

# Myoepithelioma Presenting as a Midline Cystic Tongue Lesion: Cytology, Histology, Ancillary Studies, and Differential Diagnosis

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*Salivary gland myoepithelioma (ME) is a neoplasm derived from myoepithelial cells that lacks the ductal and broad mesenchymal differentiation seen in the vast majority of mixed tumors. This report describes the cytologic findings of a cystic ME presenting in the midline of the dorsal tongue, a site where no salivary glands are generally present. The tumor was well circumscribed and composed of sheets of monotonous epithelioid cells without ductal cells. The cells were positive for S-100 protein and ultrastructurally had features of myoepithelial cells. The fine needle aspiration (FNA) biopsy findings, differential diagnosis, histology, immunohistochemistry, and electron microscopic features of this interesting and uncommon neoplasm are presented. To the best of our knowledge, there have been no cytologic reports of ME of the tongue. Diagn. Cytopathol. 2001;24:403–407.*

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**Key Words:** salivary gland neoplasm; tongue; myoepithelioma; fine-needle aspiration

Since its first description in 1943,<sup>1</sup> salivary gland myoepithelioma (ME) has been a subject of discussion. Its similarity to pleomorphic adenoma (PA) made its diagnosis as a different entity controversial.<sup>2</sup> Currently, ME is considered a unique entity with specific histomorphologic features and biological behavior.<sup>2–4</sup>

MEs are uncommon, representing approximately 1% of salivary gland tumors.<sup>5,6</sup> The vast majority are benign, with only rare malignant examples reported in the literature.<sup>6</sup> There is no sex predilection, and the peak age of occurrence is in the third decade of life (range, 9–85 yr).<sup>5</sup> The most common locations of this neoplasm are the parotid gland

and soft palate.<sup>5</sup> The present article describes the cytologic findings, differential diagnosis, histology, and ancillary studies of a cystic ME presenting in the midline of the dorsal tongue.

## Case Report

A 65-yr-old male presented to our institution with an 8-yr history of a 1.0-cm anterior dorsal midline nodule in the submucosa of the tongue. The lesion was soft, was slightly tender to palpation, and had become intermittently painful over the last year. The remainder of the physical examination and laboratory studies were normal. A fine-needle aspiration (FNA) biopsy was performed, which was initially interpreted as PA. Subsequently, a complete excision of the tumor was performed. The excised cystic mass measured 1.0 × 1.0 × 1.5 cm and contained a central liquefied hematoma, surrounded by a rim of tan, rubbery tissue. Based on the histologic examination, the diagnosis of ME was rendered. Confirmatory immunohistochemical stains and electron microscopic studies supported the diagnosis. Ten months after complete resection of the lesion, the patient is well, without disease recurrence.

## Materials and Methods

The FNA biopsy was performed by the cytopathologist, using a 25-gauge needle attached to a 10-cc syringe. Aspirated material was immediately smeared onto glass slides. Half of the slides were air-dried and stained by a rapid, modified Wright stain (Diff-Quik), while the others were immediately wet-fixed with 95% ethyl alcohol for Papanicolaou (PAP) staining. Tissue from the subsequent resection specimen was fixed in 10% buffered formaldehyde and embedded in paraffin. Sections were stained with hematoxylin-eosin (H&E). Immunoperoxidase stains were performed using an indirect biotin-avidin system (Ventana Medical Systems, Inc., Tucson, AZ). The immunoperoxi-

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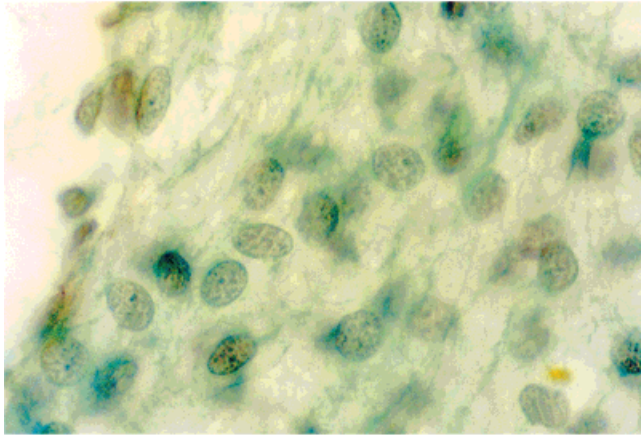


