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Soft tissue myoepithelial carcinoma

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Abstract

Background. Myoepitheliomas are tumors composed predominantly or exclusively of myoepithelial cells, usually arising in salivary glands. Cutaneous/soft tissue localization is very rare, especially for the malignant myoepitheliomas.

Case report. We presented a case of myoepithelial carcinoma involving subcutaneous adipose tissue of the left forearm in a woman aged 62 years. The tumor was composed of epithelioid and hyaline cell types, arranged in diffuse sheets, nests and loose clusters within hyalinized and myxoid matrix. The neoplasm displayed high-grade cytologic atypia with some cells having pleomorphic, hyperchromatic nuclei, and others showing vesicular nuclei, large nucleoli with scattered bizarre giant cells. High mean mitotic count of 7 mitoses/10 high power fields and extensive necrosis favoured the diagnosis of malignancy. Immunohistochemical staining was positive for cytokeratin (AE1/AE3), epithelial membrane antigen, S-100 protein, glial fibrillary acidic protein, and vimentin.

Conclusion. Considering the subcutaneous localization, myoepithelial immunophenotype and high-grade cytologic atypia the neoplasm was classified as a soft-tissue myoepithelial carcinoma.

Key words: myoepithelioma; skin; soft tissue neoplasms; immunohistochemistry.

Introduction

Benign and malignant neoplasms of myoepithelial cells comprise a rare, but well-characterized group of tumors, among which salivary gland myoepitheliomas are the best known [1–5]. Extrasalivary tumors have been also described in the breast, lung [6, 7], and, recently, in the skin and soft tissues [8–13]. Cutaneous and soft-tissue myoepitheliomas have been considered to be the monophasic, purely myoepitheliomatous, variant of cutaneous mixed tumor (chondroid syringoma) [10–13]. Soft tissue myoepitheliomas are rare tumors, histologically mostly benign [5, 8, 12, 14–16]; malignant myoepitheliomas arising in soft tissues have been reported only in a series of Hornick and Fletcher [12].

We report an additional case of soft tissue myoepithelial tumor which exhibited overt histological features of malignancy.

Case report

Clinical history

A 62-year-old woman presented with a painless mass in the left forearm. After a 15-year period of slow growth, the lump suddenly increased in size. Clinical examination re-
revealed a 5-cm-wide, firm, non-tender, circumscribed tumor deep in subcutaneous tissue, with no obvious involvement of the overlying skin. Excision of the lesion with the surrounding adipose tissue had been carried out and four months after the excisional biopsy reexcision of the scar site was performed. After a 12-month follow-up period there was no evidence of tumor recurrence or metastases.

Tissue samples were fixed in 10% formalin and routinely processed for microscopic analysis. The 5 μm thick sections were stained with hematoxylin and eosin, and immunostaining was performed using the streptavidin-biotin technique with DAKO’s LSAB+ kit (Dako, Glostrup, Denmark). The list of primary antibodies utilized is given in Table 1.

### Table 1

<table>
<thead>
<tr>
<th>Antibody specificity</th>
<th>Clone</th>
<th>Dilution</th>
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<tbody>
<tr>
<td>Keratin</td>
<td>AE1/AE3</td>
<td>1 : 100</td>
</tr>
<tr>
<td>EMA*</td>
<td>E29</td>
<td>Prediluted</td>
</tr>
<tr>
<td>S-100 protein</td>
<td>Polyclonal</td>
<td>1 : 1 500</td>
</tr>
<tr>
<td>GFAP†</td>
<td>Polyclonal</td>
<td>Prediluted</td>
</tr>
<tr>
<td>Calponin</td>
<td>CALP</td>
<td>1 : 200</td>
</tr>
<tr>
<td>αSMA‡</td>
<td>IA4</td>
<td>1 : 100</td>
</tr>
<tr>
<td>MSA§</td>
<td>HHF35</td>
<td>1 : 50</td>
</tr>
<tr>
<td>Desmin</td>
<td>D33</td>
<td>1 : 50</td>
</tr>
<tr>
<td>Vimentin</td>
<td>Vim 3B4</td>
<td>1 : 100</td>
</tr>
<tr>
<td>Melanosome</td>
<td>HMB-45</td>
<td>1 : 50</td>
</tr>
</tbody>
</table>

*EMA – epithelial membrane antigen; †GFAP – glial fibrillary acidic protein; ‡αSMA – alpha-smooth muscle actin; §MSA – muscle-specific actin. All primary antibodies supplied by DAKO (Glostrup, Denmark)

#### Pathological findings

The first specimen received consisted of three irregular parts of a tumor mass, without the overlying skin, measuring 4 cm, 2 cm, and 1.8 cm in diameter. The largest specimen had the central necrotic cavity. Histological examination showed a well delineated, partially encapsulated tumor in the subcutaneous adipose tissue (Figure 1a).

**Fig. 1a** – A well circumscribed myoepithelial carcinoma in subcutaneous adipose tissue (HE, × 40)

Tumor cells were arranged in diffuse sheets and nests within the hyaline matrix or in small loosely arranged clusters in a myxoid background. These clusters contained small cystic spaces filled with myxoid material, giving the impression of pseudo acinar/glandular structures (Figure 1b).

