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CASE REPORT

Myoepithelioma of the upper lip



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Abstract Myoepithelioma is a rare form of salivary gland tumor composed entirely of myoepithelial cells. This tumor was formerly considered to be a subtype of pleomorphic adenoma; however, in the 1991 World Health Organization classification, it is listed as an independent entity. The most favorable site of occurrence of myoepithelioma is the parotid gland. Here, we report an extremely rare case of myoepithelioma of the upper lip. A 56-year-old woman presented with a painless mass on her upper lip. Magnetic resonance imaging revealed a 23 mm × 18 mm well-defined ovoid tumor. A benign minor salivary gland tumor was clinically suspected, and the patient underwent complete resection of the tumor under general anesthesia. The tumor was histopathologically diagnosed as a benign myoepithelioma of the minor salivary gland. Immunohistochemically, the tumor cells were positive for S-100 protein, AE1/AE3, CAM5.2, CK7, vimentin, and calponin, confirming the morphologic diagnosis of myoepithelioma. The patient's postoperative clinical course was uneventful, and satisfactory results were obtained both functionally and esthetically. To the best of our knowledge, this is the sixth case of myoepithelioma of the upper lip reported in English-language research.

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Introduction

Myoepithelial cells are ectoderm-derived contractile cells that exhibit both epithelial and smooth muscle properties. There are myoepithelial cells in salivary glands and other exocrine organs situated between the basal lamina and the acinar and ductal cells.¹ Sheldon first used the term myoepithelioma to describe those rare benign tumors composed entirely of myoepithelioma cells that account for less than 1% of all salivary gland tumors.² The most common site for salivary gland myoepitheliomas is the parotid gland, but this tumor can also arise from the submandibular gland and intraoral minor salivary gland.^{3–5} Because myoepithelioma cells are difficult to identify on routine microscopic preparations, analysis of the expression of cytoplasmic filaments and ultrastructural features of these cells is important for identifying the criteria providing a diagnosis of myoepithelioma.^{6,7} Here, we describe an extremely rare case of myoepithelioma of the upper lip that was successfully treated by surgical excision. To the best of our knowledge, only five cases have been reported in the English-language literature to date.^{8–10}

Case report

On June 11, 2007, a 56-year-old Japanese woman was referred to our clinic with a painless mass on her upper lip that had gradually increased in size over a period of 3 years. Her medical history was noncontributory. On physical examination, a soybean-sized, hard, mobile, and nontender submucosal mass was observed on the left side of her upper lip (Fig. 1). There were no palpable cervical lymph nodes. Magnetic resonance imaging (MRI) revealed a 23 mm × 18 mm well-defined, ovoid tumor. The peripheral area of the tumor was uniformly thickly enhanced, while the central area showed a partially cystic structure. No absorption or destruction of the maxillary bone was observed (Fig. 2). Based on these findings, a benign minor salivary gland tumor was clinically suspected.

On July 5, 2007, the patient underwent tumor excision under general anesthesia. During the surgery, rapid pathologic examination using frozen sections suggested a diagnosis of myoepithelioma. Because an increased nuclear



Figure 1 A mass was observed on the left side of the patient's upper lip.

division was found in one region, the tumor was completely resected with a safety margin of 5 mm. The surgical defect was covered by an artificial dermis.

On gross inspection, the resected tumor had a smooth surface and was well-circumscribed and encapsulated (Fig. 3). The cut surface of the tumor appeared solid, homogeneous, and white in color. Microscopically, the tumor was composed of myoepithelial cells. The parenchyma also contained clear cells and epithelial cells with a myxoid matrix (Fig. 3). There was a very small number of nuclear divisions (Fig. 3). Immunohistochemically (Table 1), the tumor epithelioid cells were diffusely and strongly immunoreactive for S-100 protein and cytokeratins (AE1/AE3, CAM5.2, and CK7). Most of the cells were also reactive for both vimentin and calponin. However, they were negative for α -smooth muscle actin and p63 (Fig. 4). The proliferative index Ki-67 was about 3% (Fig. 5).

The patient's postoperative clinical course was uneventful. Neither clinical findings nor MRI scans have shown any tumor recurrence over the intervening period of about 4 years.

Discussion

The diagnostic term myoepithelioma was first used by Sheldon in 1943,² but the tumor was reclassified as an independent entity in 1991 in the World Health Organization international classification of salivary gland tumors.⁵ Myoepithelioma occurs in both men and women, most frequently between 30 and 40 years of age, but these tumors have been observed over a very wide age range from children to the elderly.¹¹ Like pleomorphic adenoma, myoepithelioma frequently arises in the parotid gland, which accounts for approximately 40% of cases, followed by the palatine glands (approximately 21%). However, myoepitheliomas of the lip are extremely rare.

