Mucoepidermoid Carcinoma Misdiagnosed as Palatal Odontogenic Infection: An Overview on the Differential Diagnosis of Palatal Lesions

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ABSTRACT

Mucoepidermoid carcinoma (MEC) accounts for approximately 30% of malignant salivary gland tumors and approximately 30% occur in minor salivary glands. The palate is the most frequent localization for those arising in minor glands. A 33-year-old male patient with MEC of the hard palate was treated as an acute odontogenic infection, which was not cured after tooth endodontic treatments, repeated incisions and antibiotics. On the hard palate ovoid, a hard painless mass, which had not extended over the middle palatal line, was observed. Partial maxillectomy was performed. A review of the literature was performed in order to provide a coherent overview on the differential diagnosis of palatal lesions. To the best of authors’ knowledge, this is the first report in English literature describing palatal MEC misdiagnosed and treated as odontogenic infection. Considering the extensive list of MEC’s differential diagnoses on the hard palate, acute odontogenic infection can now be added to that list.

Key words: oral cancer, salivary gland tumor, mucoepidermoid carcinoma, odontogenic infection, hard palate tumors

Introduction

In 1945, Stewart et al.1 published the first large series of mucoepidermoid carcinomas (MECs) and suggested the term MEC. They divided these tumors into benign and malignant varieties, however, due to the appearance of metastases, Foote and Franzell considered all MECs malignant2, and it is the most common malignant tumor of minor salivary glands (MSGT) in the oral cavity3–7.

The incidence of salivary gland tumors increased with age8. However, it is important to realize that the relative incidence of malignant tumors increases, as the size of the glands in which they develop decrease9. MEC accounts for up to 47% of all malignant salivary gland tumors10,11 and 21.1% of benign and malignant salivary gland tumors with 30% appearing in the minor salivary glands12. In studies after 1990, MEC represented 45%, a twofold increase in comparison with studies before 1990 (an average of 27% of all malignant salivary tumors)13. These findings are inconsistent and not sufficient to suggest a geographic related appearance14. Reviewing the English-language literature, Buchner et al.15 concluded that it was very difficult to make a valid comparison between intra-oral minor salivary gland tumors because many reports were based on outdated classification, the small number of some cases, limited list of tumors, and new entities are not included. Pires et al.16 concluded that reports from different populations using the same diagnostic criteria are essential to compare and estimate true racial and geographic variations in MSGT. The palate is the most frequent localization for those arising in the minor glands8. Some authors4–7,17–21 found a higher incidence of palatal involvement by salivary gland tumors, including MEC. Wang et al.22 found that palate was...
the most commonly affected site among intraoral minor salivary gland tumors in a Chinese population.

In adults, MEC is most common in the fourth to sixth decades with no established gender predominance. Microscopically, MEC is composed of mucous cells, epidermoid cells and intermediate cells.

Low-grade carcinomas appear as painless, slowly enlarging ovoid masses, which are greater than 2–3 cm in diameter and rarely larger than 4 cm, may produce metastases and have a 5-year determinate cure rate of approximately 90% with a recurrence rate of 6%. Oncocytic MEC (OMEC) has been rarely reported with previous cases suggesting they are largely cystic low-grade neoplasms with a favorable prognosis. The differential diagnosis of OMEC includes numerous oncocytic/oncocytoid neoplasms. Although recent evidence suggests that, unlike in OMEC, p63 is a reliable marker in the diagnosis of conventional MEC, OMEC behaved as a low-grade tumor, and is diffusely positive for p63, which may aid in its differential diagnosis. High-grade MECs present as painful, rapidly enlarging masses that tend to be firmer and less moveable, with a 5-year determinate cure rate of 27%. These are associated with a high recurrence rate (78%) and metastases. Okami et al. found a metastatic MEC in the lung 43 years after the initial treatment for the primary tumor.

Intraosseous salivary gland tumors are most commonly MECs, usually asymptomatic, three-fold more common in the mandible then in the maxilla in the region of the third molar and occur twice as often in women. It is believed that these tumors arise from the odontogenic cysts or salivary glands entrapped during embryological development.

Differential diagnosis on the hard palate includes all benign and malignant tumors of the hard palate, mostly pleomorphic adenoma, polymorphous low-grade adenocarcinoma, adenoid cystic carcinoma and squamous cell carcinoma. Chronic sialadenitis or mucocele, which is histologically similar, could be misdiagnosed as a low-grade MEC or necrotizing sialometaplasia. Odontogenic cysts, lymphoma, plasmacytoma, Langerhans cell histiocytosis or metastatic carcinoma could also be included as well as a rare papillary oncocytic cystadenoma.

To the best of authors’ knowledge, this is the first report in English literature describing palatal MEC misdiagnosed and treated as odontogenic infection.

Case Report

A 33-year-old male patient visited the dentist complaining of upper first molar toothache. On the left side of the hard palate ovoid, a hard painless mass, which had not extended over the middle palatal line, was observed. The dentist, who began the initial endodontic treatment and filled root canals, using iodoform paste (Vitapex) for one week, did not indicate an incision. After 7 days, the dentist performed the palatal incision, no puss was detected and no improvement occurred.

One month later, the patient was referred to the outpatient oral surgeon who performed a re-incision. Seven days later, some improvement had occurred. The oral surgeon advised the endodontic treatment to be continued. Three months later, the patient visited his dentist with the same palatal ovoid mass; however, the patient experienced no toothache. The patient was subsequently admitted to our Department.

