrangement, and the patient tested negative for both (Examinations No. 0SSL001100 and No. 0SSL001200). Based on these results, myoepithelioma was diagnosed. The surgical margin was negative for malignant cells. At the time of writing, 3 years postoperatively, no evidence of recurrence has been observed, and the patient has full shoulder function.

The patient provided her written informed consent for the publication of this information.

Discussion and Conclusions

The first report on myoepithelioma of the soft tissue was published in 1997 [5]. Myoepitheliomas of the soft tissue are rare but have been increasingly characterized over the past decade [6]. Men and women are affected equally, and approximately 20% of the incidence occurs in pediatric patients [7]. Myoepitheliomas are also known to occur over a wide age range (0.5-93 years), with a mean patient age of 32 years [7, 8]. To the best of our knowledge, the present patient is the oldest reported patient (Table 1). Soft tissue myoepitheliomas often occur subcutaneously [1], however, their origin remains unclear [3, 7]. In the present case, it was suspected that the tumor may have developed between muscles. As observed in the present case, myoepitheliomas show high concentrations of ^{18}FDG, as do malignant tumors [9]. The characteristics of myoepitheliomas include the proliferation of tumor cells with round, ovoid, or spindle-shaped nuclei and clear acidophilic cytoplasm; these were observed in the present case. A previous study reports that myoepithelial cells express cytokeratin

Table 1 Clinical and immunohistological features of primary myoepitheliomas of the shoulder and the present case

Author and year	Age (years)	Sex	Location	Size (cm)	Treatment	Follow-up period	IHC; Epithelial markers	IHC; Myogenic markers	IHC; Other markers
[3]Sasaguri *et al*. 1999	28	M	Subcutaneous	3 × 2.8	Marginal resection	2 years	CAM5.2	α SMA, HHF35	None
[4]Min *et al*. 2005	43	F	Subcutaneous	2.5 × 2.0 × 1.2	Marginal resection	11 weeks	Vimentin	P63, H-caldesmon	S-100, collagen IV
Current case	72	F	Muscle	8.3 × 6.5	Extended resection	3 years	AE1/AE3, CAM5.2, Vimentin	α SMA, calponin, H-caldesmon, desmin	None

