



Sialadenoma Papilliferum: "A Rare Benign Salivary Gland Tumor"

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ABSTRACT

Sialadenoma papilliferum is an uncommon, benign salivary gland neoplasm characterized by a distinctive papillary growth pattern. It most frequently arises in the minor salivary glands of the oral cavity, particularly the hard palate, though other intraoral sites have been reported. Clinically, the lesion presents as a slow-growing, painless, exophytic or nodular mass, often mimicking more common papillary or verrucous lesions. Histopathologically, sialadenoma papilliferum demonstrates a biphasic pattern consisting of a papillary squamous epithelial surface component and a sub epithelial proliferation of ductal and glandular salivary elements. Complete surgical excision is the treatment of choice and is associated with an excellent prognosis, with recurrence being rare. Awareness of this entity is important to ensure accurate diagnosis and appropriate management, as its clinical and microscopic features may overlap with other benign or malignant lesions of the oral cavity.

Keywords: Sialadenoma papilliferum, Benign salivary gland tumor, Minor salivary glands, Oral cavity, Papillary lesion, Histopathology, Surgical excision, Differential diagnosis

INTRODUCTION

Mucoepidermoid Carcinoma (MEC) is the most common malignant tumor of the salivary glands, accounting for approximately 30% of cases [1]. It arises from the pluripotent reserve cells of the excretory ducts and is characterized by a histological mixture of squamous, mucous, and intermediate cells [2]. MEC can affect both major and minor salivary glands, with frequent involvement of the parotid gland and the posterior hard palate [3]. Clinically, it presents with a broad spectrum of features, ranging from painless, slow-growing masses in low-grade cases to aggressive, infiltrative lesions with nerve involvement in high-grade cases [4].

Grading of MEC into low, intermediate, and high grades plays a critical role in determining prognosis and management [5]. Low-grade tumors are typically cystic and well-differentiated, with excellent outcomes following surgical excision, while high-grade tumors exhibit solid, infiltrative growth, perineural invasion, and a higher potential for recurrence and metastasis [6]. The histological diversity of MEC often overlaps with other salivary gland tumors and non-neoplastic lesions, such as Adenoid Cystic Carcinoma (ACC), Secretory Carcinoma (SC), Acinic Cell Carcinoma (AcICC), Necrotizing Sialometaplasia (NS), and even Oral Squamous Cell Carcinoma (OSCC) [7]. This overlap presents significant diagnostic challenges, particularly in small biopsy samples.

Accurate diagnosis of MEC relies on a comprehensive evaluation of clinical, histopathological, and immunohistochemical features [8]. Commonly used immunohistochemical markers include p63, CK7, and mucicarmine, while molecular markers such as MAML2 rearrangements provide additional diagnostic and prognostic value [9]. This report presents a case of low-grade MEC in a 20-year-old female, emphasizing the diagnostic process, differential considerations, and the importance of histopathological and immunohistochemical analyses in establishing the final diagnosis.

CASE PRESENTATION

A 20-year-old female presented with a painless lesion, that persisted for 1 to 2 years, and hasn't changed in size for the last 6 months. Clinical examination showed a 1.5×0.5 cm elevated lesion of the posterior hard palate with a central ulcerated area. Incisional biopsy demonstrated evidence of increasing tumor islands some of which were connected to overlying surface epithelium. That consisted of predominantly epidermoid cells, with scattered mucinous components. Small cystic islands lined by mucous, intermediate, and epidermoid cells, that contributed to less than 20% of tumors were noted. Mucicarmine and PAS-diastrase positive highlighted scattered mucous cells. Tumor cells were p63 positive, and negative for Calponin and GATA-3. Findings were consistent with MEC, low grade. Upon excision, surgical impression included erosion of underlying bone. Excisional biopsy showed tumor infiltration of the terminal duct and overlying surface epithelium and a more prominent cystic component. S100 highlighted perineural invasion. The final diagnosis of MEC, low grade, according to AFIP classification criteria was rendered.

