

Myoepithelial Cell Carcinoma of the Oral Tongue: Case Report and Review of the Literature

Robert G Nicholas¹ , Josh A Hanson² and Duncan A Meiklejohn¹

¹Division of Otolaryngology-Head and Neck Surgery, Department of Surgery, University of New Mexico Hospital, UNM School of Medicine, Albuquerque, NM, USA. ²Department of Pathology, University of New Mexico Hospital, UNM School of Medicine, Albuquerque, NM, USA.

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ABSTRACT

BACKGROUND: Myoepithelial cell carcinoma is a rare malignant neoplasm of salivary gland origin that typically presents in the parotid gland and minor salivary glands. It has been described previously in head and neck sites such as buccal mucosa, alveolar ridge, and base of tongue.

METHODS: A 55-year-old man presented with 30 years of right-sided tongue pain and 10 years of gradually worsening ulceration. Physical examination demonstrated a 2.5 cm ulcerative lesion of the anterior right oral tongue. An initial biopsy was consistent with moderately to poorly differentiated squamous cell carcinoma. Imaging included a positron emission tomography (PET)/computed tomography (CT) scan that demonstrated the right tongue lesion as well as hypermetabolic right level II adenopathy. The patient underwent surgical excision of the right tongue, upper aerodigestive tract endoscopy, and a bilateral supraomohyoid neck dissection. The tongue defect was closed primarily.

RESULTS: Final pathology of the surgical specimen demonstrated myoepithelial cell carcinoma. All of the margins were free of tumor and no cervical lymph nodes showed metastasis. Immunohistochemistry demonstrated myoepithelial differentiation. The tumor did not show EWSR1 gene rearrangement on genetic testing, suggesting salivary gland origin. Multidisciplinary tumor board evaluation recommended no adjuvant therapy. The patient recovered well after surgery and nearly a year later is without evidence of recurrent or residual disease.

CONCLUSIONS: We present the first reported case of myoepithelial cell carcinoma with primary origin in the oral tongue and review the available literature on this unusual tumor. We discuss the clinical, pathological, and immunohistochemical features and treatment of myoepithelial cell carcinoma.

KEYWORDS: Myoepithelial cell carcinoma, oral tongue, head and neck neoplasms, myoepithelioma, salivary gland neoplasm

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CORRESPONDING AUTHOR: Duncan A Meiklejohn, Division of Otolaryngology-Head and Neck Surgery, Department of Surgery, University of New Mexico Hospital, UNM School of Medicine, MSC 10 5610, 1 University of New Mexico, Albuquerque, NM 87131, USA. Email: dmeiklejohn@salud.unm.edu

Introduction

Myoepithelial cells are physiologically important components of salivary glands and play a significant role in contractile function. Benign tumors arising from these cells are known as myoepitheliomas (ME) and typically present in the head, neck, and extremities. Myoepithelial cell carcinoma (MCC) is a malignancy of myoepithelial cell origin and typically arises from pleomorphic adenomas or de novo and less commonly from ME. New immunohistochemistry findings have made this diagnosis more common. Here, we report the first case of MCC of the oral tongue with a review of the current literature.

Case Report

A 55-year-old man presented to the otolaryngology clinic on referral from his primary care provider for a chief complaint of tongue pain. He reported 30 years of right-sided tongue pain without an inciting factor or event, which over the preceding 10 years had developed into an open wound. This was accompanied by generalized radiation of his pain into his head and neck. He had no other significant medical history and was an

active cigarette smoker with a 14 pack-year history. He reported heavy alcohol use as a young adult but had been alcohol free for several years.

Physical examination revealed a 2.5-cm ulcerative lesion of the anterior right oral tongue with central necrosis, with palpable deep extension of abnormal tissue to the midline (Figure 1). Full motor and sensory functions of the tongue were intact. No floor of mouth involvement was detected, and there was no palpable cervical lymphadenopathy. The remainder of the head and neck examination, including flexible fiberoptic nasopharyngolaryngoscopy, was unremarkable.

Punch biopsy tissue obtained at the first clinic visit was reported to be most consistent with moderately to poorly differentiated squamous cell carcinoma with moderate p16 immunostaining. A positron emission tomography (PET)/computed tomography (CT) scan was performed confirming the right tongue lesion (Figure 2), and mildly hypermetabolic right level II nodes were visualized.

The patient underwent direct laryngoscopy with biopsies, bronchoscopy, partial glossectomy, and bilateral supraomohyoid





Figure 1. Right anterior oral tongue lesion at initial presentation.