Myoepithelioma presents as a solid tumor with a distinct peripheral border. The core is white to yellowish or white in color. The tumor becomes semi-translucent when myxoid extracellular matrix is abundantly present.

Histologically, myoepithelioma is normally covered by a fibrous membrane, but when it originates in a minor salivary gland, the membrane is sometimes incomplete. The parenchyma exhibits a diverse histologic profile depending on morphologic variations in the neoplastic myoepithelial cells and tissue architecture.^{12,13} According to Dardick et al,¹⁴ epithelioid or epithelial cells account for 45.0% of the main body of the tumor, followed, in order, by spindle cells (32.5%), plasmacytoid cells (7.5%), and clear cells (2.5%). They also report that the remaining 12.5% of tumors have a main body with a mixed cell type.

The morphologic architecture can exhibit several possible growth patterns including: (1) a solid pattern with tumor cells growing densely and accompanied by a fibrous stroma; (2) a myxoid pattern with tumor cells growing in an insular, trabecular, and sporadic manner in an abundant myxoid matrix; (3) a reticular pattern with a trabecular structure of tumor cells against a backdrop of myxoid or hyaline matrix; and (4) a mixture of these three growth pattern types. About 60% of myoepithelioma tumors have a solid growth pattern. Our case showed about 80% solid pattern and about 20% myxoid pattern.

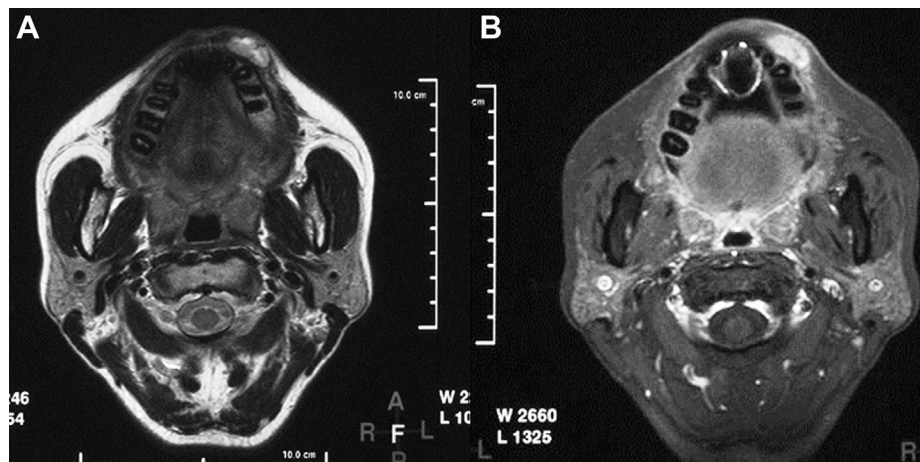


Figure 2 (A) T1-weighted magnetic resonance imaging (MRI), showing that the tumor was heterogeneously enhanced. (B) T2-weighted MRI scan, showing that the tumor had a heterogeneous, predominantly increased signal and internal septa of low signal isointensity.