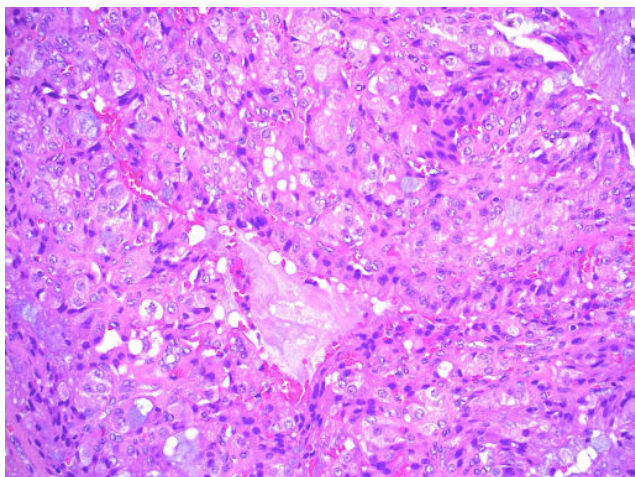


Figure 1 Low-grade Mucoepidermoid Carcinoma (MEC) of the posterior hard palate

RESULTS AND DISCUSSION

Mucoepidermoid Carcinoma (MEC) is the most common malignant salivary gland tumor, yet its clinical and histological overlap with various benign and malignant lesions makes accurate diagnosis challenging. In this case, a 20-year-old female presented with a slow-growing lesion on the posterior hard palate, which, due to its clinical and histological features, necessitated careful differential diagnosis. The diagnosis of low-grade MEC was confirmed based on histopathological findings, supported by immunohistochemical staining and careful exclusion of other salivary gland neoplasms and non-neoplastic entities.

Differential diagnoses considered

Oral Squamous Cell Carcinoma (OSCC): OSCC is a key differential diagnosis due to its ability to mimic MEC when the lesion is dominated by epidermoid cells. OSCC arises from the surface epithelium and lacks the mucin-producing and intermediate cells characteristic of MEC. Special stains such as mucicarmine and PAS-diastrase are crucial in highlighting mucin-producing cells in MEC, as was observed in this case. The absence of keratin pearls, a hallmark of OSCC, further supported the diagnosis of MEC.

Adenoid Cystic Carcinoma (ACC): ACC often overlaps with MEC, especially when perineural invasion is observed. However, ACC typically exhibits a cribriform or solid growth pattern and lacks the mucinous components seen in MEC. ACC is also distinguished by its strong positivity for SOX10 and C-kit, which were absent in this case. Furthermore, ACC tends to exhibit more aggressive behavior and poorer prognosis than low-grade MEC.

Secretory Carcinoma (SC): SC is another low-grade salivary gland malignancy that may exhibit cystic and papillary structures similar to MEC. SC is characterized by the ETV6-NTRK3 gene fusion and immunohistochemical positivity for S100 and mammaglobin, which were absent in this case. The lack of these molecular and IHC markers helped differentiate SC from MEC.

Acinic Cell Carcinoma (AciCC): AciCC is a salivary gland tumor with serous acinar differentiation and occasional cystic patterns, making it another differential for MEC. However, AciCC typically demonstrates cytoplasmic PAS-positive, diastase-resistant granules and DOG1 positivity, features not observed in this patient. AciCC also lacks the mucinous and intermediate cells characteristic of MEC.

Necrotizing Sialometaplasia (NS): NS, while benign, can mimic MEC due to its ulcerative presentation and extensive squamous metaplasia. However, NS lacks the invasive features seen in MEC and is negative for p63 and mucicarmine, distinguishing it from MEC. Additionally, the absence of tumor infiltration into surrounding structures further rules out NS.

Histopathological and immunohistochemical findings

The histopathological evaluation in this case revealed tumor islands composed of epidermoid, mucinous, and intermediate cells, with small cystic spaces lined by mucous cells. These features are hallmark characteristics of MEC. Immunohistochemical staining further confirmed the diagnosis, with tumor cells being positive for p63 and negative for Calponin and GATA-3, ruling out other salivary gland neoplasms such as ACC and SC. Perineural invasion, highlighted by S100 staining, reinforced the malignant nature of the lesion. These findings, combined with the low mitotic activity and cystic growth pattern, confirmed the diagnosis of low-grade MEC according to the AFIP classification criteria.

Management and prognosis

Management of MEC is grade-dependent, with low-grade tumors like the one in this case having an excellent prognosis following complete surgical excision. In this patient, excisional biopsy revealed tumor infiltration of the terminal duct and overlying epithelium, necessitating thorough removal to prevent recurrence. The patient experienced an uneventful recovery, and no recurrence was noted during follow-up. High-grade MECs, in contrast, require multimodal therapy, including radiation and chemotherapy, due to their aggressive behavior and higher recurrence rates.

Prognosis for MEC varies with grade and stage. Low-grade MEC is associated with a 5-year survival rate exceeding 90%, whereas high-grade MEC may exhibit poorer outcomes. Molecular markers such as MAML2 rearrangements have been identified as favorable prognostic indicators, further emphasizing the importance of comprehensive diagnostic evaluation.

CONCLUSION

This case highlights the diagnostic complexity of MEC and the importance of distinguishing it from mimics such as OSCC, ACC, SC, AciCC, and NS. Comprehensive histopathological evaluation, supported by immunohistochemically and molecular studies, is essential for accurate diagnosis. Surgical excision remains the cornerstone of treatment for low-grade MEC, offering excellent outcomes. Ongoing advancements in diagnostic techniques promise improved precision and better outcomes for patients with salivary gland malignancies.

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