**Fig. 1b** – The tumor consists of solid nests of tumor cells and loose clusters of epithelioid and hyaline cells with cystic spaces (HE, × 200)

True glands and ducts were not present. Large areas of coagulative necrosis were centrally placed. The tumor consisted of two cell types: epithelioid and hyaline/plasmacytoid (Figure 1b). Epithelioid cells were round or polygonal with variable amount of eosinophilic cytoplasm, ill defined cell borders and centrally placed nuclei. Hyaline cells contained copious, intensively eosinophilic cytoplasm and peripherally placed nuclei. High-grade cytologic atypia and nuclear pleomorphism, with enlarged irregular ovoid, hyperchromatic nuclei, were found predominantly in the epithelioid cell-type (Figure 2a).

**Fig. 2a** – Myoepithelial carcinoma displaying high-grade cytologic atypia with nuclear pleomorphism (HE, × 400)

Scattered bizarre mono- and multinucleated-giant cells were also present. In less differentiated portions, the cells displayed vesicular nuclei with prominent large nucleoli and the mitotic count up to 7 mitoses/10 high power fields (HPF) (Figure 2b). Tumor infiltration into surrounding adipose tissue was also noted.

Immunohistochemistry showed strong positive staining with cytokeratin (AE1/AE3), epithelial membrane antigen (Figure 3a), glial fibrillary acidic protein (GFAP) (Figure 3b), S-100 protein, and vimentin. Immunostaining for calponin, α-smooth muscle actin, muscle-specific actin, desmin, and HMB-45 was negative.

The second excisional biopsy of the scar site showed two small foci of residual tumor in the subcutaneous fat at the deep margin of the specimen.

Discussion

In the skin, myoepithelial cells are seen mainly around apocrine and eccrine sweat glands. Morphologically, the neoplastic myoepithelial cells may show spindled, epithelioid, hyaline (plasmacytoid) and clear cell features. Such variations result in the extremely heterogeneous appearances of myoepitheliomatous neoplasms, with a morphologic continuum ranging from ductal neoplasms (cutaneous mixed tumors, or chondroid syringomas) to pure myoepitheliomas with no ductal differentiation. The current view is that both tumors represent ends of a single spectrum of neoplasms with myoepithelial differentiation. According to the similar clinical behavior of chondroid syringoma and myoepithelioma, the distinction in classification is only useful to recognize their diverse morphology and to avoid confusion with unrelated neoplasms.

The occurrence of myoepitheliomas in soft tissues has been recently recognized. Soft tissue localization has been defined as subcutaneous, intramuscular, fascial and subfascial, where myoepitheliomas are possibly derived from deeply located, heterotopic adnexal structures. In 1997, Kilpatrick et al. first described 13 cases of soft tissue myoepitheliomas, which were included later by Hornick and Fletcher into the largest series of myoepithelial tumors of soft tissue. They classified 35 tumors as myoepithelial carcinomas upon histological criteria. Since then, according to the MEDLINE database, no additional case of soft tissue myoepithelial carcinoma has been reported.

In the case described, a diagnosis of myoepithelial carcinoma was based on morphological and immunohistochemical features. Malignant chondroid syringoma was excluded due to the lack of ductal differentiation. According to Savera et al. our case could be classified as a mixed cell type, consisting of hyaline (plasmacytoid) and epithelioid cells. Myoepithelial cells possess the capacity for epithelial and myoid differentiation and therefore, variable immunoreactivity for cytokeratins, EMA, S-100 protein, GFAP, muscle actins, and calponin. This case exhibited the immunophenotype required for a myoepithelial tumor, being positive for epithelial markers (cytokeratin and EMA), S-100 protein and GFAP. The tumor was immunonegative for myogenic markers. The latter finding does not exclude the diagnosis of a myoepithelial tumor, as it has been well established that neoplastic myoepithelial cells often lose expression of myogenic markers, and such immunoreactivity is not required to confirm myoepithelial differentiation.

The prognosis of soft tissue myoepitheliomas is uncertain, although most appear to behave in a benign fashion. Histologic criteria for malignancy in cutaneous/soft tissue myoepitheliomas have been established analogously to salivary gland myoepithelial carcinoma and cutaneous malignant mixed tumor (malignant chondroid syringoma). The present case displayed frank histological features of...
malignancy: severe cytologic atypia (nuclear pleomorphism, enlarged vesicular and hyperchromatic nuclei, large nucleoli, high mitotic activity, coagulative necrosis and satellite tumor nodules. No specific mitotic rate cutoff exists for making the distinction between benign and malignant myoepitheliomas, but >7 mitoses per 10 HPF was diagnostic of malignancy in one series, a finding identical to the mean mitotic count in our case. In a soft tissue myoepithelioma series of Hornick and Fletcher there was a statistically significant difference in recurrence rate and the frequency of metastasis between the tumors classified histologically as benign and malignant, and the only histological feature significantly associated with the recurrence or metastasis was severe cytological atypia. Clearly, myoepithelial tumors of soft tissue with high-grade cytologic atypia are malignant. Accordingly, on the basis of high-grade cytologic atypia, we classified the present case of soft tissue myoepithelial tumor as a myoepithelial carcinoma, which warranted a close follow-up for early detection of a possible local recurrence or metastasis.

Conclusion

Considering the subcutaneous localization, myoepithelial immunophenotype and high-grade cytologic atypia the neo-plasm was classified as a soft-tissue myoepithelial carcinoma.

LITERATURA


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