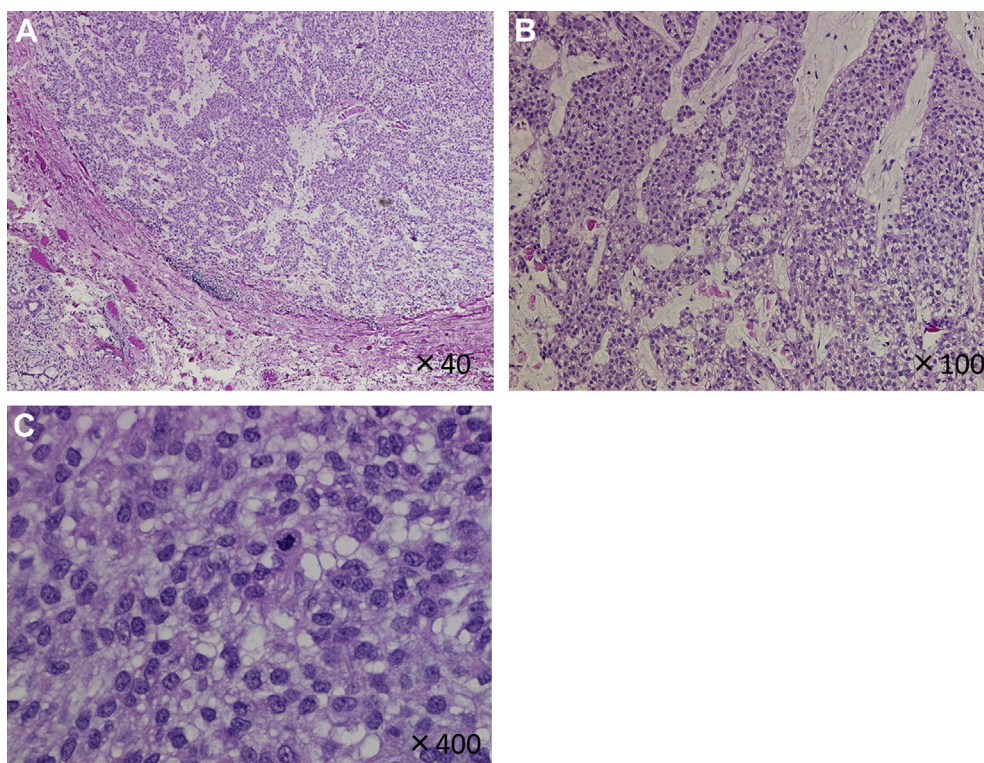


Figure 3 (A) Photograph showing the tumor covered by a fibrous capsule (40× magnification). (B) Clear cell and epithelial cells with a myxoid matrix (100× magnification). (C) A very small number of nuclear mitoses can be seen (400× magnification). All hematoxylin-eosin stain.

Table 1 A profile of immunohistochemical markers staining positive or negative in the tumor tissue.

Antibody (clone)	Immunoglobulin isotype	Antigen retrieval	Immunoreactivity	Source
S-100 protein	Rabbit, polyclonal	Autoclave, pH 6.0	Positive	Nichivei
Cytokeratin (AE1/AE3)	Mouse, IgGK	Trypsin	Positive	Nichivei
Cytokeratin (CAM 5.2)	Mouse, IgG2a	Trypsin	Positive	Becton-Dickinson
CK 7 (OV-TL12/30)	Mouse, IgG1	Autoclave, pH 6.0	Positive	Zymed
Vimentin (sp 20)	Rabbit, IgG	Autoclave, pH 6.0	Positive	Nichivei
Calponin (CALP)	Mouse, IgG1K	Trypsin	Positive	DAKO
p63 (4a4)	Mouse, IgG2a,K	Autoclave, pH 6.0	Negative	DAKO
α -smooth muscle antigen (1A4)	Mouse, IgM,K	Autoclave, pH 6.0	Negative	DAKO