Fig. C-1

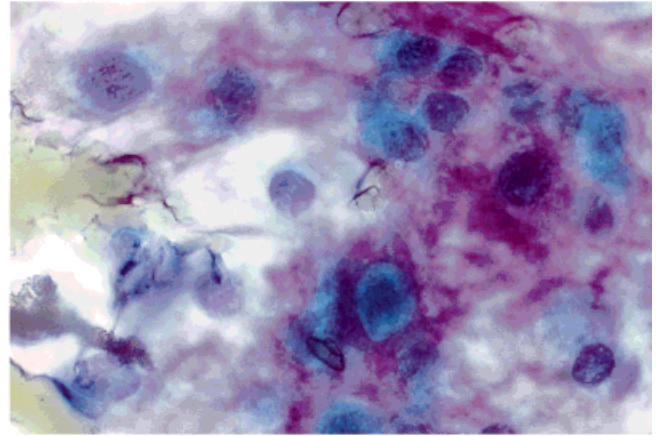


Fig. C-2

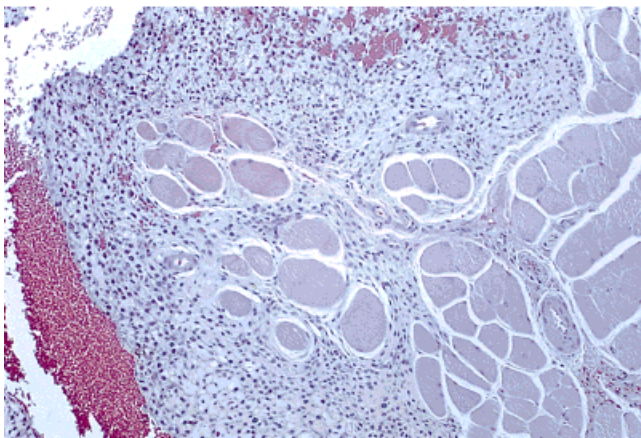


Fig. C-3

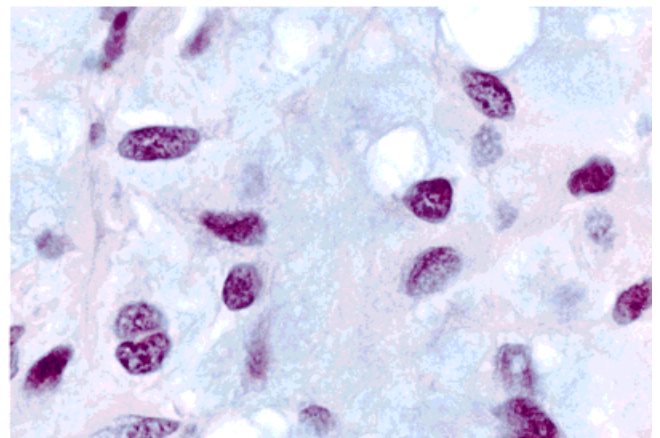


Fig. C-4

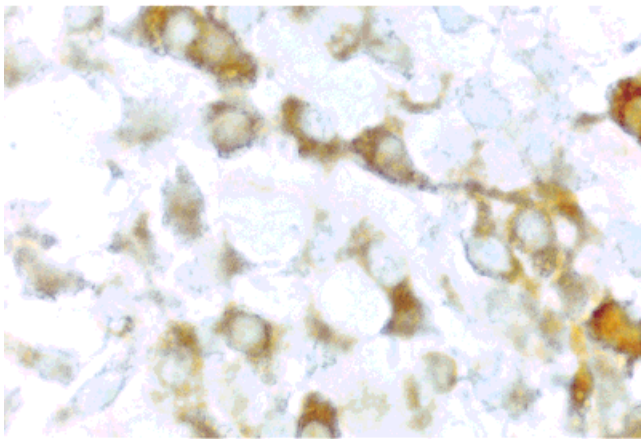


Fig. C-5

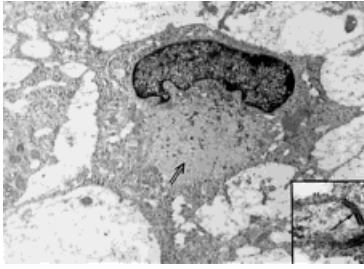
**Fig. C-1.** Aspirate smear. Tumor cells with rounded and well-spaced nuclei, displaying fine, granular, and evenly distributed chromatin. The extracellular fibrillary material is pale green on Papanicolaou stain (Papanicolaou stain,  $\times 1,000$ ).