M, male; F, female; IHC, immunohistochemistry; SMA, smooth muscle actin

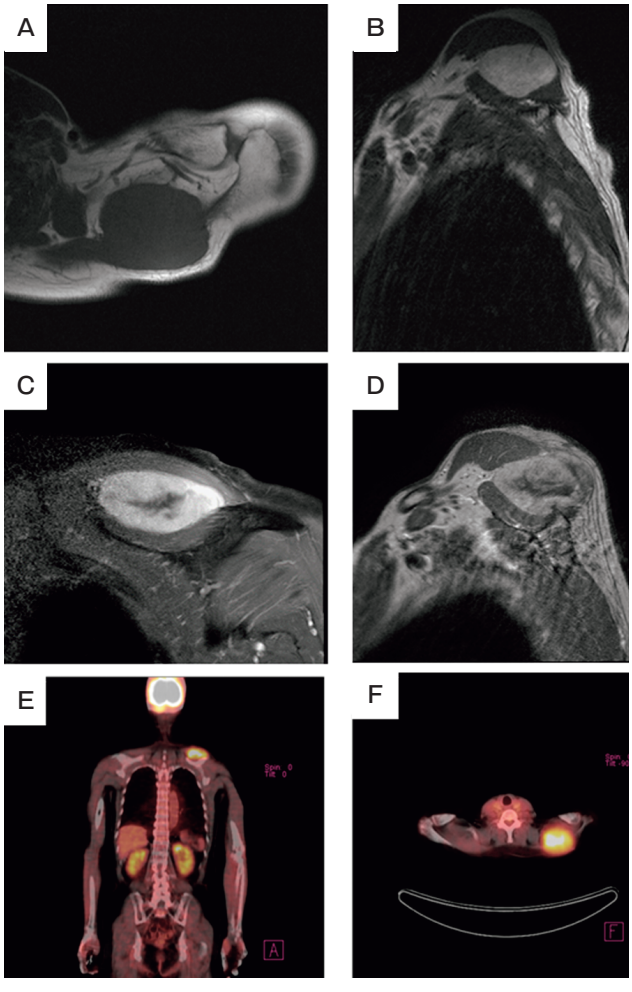

Fig. 1 **A**, Coronal view of the tumor on T1-weighted magnetic resonance imaging MRI; **B**, Sagittal view of the tumor on T2-weighted MRI; **C**, Coronal view of the tumor on gadolinium Gd-enhanced T1-weighted MRI; **D**, Sagittal view of the tumor on Gd-enhanced T2-weighted MRI; **E** Frontal and **F** coronal views of the tumor on ^{18}F-fluorodeoxyglucose positron emission tomography (^{18}FDG-PET). **A** and **B** are images from the MRI scans recorded at a nearby hospital in October 2014. **C** and **D** are images from the Gd-enhanced MRI scans recorded at our hospital in January 2015.

(100%), EMA (79%), SMA (57%), calponin (91%), desmin (17%), S-100 protein (93%), CK14 (57%), GFAP (50%), and p63 (27%) [10]. As our patient tested positive for epithelioid markers such as AE1/AE3 and CAM5.2, and for muscle-specific antigens such as αSMA, calponin, h-caldesmon, and desmin, we diagnosed her with myoepithelioma. It is known that the spindle cell patterns of myoepitheliomas might mimic the histological patterns of other more common smooth muscle tumors, such as leiomyomas and synovial sar-

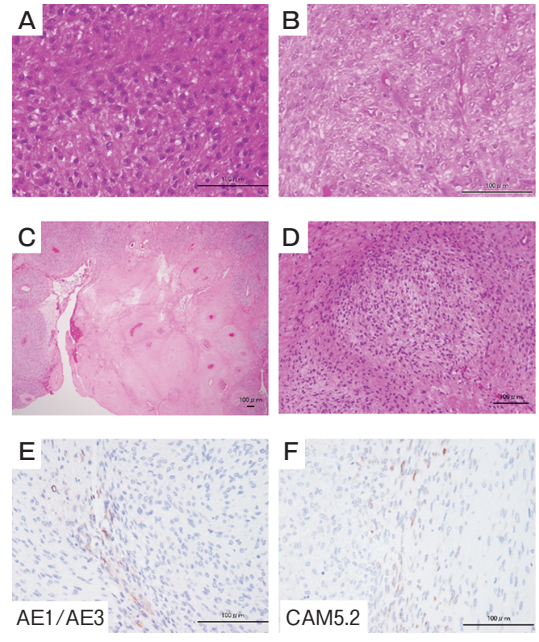

Fig. 2 Hematoxylin and eosin stained images **A**–**D** and immunohistochemical staining images **E**, **F**. **A**, Proliferation of tumor cells, with round, ovoid, or spindle-shaped nuclei and clear acidophilic cytoplasm; **B**, Heterogeneous nuclear staining was observed and mitosis and differences in nuclear size were detected; **C**, Necrosis can be seen; **D**, A predominantly reticular or trabecular growth pattern with prominent myxoid stroma; **E**, Immunohistochemical staining for AE1/AE3; **F**, Immunohistochemical staining for CAM5.2. Scale bars are 100 μm.

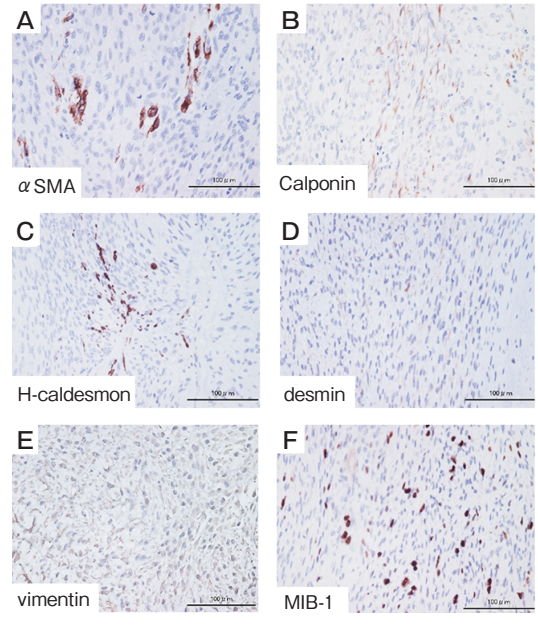

Fig. 3 Immunohistochemical staining images for **A**, α-smooth muscle actin SMA (αSMA); **B**, calponin; **C**, h-caldesmon; **D**, desmin; **E**, vimentin, and; **F**, MIB-1. Scale bars are 100 μm.

