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Case study

Mucoepidermoid carcinoma with extensive spindled morphology and melanocytic marker expression ☆

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Summary Mucoepidermoid carcinoma (MEC) is the most common malignant neoplasm of the salivary gland. Albeit common, histologic variants have rarely been noted in MEC. Here, we report a 49-year-old man with a sublingual gland tumor. Histologically, the tumor was composed of spindle cells arranged in interlacing fascicules or globular nests. A few bland small glands containing mucous cells were also scattered. The spindle tumor cells completely lacked immunoreactivity for cytokeratin, and exhibited immunoreactivity for vimentin, S-100, HMB-45, Melan A, and SOX10. The tumor was initially suspected to be clear cell sarcoma, malignant melanoma, or perivascular epithelioid cell tumor with a few entrapped nonneoplastic duct epitheliums. However, reverse-transcription polymerase chain reaction revealed the *CRTC3-MAML2* fusion gene product diagnostic of MEC. In fact, a very minor component of the epithelial cells was reminiscent of conventional MEC, whereas major spindled tumor cells possessed markedly altered differentiation. This is the first case report of MEC with extensive spindled morphology and melanocytic marker expression.

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1. Introduction

Mucoepidermoid carcinoma (MEC) is the most common malignant epithelial neoplasm of the salivary gland in both adults and children [1]. Histologically, MEC is composed of epidermoid, mucus-producing, and intermediate-type epithelial cells, with varying proportions of these different cell populations. Although some histologic variants of MEC have been described, such as columnar, clear cell, oncocytic, and sclerosing, these forms are thought to be within the range of conventional MEC [1]. Although it is a common neoplasm, histologic variants other than the above usual types have rarely been noted in MEC. Here, we report a quite unusual case of sublingual gland MEC showing previously unreported histologic and immunohistochemical features, which resulted in considerable diagnostic confusion. Recognition of histopathologic variations in MEC may play an important role in the precise diagnosis and appropriate treatment of the tumor in the future. The pathological findings of this novel form of MEC are described herein.

2. Case report

2.1. Clinical presentation

A 49-year-old man visited our hospital with the chief concern of a painless oral tumor. His medical history was unremarkable, and he had no history of neoplasms including malignant melanoma. He had noticed a contractive sensation on his tongue with tongue protrusion for over a year preceding his visit. Palpation revealed an elastic hard movable mass in the right oral floor covered by normal mucosa. No palpable lymph nodes were noted. Head and neck computed tomographic scans revealed a circumscribed solid mass 2.9 cm in size located closely adjacent to the right sublingual gland. Fluorodeoxyglucose positron-emission tomography demonstrated fluorodeoxyglucose uptake solely in the right oral floor. The mass was clinically diagnosed as a right sublingual gland tumor classified as cT2N0M0: cStage II, and was surgically removed. Lymph node dissection was not performed. The patient had an uneventful postoperative course and had no tumor recurrence for 9 months after the tumor resection.

2.2. Pathological findings and molecular analysis results

The tumor was 3.0 ×2.0 ×1.8 cm in size, elastic hard, and well circumscribed with a thin fibrous capsule (Fig. 1A and B). Upon sectioning, the cut surface of the tumor was somewhat lobulated and white (Fig. 1C). No cyst formation, mucin retention, or pigmentation was seen. The entire surgical specimen was embedded for histologic examination. Microscopically, the tumor was located adjacent to the normal sublingual gland lobules but was roughly separated by an intercalated thin fibrous capsule (Fig. 1D). The margin of the resection was entirely free of tumor tissue.

The tumor was largely composed of plump or elongated spindle cells, with the spindle cell component forming more than 99% of the entire tumor. These spindle cells were arranged in interlacing fascicules (Fig. 1E) or globular nests surrounded by collagen fibers (Fig. 1F). These globular nests somewhat resembled the zellballen structures of paraganglioma. Each spindle cell had an oval to fusiform vesicular nucleus with a conspicuous nucleolus (Fig. 1G). The cytoplasm was abundant and amphophilic, and had fine granularity. Some spindle tumor cells fused and formed multinucleated giant cells (Fig. 1H). Those of osteoclast type were also intermixed. In addition, a few tiny epithelial cell nests were observed in the spindle cell tumor. These epithelial cells had bland, small- to medium-sized round nuclei. The epithelial cells occasionally formed small glandular structures, and some of them had intracytoplasmic mucin (Fig. 1I). A few mitotic figures were observed in spindle cells (0.3/10 high-power field), but none were observed in epithelial cells. Although the tumor grew expansively with a circumscribed contour, a careful observation revealed small nerve fiber bundles within the tumor, thus suggesting the expansile invasive nature of the tumor.

The items of histologic differential diagnosis were thought to encompass myoepithelial tumors (myoepithelial carcinoma or, less likely, myoepithelioma) as primary salivary gland tumors, and clear cell sarcoma of soft tissue, malignant melanoma, and perivascular epithelioid cell tumor (PEComa) as non–salivary gland type tumors. Although atypia of the minor epithelial component was light and was likely due to entrapped nonneoplastic duct epithelium with mucous metaplasia, a possibility of MEC was included. Thus, immunohistochemical examination was performed, including epithelial, myoepithelial, and melanocytic markers.

Immunohistochemical reactions were performed using a Dako Autostainer Link 48 (Dako, Glostrup, Denmark). The primary antibodies used and the immunohistochemistry results are shown in the Table. As a result, the epithelial cells forming small glands were cytokeratin immunopositive, whereas the spindle tumor cells completely lacked immunoreactivity for cytokeratin and exhibited diffuse strong immunoreactivity for vimentin (Fig. 2A-D). Immunoreactivity for p63 was observed in some nonmucous epithelial cell nuclei, but none of the spindle tumor cells showed immunoreactivity for p63. A large number of spindle tumor cells exhibited S-100 immunoreactivity (Fig. 2E). All other myoepithelial markers showed no immunoreactivity. HMB-45–positive spindle tumor cells were widely scattered within the samples (Fig. 2F). A few Melan A–positive plump tumor cells were also observed (Fig. 2G). Moreover, almost all spindle tumor cells exhibited strong nuclear expression of SOX10 (Fig. 2H).

After these immunohistochemical observations, a careful microscopic reexamination revealed a small amount of melanin granules in limited areas of the globular nests. A serial