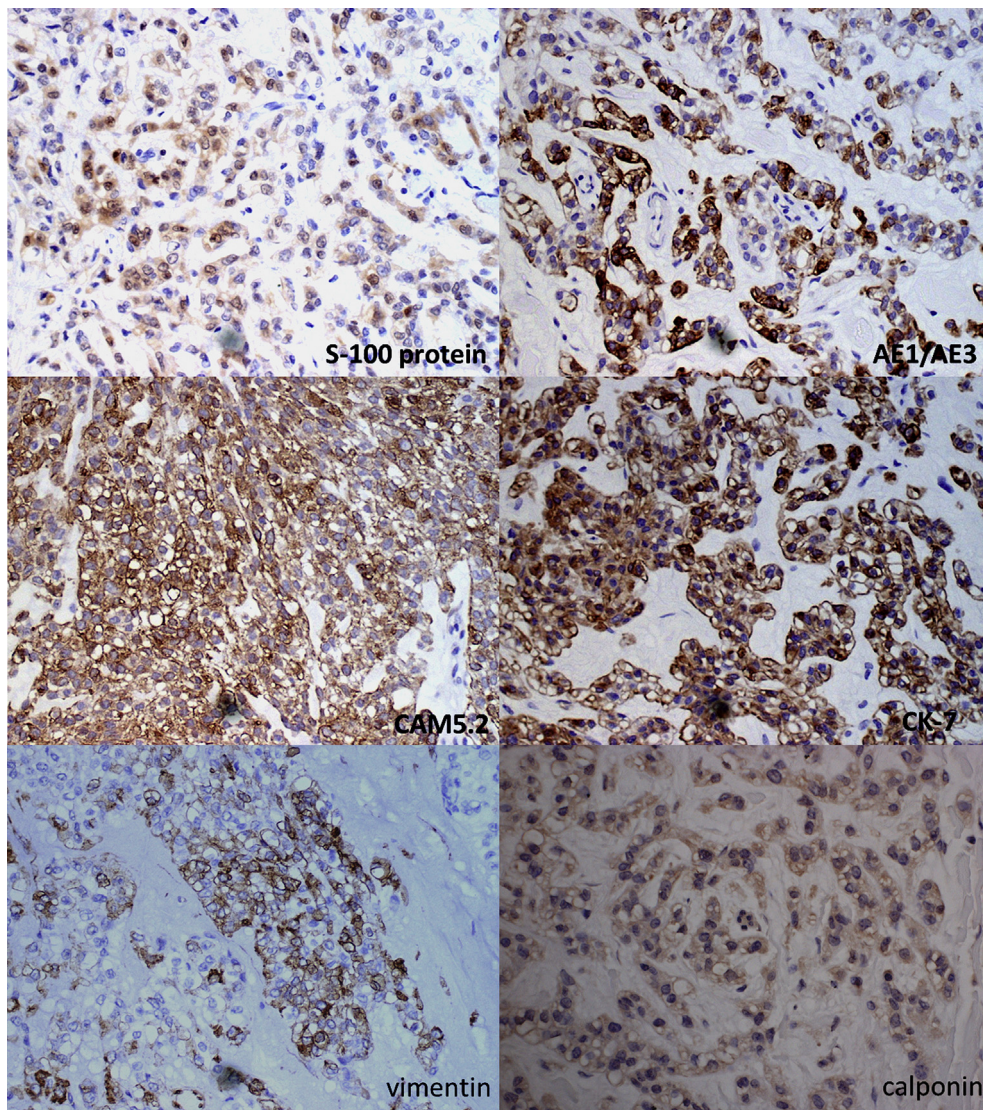


Figure 4 Immunohistochemical findings. The tumor cells are positive for S-100 protein, AE1/AE3, CAM5.2, CK7, vimentin, and calponin. Original magnifications 200 \times .

Generally, on immunostaining, the tumor cells positively express cytokeratin and α -smooth muscle actin and S-100 protein. However, the frequently intensity of positive

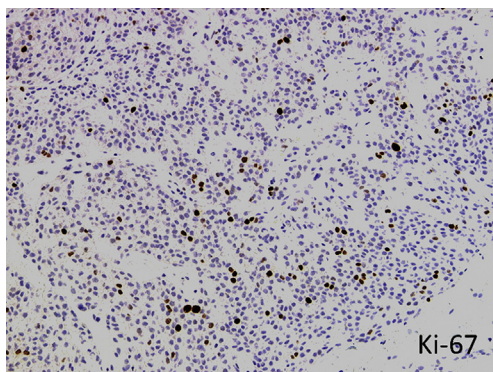


Figure 5 Immunohistochemical finding. The Ki-67 labeling index is about 3%. Original magnifications 100 \times .

stained cells varies according to cell type. Tumors characterized by spindle cells often show a weak expression of cytokeratin but a strong expression of α -smooth muscle actin. By contrast, plasmacytoid and epithelioid or epithelial cells clearly express cytokeratin, but very few express α -smooth muscle actin. Clear cells exhibit weak expression of both molecules. Thus, one cannot reject a diagnosis of myoepithelioma in patients without an extensive expression of α -smooth muscle actin. From an immunohistologic standpoint, the S-100 protein is a significant and important marker in the diagnosis of myoepithelioma because a high percentage of tumor cells stain positive for this protein.

In the present case, the tumor was positive for cytokeratins (AE1/AE3, CAM5.2, and CK7), vimentin, calponin, and S-100 protein, but negative for α -smooth muscle actin and p63. We made a diagnosis of myoepithelioma because histologic examination showed a scattered mixture of clear cells and epithelial cells with a myxoid matrix and a clear boundary between the parenchyma and stroma. This tumor

stained negative for α -smooth muscle actin because the main body of the tumor consisted of epithelioid or epithelial cells that contained few positive smooth muscle cells. We found no clear ductal structures or chondroid profile as is seen in pleomorphic adenoma. The cellular morphology was diverse, and there was no sign of separation of the neoplastic myoepithelial cells into the stroma. No cellular atypia was recognized. The Ki-67 labeling rate was approximately 3%, and growth was localized.

Because the mitotic activity was found in one region on rapid pathologic examination during surgery, the tumor was excised with a safety margin of approximately 5 mm. The patient's clinical course was uneventful. However, further periodic follow-up must be carried out because a case of recurrence has been reported 24 years after removal of such a tumor.¹⁵

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