

Cutaneous syncytial myoepithelioma: A case report with emphasis on the differential diagnosis of problematic dermal tumors

JUN-HSIUNG LEE¹, HSUAN-YING HUANG², JUI LAN², CHENG-CHENG HWANG³ and CHIH-YI LIU^{1,4}

¹Department of Pathology, Sijhih Cathay General Hospital, Sijhih, New Taipei City; ²Department of Pathology, Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung;

³Department of Pathology, Chang Gung Memorial Hospital, Keelung;

⁴College of Medicine, Fu Jen Catholic University, New Taipei City, Taiwan, R.O.C.

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Abstract. Cutaneous myoepithelioma is a peculiar and recently recognized neoplasm exhibiting purely myoepithelial differentiation. These lesions affect different areas of the body, and are characterized by heterogenous morphological and immunophenotypical features. The majority of cutaneous myoepitheliomas behave in a benign fashion, however, the risk for local recurrence is higher with incomplete resection. A relatively newly described variant of myoepithelioma exhibits syncytial cytological features. The current study reports a case of cutaneous syncytial myoepithelioma presenting as a painless and papular skin lesion. The presence of the Ewing sarcoma RNA-binding protein 1 gene rearrangement in the present case supported the diagnosis of a myoepithelial tumor. The patient subsequently underwent local excision of the tumor and was followed up twice in the year after surgery. At the time of writing, the patient was alive and no recurrences had been identified. Furthermore, the current study discusses how this myoepithelial neoplasm may be distinguished from other problematic spindle or epithelioid cell tumors, particularly superficial dermal lesions.

Introduction

Myoepithelial tumors comprise a peculiar group of lesions displaying heterogeneous morphological features, including dual epithelial and myoid differentiation. As a relatively newly recognized entity, cutaneous myoepithelioma is continually being assigned novel gradings and classifications. To date, <40 cases of cutaneous syncytial myoepithelioma have been

reported (1,2). Recently, a distinctive variant, designated as cutaneous syncytial myoepithelioma, has been identified as part of this group (1). This particular entity has been reported to occur predominantly on the extremities and trunk. Clinically, these lesions present as a solitary papule or polypoid nodule. Histologically, cutaneous syncytial myoepithelioma is characterized by the well-circumscribed, solid, sheet-like growth of ovoid to spindled or histiocytoid cells, with pale eosinophilic syncytial cytoplasm (1). Due to the rarity of cutaneous syncytial myoepithelioma, the incidence of this tumor remains unclear. The current study describes a case of cutaneous syncytial myoepithelioma arising in the thigh. Given the unusual histological features, myoepithelioma must also be considered in the differential diagnosis of a superficial dermal tumor. Written informed consent was obtained from the patient.

Case report

In January 2014, a 50-year-old female patient presented to Sijhih Cathay General Hospital (New Taipei City, Taiwan) with a small, painless and papular lesion on the right thigh, which had grown slowly over the previous 6 months. Subsequently, a dermatologist performed a local excision of the tumor. Histopathological examination revealed a well-circumscribed nodule of 4 mm in maximum diameter in the superficial dermis. The tumor was composed of ovoid to histiocytoid cells, of uniform size, growing in solid sheets or a vaguely fascicular pattern, and abutting the overlying epidermis (Fig. 1 and 2). The tumor cells exhibited an eosinophilic syncytial cytoplasm (Fig. 3). Sparse mitotic activity was observed, with 4 or fewer mitotic figures per 10 high-power microscopic fields (HPF). Chondromyxoid stroma, ductal components or melanin pigment were not identified.

Immunohistochemically, the tumor cells were positive for S-100 protein (Fig. 4A), focally positive for smooth muscle actin (SMA; Fig. 4B) and epithelial membrane antigen (EMA). Notable immunoreactivity was not observed for cluster of differentiation (CD)68 and CD34. Subsequent molecular genetic tests were performed, and a fluorescence *in situ* hybridization assay of the tumor cells revealed Ewing

Correspondence to: Dr Chih-Yi Liu, Department of Pathology, Sijhih Cathay General Hospital, No. 2, Lane 59, Jiancheng Road, Sijhih, New Taipei City 22174, Taiwan, R.O.C.
E-mail: cyl1124@gmail.com

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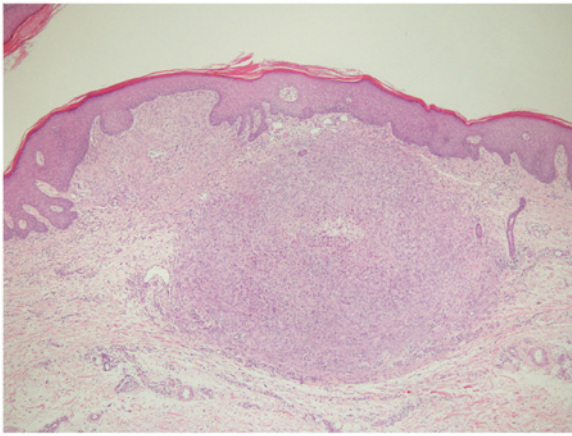


Figure 1. Histopathological staining revealing a well-circumscribed, dermal-based tumor abutted to the overlying epidermis (hematoxylin and eosin staining; magnification, x40).