comas [7,10]. Almost all cases of leiomyosarcoma show positive immunostaining for desmin and negative immunostaining for vimentin [11]. In contrast, myoepithelioma shows positive immunostaining for both desmin and vimentin. Because cytokeratin-positive tumor cells are observed in synovial sarcoma [12], this tumor should also be considered in the differential diagnosis. Synovial sarcoma usually stains positive for S-100 [12], but the present case showed negative S-100 staining [13]. Recently, myoepithelial carcinoma has come to be recognized as a malignant myoepithelial neoplasm of the soft tissue [8], and should be considered in the differential diagnosis of myoepithelioma. Myoepithelial carcinoma often recurs or becomes metastatic, unlike myoepithelioma [8,14], however, the histological and immunohistochemical features of these two entities are similar, thus rendering it difficult to distinguish between them [8,14]. Important points of differentiation are that myoepithelial carcinoma, unlike myoepithelioma, is often positive for p63 and has a mean mitosis rate of 13/10 HPF [14]. Recent reports have shown that the malignant potential is determined by the degree of nuclear atypia [1,6]. A recent systematic review revealed that the long-term prognosis for myoepithelioma of the soft tissue is poor, and local recurrence is associated with poorer resection margins (R1,R2) [15]. The same review also reported that the percentage of severe atypia was above 50% in five studies, and suggested that myoepithelioma of the soft tissue itself might be a malignancy [15]. Although the present case was considered malignant due to the presence of nuclear atypia, it may be better to treat myoepithelioma itself as a malignancy. Recent studies have reported that the detection of specific fusion transcripts can aid in better identifying myoepithelioma and facilitate an accurate differential diagnosis [16-20]. Approximately 50% of myoepitheliomas show EWSR1 translocations in various patterns [2,16,17]. Moreover, myoepithelial tumors that do not show EWSR1 rearrangement are often benign and superficially located and show ductal differentiation [2]. PLAG1 translocations have also been described in cases of myoepithelioma with ductal differentiation [18]. Other fusion events have been identified in a small subset of myoepithelial tumors involving the FUS gene [19]. A recent study reports that SRF-E2F1 fusion transcripts have been detected in EWSR-negative soft tissue myoepitheliomas. [20]. We confirmed our diagnosis based on the overall histological features, including the results of our immunohistochemical analysis, which indicated positivity for epithelial and myogenic markers. Although EWSR1 rearrangement was not observed in the present case, the tumor had spread to a substantial depth and the pathological findings indicated nuclear atypia, suggesting malignancy. In the World Health Organization (WHO) classification, myoepithelioma is considered an intermediate (rarely metastasizing) tumor [2]. Although rare, recurrence or metastasis can sometimes occur [7,8,10,15], and tumors extending to a greater depth show a poorer prognosis compared to subcutaneous tumors [21]. Moreover, as mentioned above, a recent systematic review suggests that myoepithelioma itself should be treated as a malignant tumor [15]. Thus, wide resection and careful follow-up may be necessary.

In summary, we present a case of deep soft tissue myoepithelioma of the shoulder, which was initially treated by a non-specialist. In cases in which myoepithelioma is initially treated by a non-specialist, prompt and effective intervention by a specialist will help avoid unnecessary loss of function.

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References

1. Elsensohn A, Mo JH, Maly TJ, Lee PK and de Feraudy S: Myoepithelioma of soft tissue with both squamous and adipocytic metaplasia. Am J Dermatopathol (2018) 40: 142–144.
2. Fletcher CD, Bridge JA, Hogendoom PC and Mertens F: WHO Classification of Tumors of Soft Tissue and Bone, 4th Ed, IARC Publications, France (2013) pp 208.
3. Sasaguri T, Tanimoto A, Arima N, Hamada T, Hashimoto H and Sasaguri Y: Myoepithelioma of soft tissue. Pathol Int (1999) 49: 571–576.
4. Min KW, Seo IS and Pitha J: Ossifying fibromyxoid tumor: modified myoepithelial cell tumor? Report of three cases with immunohistochemical and electron microscopic studies. Ultrastruct Pathol (2005) 29: 535–548.
5. Kilpatrick SE, Hitchcock MG, Kraus MD, Calonje E and Fletcher CD: Mixed tumors and myoepitheliomas of soft tissue: a clinicopathologic study of 19 cases with a unifying concept. Am J Surg Pathol (1997) 1: 13–22.
6. Jo VY and Fletcher CD: Myoepithelial neoplasms of soft tissue: an updated review of the clinicopathologic, immunophenotypic, and genetic features. Head Neck Pathol (2015) 1: 32–38.
7. Hornick JL and Fletcher CD: Myoepithelial tumors of soft tissue: a clinicopathologic and immunohistochemical study of 101 cases with evaluation of prognostic parameters. Am J Surg Pathol (2003)