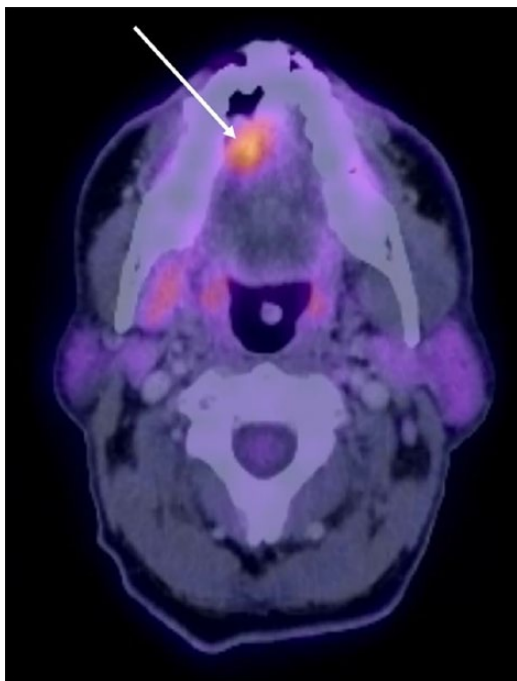


Figure 2. PET/CT imaging demonstrating a hypermetabolic lesion of the right anterior tongue (arrow). CT indicates computed tomography; PET, positron emission tomography.

neck dissection. Laryngoscopy, esophagoscopy, and bronchoscopy were normal. All intraoperative frozen section margins were free of disease. The glossectomy defect was closed primarily. His postoperative course was unremarkable, and he was discharged on postoperative day 5. At his first clinic follow-up on postoperative day 8, he was recovering well overall but had some minor dysarthria.

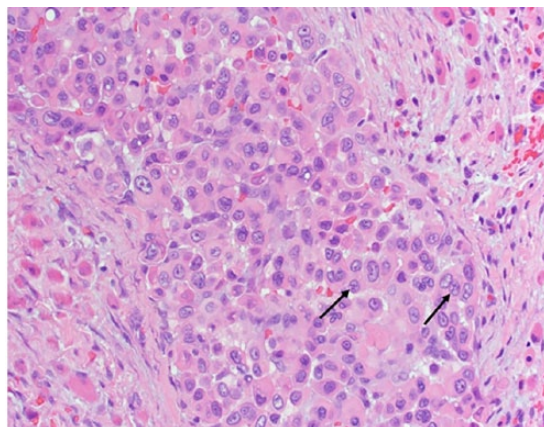


Figure 3. H&E stain of right anterior oral tongue mass demonstrating mitotically active infiltrating nests of epithelioid cells (arrows).

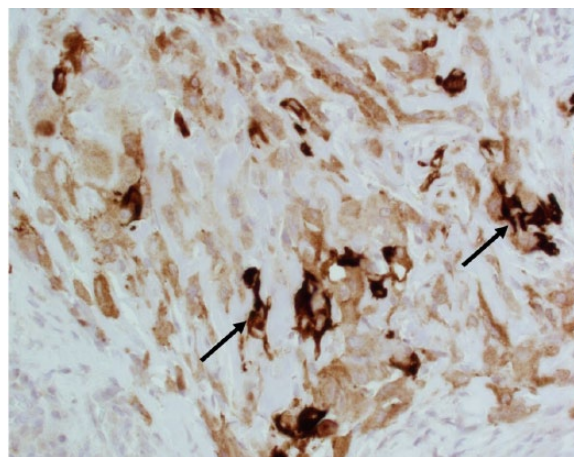


Figure 4. Immunohistochemistry demonstrating positivity for pancytokeratin (arrows).

Although the initial biopsy was most consistent with squamous cell carcinoma, the final specimen demonstrated findings inconsistent with this diagnosis, prompting further investigation with immunohistochemical staining. The final pathology analysis confirmed a 2.5-cm tumor with a thickness of 5 mm, consistent with MCC. The tumor itself comprised invasive mitotically active infiltrating nests of epithelioid cells, many of which had a rhabdoid appearance. These cells demonstrated a high degree of cellular atypia with eccentrically placed nuclei with prominent nucleoli and dense pink cytoplasm (Figure 3), which combined with the infiltrative growth pattern confirmed a malignant tumor. There was little evidence of chondroid stroma or ductal differentiation, which assisted in ruling out pleomorphic adenoma. Immunohistochemical stains demonstrated positivity for pancytokeratin (Figure 4), epithelial membrane antigen (EMA) (Figure 5), calponin (Figure 6), and glial fibrillary acidic protein (GFAP) (Figure 7), consistent with myoepithelial differentiation. To differentiate between an MCC of soft tissue versus salivary gland origin, a fluorescence in situ hybridization (FISH) study using an *EWSR1* break-apart probe was employed. This study showed no evidence of an