**Fig. C-2.** Aspirate smear. Abundant metachromatic extracellular material surrounding plasmacytoid tumor cells (Diff-Quik stain,  $\times 1,000$ ).

**Fig. C-3.** Tissue section. Well-demarcated tumor composed of sheets of monotonous epithelioid cells, in direct contact with the lingual skeletal muscle (H&E,  $\times 40$ ).

**Fig. C-4.** Tissue section. Tumor cells with eosinophilic cytoplasm and oval to rounded nuclei, surrounded by abundant extracellular pale blue material (H&E,  $\times 1,000$ ).

**Fig. C-5.** Neoplastic cells of myoepithelioma, demonstrating strong cytoplasmic immunoreactivity for S-100 protein (immunoperoxidase,  $\times 1,000$ ).



**Fig. 1.** Ultrastructure of a neoplastic cell of myoepithelioma. The cytoplasm is packed with haphazardly arranged intermediate filaments (arrow). Elongated, eccentrically located nuclei show peripheral margination of the chromatin. Electron micrograph printed at  $\times 6,000$ . **Inset:** Desmosomes connecting tumor cells are presented (arrow). Electron micrograph printed at  $\times 19,600$ .

dase markers included cytokeratin (AE1/3) (1:200; Cell Marque, Austin, TX), glial fibrillary acidic protein (GFAP) (1:600; Dako, Carpinteria, CA), S-100 protein (1:600; Dako), and muscle-specific actin (MS-ACTN) (predilute; Biocare Medical, Walnut Creek, CA).

Electron microscopy (EM) studies were performed from paraffin-embedded tissue. Tumor submitted for EM was deparaffinized, postfixed in Caulfield  $O_5O_4$ , dehydrated in series of graded alcohol, and embedded in Epon-Spurr. Ultrathin sections (900 Å) were examined with a Hitachi H-600 electron microscope (Hitachi, San Jose, CA). Clinical information and follow-up data were obtained from hospital charts and from the referring physician.

## Results

### *Cytologic Findings*

Aspirate smears demonstrated a cellular specimen composed of sheets and small clusters of monotonous epithelioid cells, with moderate amounts of pale blue cytoplasm. Their rounded and well-spaced nuclei had a finely granular, evenly distributed chromatin and inconspicuous nucleoli (Fig. C-1). Single tumor cells with a plasmacytoid appearance were also present. Extracellular matrix composed of fibrillary material, which appeared purple with Diff-Quik (Fig. C-2) and pale green with Papanicolaou stains, was relatively abundant. This material surrounded many tumor cells, obscuring their cytoplasm and cell borders. Glandular structures, tubule formations, crystals, and chondroid matrix were not seen. Mitosis, necrosis, and cytologic atypia were absent.

### *Histopathology, Immunohistochemical Profile, and Ultrastructural Findings*

H&E-stained tissue sections showed a sharply demarcated tumor composed of sheets of epithelioid cells without duct formations (Fig. C-3). Cells had a relatively uniform appearance, moderate amounts of pale eosinophilic cytoplasm, oval to rounded nuclei, and small inconspicuous nucleoli. Abundant pale blue material around neoplastic cells was

present throughout the neoplasm (Fig. C-4). The tumor cells were in direct contact with large blood lakes scattered within the neoplasm and the skeletal muscle around the tumor. Normal salivary gland tissue was not present. Nuclear atypia, mitotic activity, and areas of necrosis were not identified.

Immunoperoxidase studies performed on tissue sections showed a strong and diffuse immunoreactivity of tumor cells for S-100 protein (Fig. C-5), and focal reactivity with muscle-specific actin and glial fibrillary acidic protein. The neoplastic cells did not react with cytokeratin (AE1/3).