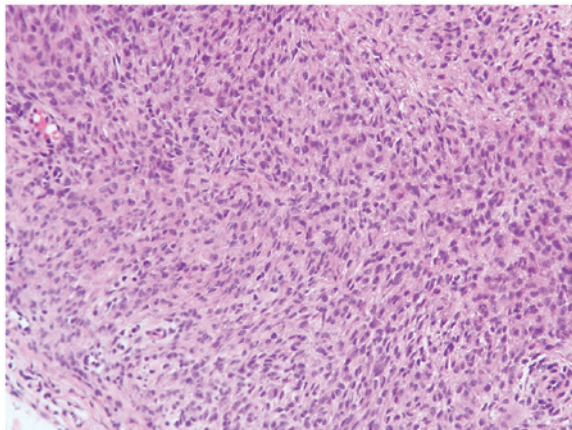


Figure 2. Ovoid to histiocytoid cells, relatively uniform in size, growing in solid sheets or a vaguely fascicular pattern (hematoxylin and eosin staining; magnification, x200).

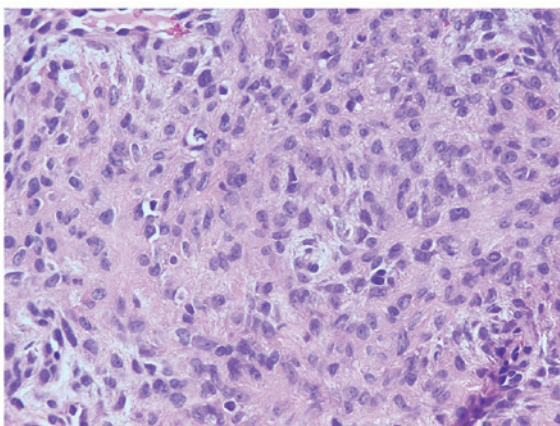


Figure 3. Tumor cells displaying vesicular nuclei, eosinophilic syncytial cytoplasm and sparse mitotic activity (hematoxylin and eosin staining; magnification, x400).

sarcoma RNA-binding protein 1 (EWSR1) rearrangement. The results of immunohistochemical analysis and cytogenetic aberration confirmed a diagnosis of cutaneous syncytial myoepithelioma. Subsequently, the tumor was excised with

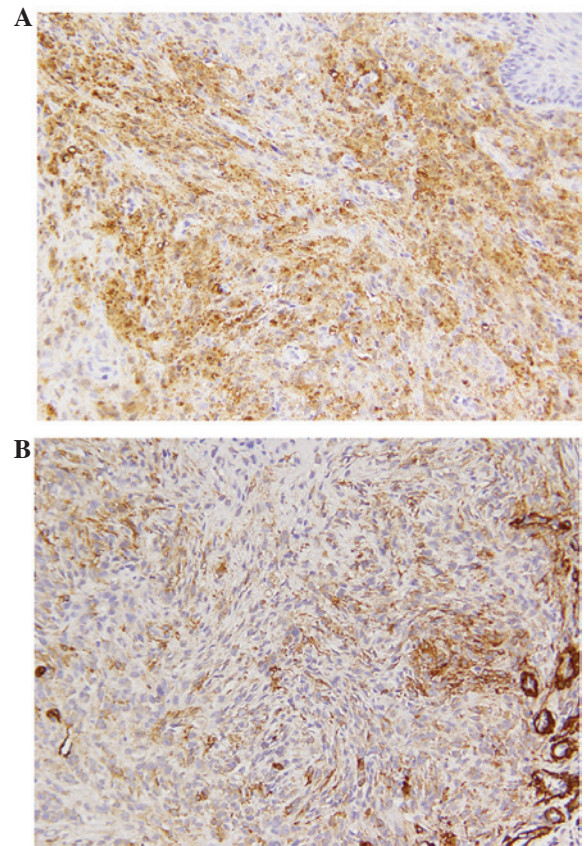


Figure 4. Immunohistochemical staining for (A) S-100 protein, diffusely positive in tumor cells, and (B) smooth muscle actin, focally positive in tumor cells (magnification, x200).

free margins. The patient received no further treatment and follow-up examination was performed twice in the year after surgery. At the time of writing, the patient was alive with no evidence of local recurrence or distant metastasis.

Discussion

Neoplasms of myoepithelial cells are uncommon skin tumors that consist of chondroid syringoma, cutaneous myoepithelioma and their malignant counterparts. Cutaneous myoepithelioma has only been identified recently, and in contrast to chondroid syringoma, exhibits purely myoepithelial differentiation without a ductal component (3). Clinically, cutaneous myoepithelioma typically presents as a painless cutaneous nodule, presenting with a wide anatomical distribution, with tumors commonly occurring in the extremities (2-4). Development in younger patients is relatively common. The majority of cutaneous myoepitheliomas behave in a benign manner; whilst there appears to be a significant risk for local recurrence, the tumors have a low metastatic potential (2). In a previous study conducted in Taiwan, 1 out of 3 patients developed local recurrence due to incomplete excision (5).