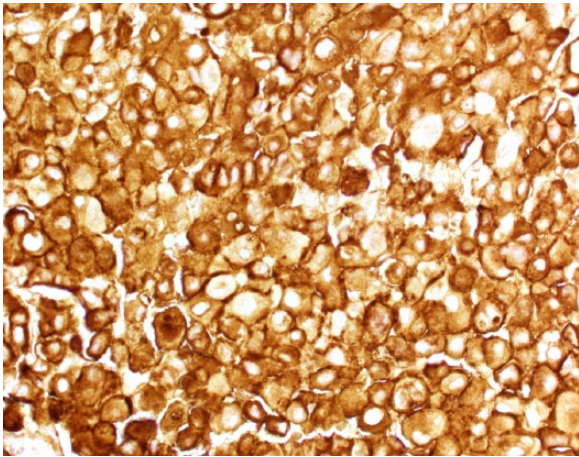


Figure 5. Immunohistochemistry demonstrating positivity for epithelial membrane antigen (EMA).

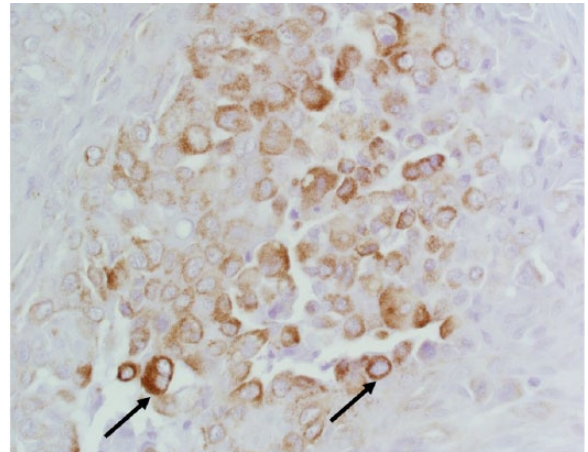


Figure 7. Immunohistochemistry demonstrating positivity for glial fibrillary acidic protein (arrows).

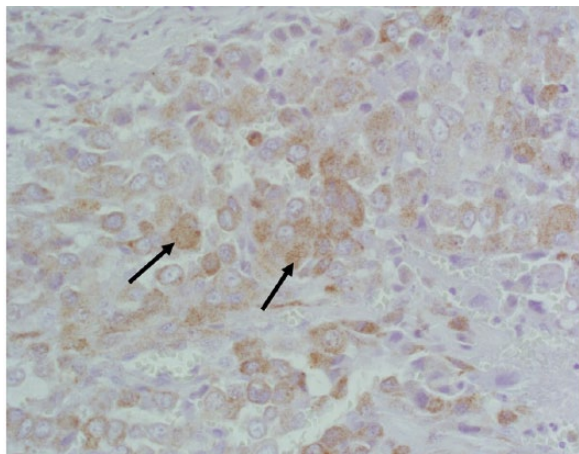


Figure 6. Immunohistochemistry demonstrating positivity for calponin (arrows).



Figure 8. Three-month postoperative photograph demonstrating well-healed surgical site and no evidence of residual disease at primary site.

EWSR1 gene rearrangement, indicating that the tumor was likely of salivary gland origin. No perineural or lymphovascular invasion was identified. All margins were negative, and the bilateral neck dissection specimens showed no metastatic tumor. Final pathologic staging was T2N0M0.

The case was presented at multidisciplinary head and neck tumor board. Due to the early stage of the tumor and lack of high-risk features, no adjuvant therapy was recommended. At 3 months postoperative visit, he reported that his speech and swallowing were normal. He had resumed his pre-operative level of physical activity. Physical examination and indirect flexible nasopharyngolaryngoscopy were normal, with a well-healed surgical defect (Figure 8). At his most recent evaluation, he had no evidence of disease 9 months after his surgery.

Discussion

History and clinical characteristics of MCC

Myoepithelial salivary gland tumors were first reported in 1943 by Sheldon.¹ Initial case series were documented in 1945 by Bauer and Fox.² The first report of an MCC was published

30 years later by Stromeyer et al³ in 1975. Larger case series, including one by Sciubba and Brannon⁴ documenting 23 cases of ME, were written throughout the 1980s, which led to MCC being included in the World Health Organization classification of salivary gland tumors in 1991.⁵ The largest case series in the English literature was published by Kane and colleagues and reported 51 cases of MCC in a tertiary cancer center. Previous literature had found that ~70% of these cancers arise in the major salivary glands; however, Kane and Bagwan⁶ found that ~71% of documented cancers in their series arose in minor salivary glands. In the oral cavity, the hard palate was the most frequent site of involvement. Case reports have documented oral cavity MCC occurring in buccal mucosa, hard palate, alveolar ridge, retromolar trigone, and lips.⁷ At the time of

publication, all current case reports of primary tongue MCC describe tumors that appear to have originated in the base of tongue.^{8,9}