27: 1183-1196.
8. Jo VY: Myoepithelial Tumors: An Update. Surg Pathol Clin (2015) 8: 445-466.
9. Hamada K, Ueda T, Tomita Y, Yoshikawa H and Hatazawa J: Myoepithelioma of soft tissue originating from the hand: ^{18}F-FDG PET Features. AJR Am J Roentgenol (2006) 186: 269-271.
10. Hornick JL and Fletcher CD: Cutaneous myoepithelioma: a clinicopathologic and immunohistochemical study of 14 cases. Hum Pathol (2004) 35: 14-24.
11. Iwata J and Fletcher CD: Immunohistochemical detection of cytokeratin and epithelial membrane antigen in leiomyosarcoma: a systematic study of 100 cases. Pathol Int (2000) 50:
12. Chase DR, Enzinger FM, Weiss SW and Langloss JM: Keratin in epithelioid sarcoma. An immunohistochemical study. Am J Surg Pathol (1984) 8: 435-441.
13. Eswaran P, Devadoss P, Narasimhan LS and Kannan K: Synovial sarcoma of the heart: A case report and literature review. J Cancer Res Ther (2015) 11: 659.
14. Frost MW, Steiniche T, Damsgaard TE and Stolle LB: Primary cutaneous myoepithelial carcinoma: a case report and review of the literature. APMIS (2014) 122: 369-379.
15. Rastrelli M, Del Fiore P, Damiani GB, Mocellin S, Tropea S, Spina R, Costa A, Cavallin F and Rossi CR: Myoepithelioma of the soft tissue: A systematic review of clinical reports. Eur J Surg Oncol (2019) 45: 1520-1526.
16. Antonescu CR, Zhang L, Chang NE, Pawel BR, Travis W, Katabi N, Edelman M, Rosenberg AE, Petur Nielsen G, Cin PD and Fletcher CD: EWSR1-POU5F1 fusion in soft tissue myoepithelial tumors. A molecular analysis of sixty-six cases, including soft tissue, bone, and visceral lesions, showing common involvement of the EWSR1 gene. Genes Chromosomes Cancer (2010) 49: 1114-1124.
17. Flucke U, Palmedo G, Blankenhorn N, Slootweg PJ, Kutzner H and Mentzel T: EWSR1 gene rearrangement occurs in a subset of cutaneous myoepithelial tumors: a study of 18 cases. Mod Pathol (2011) 24: 1444-1450.
18. Antonescu CR, Zhang L, Shao SY, Mosquera JM, Weinreb I, Katabi N and Fletcher CD: Frequent PLAG1 gene rearrangements in skin and soft tissue myoepithelioma with ductal differentiation. Genes Chromosomes Cancer (2013) 52: 675-682.
19. Huang SC, Chen HW, Zhang L, Sung YS, Agaram NP, Davis M, Edelman M, Fletcher CD and Antonescu CR: Novel FUS-KLF17 and EWSR1-KLF17 fusions in myoepithelial tumors. Genes Chromosomes Cancer (2015) 54: 267-275.
20. Urbini M, Astolfi A, Indio V, Tarantino G, Serravalle S, Saponara M, Nannini M, Gronchi A, Fiore M, Maestro R and Brenca M: Identification of SRF-E2F1 fusion transcript in EWSR-negative myoepithelioma of the soft tissue. Oncotarget (2017) 8: 60036-60045.
21. Yokose C, Asai J, Kan S, Nomiyama T, Takenaka H, Konishi E, Goto K, Ansai SI and Katoh N: Myoepithelial carcinoma on the right shoulder: Case report with published work review. J Dermatol (2016) 43: 1083-1087.