Hornick and Fletcher (2) presented a case series of 14 patients that initially described a morphologically and immunohistochemically distinct subset of cutaneous myoepithelioma exhibiting a solid syncytial growth pattern. The tumors were formed from ovoid, spindle or histiocytoid cells with eosinophilic cytoplasm, and exhibited

immunophenotypical EMA and S-100 positivity, with infrequent keratin staining (2). In 2013, the clinicopathological characteristics of cutaneous syncytial myoepithelioma were further analyzed in a large study of 38 cases (1). A wide age range (2 months-74 years) was noted, however, there appeared to be a predilection for the third to fifth decades. Males were more frequently affected than females (2.5:1). The tumor size ranged from 0.3-2.7 cm (median, 0.8 cm), and the most common sites of tumor growth were the extremities, although the trunk and the face were also affected. Grossly and histopathologically, the tumors were predominantly located in the dermis as polypoid or papular lesions (1-3). The tumor cells are reported to be uniform in size, with the presence of eosinophilic syncytial cytoplasm and vesicular nuclei. The majority of tumors display no mitotic activity, and the highest mitotic count observed is 4 per 10 HPF. Chondro-osseous differentiation is infrequent (1,2). Immunohistochemically, the tumor cells are positive for EMA and S-100 protein, whilst staining for glial fibrillary acidic protein (GFAP), SMA and p63 may be positive, and keratin staining is infrequent. The syncytial variant of cutaneous myoepithelioma appears to behave in a benign manner, and the standard treatment is complete excision with negative margins (1,2). The criteria for diagnosing a cutaneous myoepithelial carcinoma have not been well established, however, tumors exhibiting cytological atypia, a high mitotic rate and necrosis have been shown to behave in a more aggressive fashion (2,6-8).

Similar to previously reported series, the present case involved a well-circumscribed, dermal-based tumor with a typically syncytial growth pattern. The differential diagnosis of cutaneous myoepitheliomas is dependent on the predominant histological pattern (5). Epithelioid fibrous histiocytoma (EFH) may mimic cutaneous syncytial myoepithelioma to a certain extent: The two tumor types frequently present as a dermal nodule of epithelioid cells with an epidermal collarette, however, EFH usually lacks the typical syncytial architecture. Furthermore, EFH commonly contains scattered binucleated cells and more intervening collagenous or variably vascular stroma (3). Whilst the two tumors may each exhibit EMA positivity, EFH is negative for S-100 protein, GFAP and p63 (9).

Early-stage juvenile xanthogranuloma (JXG), which lacks the characteristic multinucleated giant cells and lipidization, may also mimic cutaneous syncytial myoepithelioma (3,10). JXG displays a marked predilection for young children. Immunohistochemically, JXG exhibits CD163 and CD68 positivity, however, it lacks reactivity for EMA and S-100 protein.

Cutaneous syncytial myoepithelioma contains a mixture of epithelioid, ovoid or histiocytoid cells, thus the primary diagnostic consideration includes melanocytic tumors, such as Spitz nevi (5). Spitz nevi show a nested pattern with downward maturation, but lack the sheet-like syncytial architecture of cutaneous myoepithelioma. Whilst the two tumors are each positive for S-100 protein, Spitz nevi are also positive for melanocytic markers, including human melanoma black 45, Melan A and microphthalmia-associated transcription factor. Additionally, Spitz nevi are negative for EMA and GFAP.

Epithelioid sarcoma may also enter the differential diagnosis of myoepithelioma. This lesion also commonly affects young adults on the extremities, however, more morphological uniformity is observed in epithelioid sarcoma compared with myoepithelioma. In addition, whilst the two tumor types are each positive for EMA, epithelioid sarcoma also exhibits positivity for cytokeratin and CD34, and is generally negative for other typical myoepithelial differentiation markers (S-100 protein, GFAP and myogenic markers) (3,5).

EWSR1 gene rearrangement occurs in a subset of cutaneous myoepithelial tumors (1,11), providing a genetic association between myoepithelial tumors of the skin and their counterparts in bone, soft tissue and visceral locations (11). The presence of EWSR1 gene rearrangement in the majority of cutaneous synovial myoepithelioma supports the concept of its close association to other subsets of myoepithelial tumors. However, Jo *et al* (1) hypothesized that this morphologically distinctive tumor type may be associated with a novel fusion gene.

In summary, the current study presents a unique case of cutaneous syncytial myoepithelioma. This distinct variant of myoepithelioma must be included in the differential diagnosis of superficial dermal tumors, and confirmatory immunohistochemical study may be valuable in determining a diagnosis in problematic cases. Wide excision with safe surgical margins and regular follow-up are crucial for the management of cutaneous myoepitheliomas.

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