Electron microscopic studies revealed neoplastic cells separated by widened intercellular spaces. Nuclei were eccentrically located, rounded, or elongated, and showed peripheral margination of the chromatin. The cytoplasm of many tumor cells was packed with haphazardly arranged intermediate filaments (Fig. 1). Desmosomes, and only a few profiles of rough endoplasmic reticulum, mitochondria, and lysosomes, were scattered within the cytoplasm of tumor cells.

## Discussion

Orthotopic (normally located) lingual salivary gland tissue is situated on the anterior ventral (Blandin glands), and posterior dorsolateral (von Ebner glands) portions of the tongue.<sup>5</sup> The lack of capsule and close contact with the lingual muscle are characteristic histologic features of these minor salivary glands.<sup>5</sup> A cystic salivary gland neoplasm of the anterior dorsal midline tongue is an unexpected and extremely rare finding. The main entities to be considered in the differential diagnosis of a lingual cystic lesion in an adult patient include: mucus retention cyst (MRC), lymphoepithelial cyst, lymphangioma, intraductal papilloma (IP), polymorphous low-grade adenocarcinoma (PLGA), acinic-cell carcinoma (ACC), mucoepidermoid carcinoma (MEC), squamous-cell carcinoma (SCC), and PA<sup>7</sup> (Table I).

Cytologic preparations from MRC usually yield a mucoid fluid, with histiocytes and epithelial cells reflecting their histologic counterparts.<sup>7,8</sup> Intraoral lymphoepithelial cysts can be uni- or multilocular. Their smears generally show a polymorphic population of lymphocytes, squamous cells, histiocytes, and a proteinaceous background.<sup>9-11</sup> The most common intraoral location of lymphangiomas is the tongue, and can be a cause of macroglossia.<sup>8</sup> Cytologic findings include clear, watery fluid containing red cells and lymphocytes.<sup>12</sup> Aspirate smears from IP show oncocytic and ductal-type cells arranged in papillary configurations, a proteinaceous background, and rare fibrovascular stromal fragments.<sup>13</sup> None of the above lesions yield cytologic preparations with the sort of pattern found in our case, characterized by epithelioid and plasmacytoid cells admixed with abundant extracellular myxoid fibrillary material.

Occasionally, other neoplasms may arise in lingual minor salivary glands and be cystic. PLGA has been described in

**Table I.** Cytologic Differential Diagnosis of Cystic Lesions of the Tongue<sup>a</sup>

	<i>Cell type(s) and background material</i>	<i>Comments and/or remarkable features</i>	<i>Reference numbers</i>
Mucous retention cyst (MRC)	Epithelial and inflammatory cell admixed with mucus.	MRC can mimic LGMEC.	7, 8
Lymphoepithelial cyst	Sq cells, LMN, and histiocytes in a proteinaceous background.	Generally non-HIV-associated. Unilocular or multilocular.	9–11
Lymphangioma	Clear fluid, containing LMN and RBC.	Can be a cause of macroglossia.	8, 12
Intraductal papilloma	Ductal and/or oncocytic cells. Proteinaceous background.	Papillary formations. Unilocular cystic masses.	5, 13
Polymorphous low-grade adenocarcinoma	Epithelial cells admixed with myxoid stroma.	Palisading of tumor cells around myxoid material is characteristic.	5, 13, 14
Acinic-cell carcinoma	Acinar cells with abundant granular cytoplasm, in clusters and isolated. Few or no ductal cells.	Cellular specimens. Vascular stromal fragments.	8, 15, 16
LGMEC	Intermediate, epidermoid, and mucous cells. Mucoid background.	Can mimic MRC and chronic sialoadenitis. Usually good prognosis.	7, 8, 10, 11, 15
HGMEC	Marked cytologic atypia. Mucin can be difficult to identify.	Mucin stains can demonstrate intracellular mucin. Lingual HGMEC has aggressive behavior.	8, 10, 11
SCC	Markedly atypical Sq cells. Evidence of keratinization is common. Necrotic background.	SCC of posterior one third or base of tongue have worse prognosis. Always r/o metastatic SCC.	8, 10, 11, 15
Granular-cell tumor (GCT)	Polygonal cells with abundant granular cytoplasm.	The tongue is a common location. Also, S-100-protein-positive.	8, 17
PA and ME	Epithelial/plasmacytoid/spindle cells. Extracellular metachromatic fibrillar material.	Duct formations and chondroid stroma indicate PA.	2–5, 10, 11, 18