Myoepithelial cells constitute an important component of glandular acini and ducts. They are normally located between the luminal epithelial cells and the basement membrane and have contractile function.¹⁰ They are found throughout the body, not only in salivary glands but also in lacrimal glands, sweat glands, mammary glands, Bartholin glands, and mucus-secreting glands of the aerodigestive tract.¹¹ These cells demonstrate features of both myoid and epithelioid cells, and in salivary glands function to facilitate release of saliva and regulate the exchange of electrolytes.¹¹ When myoepithelial cells contract, they rupture mucous cells in the acini.¹² They also contract along the intercalated ducts to increase pressure and have been documented to play a role in tumor suppression.¹⁰

MCC is the malignant complement of ME and is a rare tumor presenting over a wide range of ages. It comprises 0.4% to 0.6% of salivary gland tumors and 1.2% to 1.5% of salivary gland carcinomas.¹³ This tumor most commonly presents in the parotid gland (60%), but also can develop in the submandibular glands (10%), and the minor salivary glands (25%), especially of the palate.¹⁴ Case reports also have documented MCC appearing in the nasopharynx, larynx, and lungs.⁷ Patients typically present with an asymptomatic mass, but symptoms may include tenderness, dysphagia, and hoarseness. In palatal tumors, invasion of the bone can be seen in some instances. It can develop as a *de novo* neoplasm or as malignant transformation of either ME or pleomorphic adenoma.¹⁵ When arising from a pleomorphic adenoma, MCCs are thought to have worse 5-year disease free survival.¹⁶ Given the extended time course of our patient's symptoms, we suspect his tumor may have originated from ME or pleomorphic adenoma, with slow growth over many years.

The current accepted treatment for ME is complete surgical excision with clear margins, as they are less prone to recurrence than pleomorphic adenomas and malignant transformation is rare.¹⁷ Similarly, the definitive treatment for MCC is complete surgical resection.¹⁸ MCC involving a major salivary gland is an indication for complete glandular excision. In minor salivary glands, excision with tumor-free margins is the standard of care. Neck dissection is indicated if neck disease is suspected.¹⁷ The indications and potential benefit of chemotherapy and radiotherapy have not been well defined. Overall, prior reports indicate that one-third of patients will die from metastasis, one-third will have multiple local recurrences, and one-third will be disease free after resection.¹⁹

Histopathology

Due to their shape and interdigitating processes, normal myoepithelial cells are described as star-shaped or basket cells. These cells produce proteins such as proteinase inhibitors,

anti-angiogenesis factors, metalloproteinase-1, protease nexin II, and alpha1-antitrypsin.¹² ME is subdivided into 4 types based on cellular appearance: spindle, plasmacytoid, epithelioid, or clear cell. Acellular mucoid or hyalinized stroma may be present surrounding the myoepithelial cells.²⁰ The cells lack any ductal differentiation or chondroid stroma, which is the primary feature in distinguishing it from the very similar pleomorphic adenoma.²¹

In MCC, the most common histological pattern is epithelioid, which demonstrates large polygonal cells with distinct central nuclei. The spindle-shaped variant has uniform central nuclei and granular cytoplasm.⁶ The plasmacytoid variant, which is also known as hyaline or rhabdoid, presents as polygonal cells with pyknotic eccentric nuclei and dense eosinophilic cytoplasm.¹⁹ The clear cell variant demonstrates cytoplasm comprised almost entirely of glycogen.²² Malignant MCCs primarily differ from MEs in that they are infiltrative, show increased mitotic activity, marked nuclear pleomorphism, and may show lymphovascular or perineural invasion.¹⁹

Immunohistochemistry demonstrates cells that are variably positive for cytokeratins, EMA, p63, calponin, S100, smooth muscle actin, GFAP, and muscle-specific actin.²³ Electron microscopy reveals both epithelial and myoid features. Epithelial characteristics include desmosomes and tight junctions, whereas myoid characteristics include intracytoplasmic myofilaments.¹⁹ EWSR1 gene rearrangements have been detected in soft-tissue MEs, but not in their salivary counterparts.²⁴

Conclusions

To our knowledge, this is the first report of MCC primarily arising in the oral tongue. MCC is a malignancy derived from salivary acini and ductal cells and is rarely found in the oral cavity. We have discussed the clinical presentation, workup, management, unique pathology, immunohistochemistry, and treatment for this tumor. Further reports of treatment and outcomes will help to clarify the standard of care for these rare tumors.

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Author Contributions

All authors participated in original data acquisition and analysis, and contributed to manuscript preparation and review. RGN and DAM conducted literature review.

Statement on Consent

This case report was formally reviewed by the UNM HSC Human Research Review Committee on August 15, 2017 who deemed it Not-Human Research as it contained no personally identifiable information and as such did not require written informed consent.

ORCID iD

Robert G Nicholas  <https://orcid.org/0000-0001-9870-8979>

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