<sup>a</sup>GCT, granular-cell tumor; HGMEC, high-grade mucoepidermoid carcinoma; LGMEC, low-grade mucoepidermoid carcinoma; LMN, lymphomononuclear cells; ME, myoepithelioma; MRC, mucous retention cyst; PA, pleomorphic adenoma; PLGA, polymorphous low-grade adenocarcinoma; RBC, red blood cells; SCC, squamous-cell carcinoma; Sq, squamous.

the tongue and can have cystic areas.<sup>5,13,14</sup> Aspirated material can yield cohesive clusters of epithelial cells admixed with myxoid stroma, mimicking preparations from ME. However, tumor cells palisading around the myxoid stroma, a characteristic feature of PLGA,<sup>14</sup> is generally not seen in ME preparations. Aspirate smears from cystic ACC generally show polygonal cells with abundant granular cytoplasm and marked cell dissociation.<sup>15,16</sup> Preparations from low-grade MEC are usually composed of mainly cohesive bland epithelial cells, sometimes with mucinous vacuoles.<sup>7,10,11</sup> The abundant myxoid fibrillary stroma commonly observed in ME is not seen in ACC<sup>16</sup> or low-grade MEC.<sup>7,10,11</sup> FNA material from high-grade MEC and SCC generally are differentiated from ME, based on their marked cytologic atypia, and/or evidence of keratinization.<sup>7,10,11</sup>

Granular-cell tumor (GCT), a rare benign neoplasm, deserves special comment due to its common lingual location.<sup>8,17</sup> Its aspirate smears are composed of large polygonal cells, with abundant granular cytoplasm.<sup>17</sup> Both GCT and ME cells express S-100 protein; however, the prominent cytoplasmic granules seen in cells from GCT preparations are not appreciated in cytologic material from ME.

Preparations from PA are generally characterized by a combination of bland epithelial cells and fragments of metachromatic chondromyxoid stroma with spindle cells.<sup>5,10,11</sup> Their great histologic diversity is sometimes reflected in

unusual findings in aspirated material.<sup>18</sup> Duct formations and chondroid stromal fragments, commonly seen in preparations from PA,<sup>5,10,11</sup> are not features of ME. Their absence in aspirates from PA specimens makes ME and PA cytologically indistinguishable.

Salivary gland MEs present as slow-growing circumscribed tumors composed of epithelioid, spindle, and plasmacytoid cells, generally accompanied by abundant myxoid or hyalinized stroma.<sup>2,5</sup> A requirement for their diagnosis is the absence of ducts within the neoplasm.<sup>5</sup> Immunoreactivity for S-100 protein, variable reactions with other antibodies, desmosomes, and tumor-cell cytoplasm packed with intermediate filaments by electron microscopic studies also characterize these lesions.<sup>2,5</sup> Some reports have indicated that MEs have the same prognosis as PA.<sup>2,5</sup> However, other investigators believe that MEs have a worse biological behavior than PA, based on a higher rate of recurrence and malignant transformation.<sup>3,19</sup> Complete surgical excision is the treatment of choice.<sup>2,3,5,19</sup>

We have reported on the cytologic findings from a rare tumor occurring in an uncommon location, the midline of the dorsal aspect of the tongue, where no salivary glands are generally present. Abnormal budding of proliferative salivary gland primordia during embryogenesis may account for the ectopic location of this neoplasm. Moreover, ME cannot be distinguished cytologically from some variants of

PA. Therefore, in the appropriate clinical setting, we propose considering ME in addition to PA if the cytologic features show a monotonous population of epithelioid and plasmacytoid cells, extracellular myxoid fibrillary material, and neither duct formations nor chondroid stromal fragments. This case also indicates that ME can be included in the differential diagnosis of lingual cystic lesions.

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