An ortopantomograph revealed semi-ovoid transparency of the left maxillary alveolar process above the teeth roots that lifted the hard palate and floor of the maxillary sinus (Figure 1). An axial CT scan showed a pathological process of the hard palate (diameter, 25 mm) with cystic bone transformation and a small bone infraction (Figure 2). Coronal CT showed the submucous mass near the alveolar ridge and thickening of the Schneider’s membrane of the left maxillary sinus without bone destruction (Figure 3). A presumptive diagnosis was pleomorphic adenoma. A cytological diagnosis considered a low-grade MEC or cytologically similar mucocele. The histopathological diagnosis of a biopsy specimen was MEC, grade 1.

Fig. 1. An ortopantomograph reveals semi-ovoid transparency of the left maxillary process above the teeth roots, which lifts the hard palate and floor of the maxillary sinus.

Fig. 2. Axial CT scan shows the pathological process of a hard palate (25 mm in diameter) with a cystic bone transformation and a small bone infraction.
A partial maxillectomy was subsequently performed. Figure 4 shows the tumor specimen. The palatal plate was placed immediately following surgery.

Histopathological examination of the excised portion of the hard palate revealed an invagination in the central portion of the bone, occupied by a soft, partially cystic node measuring 2 cm in diameter. The tumor was composed of multiple cystic spaces lined by well-differentiated mucinous cells, intermixed with intercalated and occasionally squamous epithelial cells. One of the larger cystic spaces contained a papillary structure lined by multilayered squamous epithelium with scattered mucinous cells. Pools of mucinous material with occasional multinucleated foreign-body giant cells were present within the fibrous stroma. The tumor tissue was invaginated into the underlying bone with pushing borders showing minute evidence of infiltration. Adjacent salivary glands were normal as well as surgical margins (Figure 5). Figure 6 shows the postsurgical defect, 5 years following treatment, with no signs of recurrence.

Discussion and Differential Diagnosis of Palatal Lesions

In our case, the initial diagnosis and long term unsuccessful treatment clearly indicates that the initial diagnosis and the subsequent treatment administered should have been revised. Minor salivary gland tumors are, in fact, uncommon tumors of the oral cavity. They are found mostly on the hard palate, as in our case, but also on the tongue, buccal mucosa, soft palate and other sites.

The extensive list of differential diagnoses possibilities can result in confusion, as follows.

Pleomorphic adenoma

Pleomorphic adenoma is the most common benign tumor and MEC is the most common malignant tumor of minor salivary glands in the oral cavity. The pleomorphic adenoma, or benign mixed tumor, is the most common salivary gland tumor. The mean age of occurrence is 45 years, with a male-to-female ratio of 3:2. In minor
glands, the most common site is the palate where it usually presents as a slow-growing, painless mass. There is a small risk of recurrence, as well as a small (5%) risk of malignant transformation to a carcinoma-ex pleomorphic adenoma.12,15,17 Matsumabayashi and Yoshihara15 suggested that carcinoma ex pleomorphic adenoma acquired the particular biological behavior in contrast to the other salivary neoplasms in the long-standing process while pleomorphic adenoma undergoes malignant transformation.

Myoepithelioma

Myoepithelioma, in most studies probably included within the group of pleomorphic adenoma, is defined as a tumor composed almost exclusively of myoepithelial cells.15 Buchner et al.15 reported five intraoral lesions, two of them located in the palate. The criteria to distinguish myoepithelioma from pleomorphic adenoma with a predominance of myoepithelial cells are largely subjective.33 Myoepithelial carcinoma (MC), also known as malignant myoepithelioma, is a rare malignant salivary gland tumor with a predilection for the parotid gland. Yang et al.18 described seven cases of MC of intraoral minor salivary glands and found three cases arose in the hard palate. It is a low-grade malignant tumor with little propensity for regional or distant metastasis and low recurrence. Wide local excision is the treatment of choice. MC with predominantly clear cell morphology is rare.35

Warthin’s tumor

The papillary cystadenoma lymphomatosum or Warthin’s tumor almost exclusively affects the parotid gland, especially the tail. The peak incidence occurs during the sixth decade of life, with a male-to-female ratio of 7:1. This lesion presents itself as a slow-growing, soft painless mass with a mean age of 56 years. This tumor presents as a slow-growing, asymptomatic, circumscribed mass; the duration of the tumors prior to excision ranged 6 weeks to 15 years. Fanburg-Smith et al.38 reported one palatal out of 78 intraoral lipomas. Most patients presented with an asymptomatic, circumscribed mass; the duration of the tumors prior to excision ranged 6 weeks to 15 years. Fanburg-Smith et al.45 reported one palatal out of 14 intraoral liposarcomas which are rare in the oral and salivary gland region. They concluded that local excision and careful follow-up, without adjuvant therapy, appears to be the best treatment of salivary gland region liposarcoma.

Polymorphous low-grade adenocarcinoma

The polymorphous low-grade adenocarcinoma is, following MEC, the second most common intraoral salivary gland malignancy. It was first described in 1983 and prior to this, was probably misdiagnosed as an adenoid cystic carcinoma. The most common site is the junction of the hard and soft palate. The male-to-female ratio is 3:1, with a mean age of 56 years. This tumor presents as a slow-growing, asymptomatic mass that may be ulcerated.29,20,36

Adenoid cystic carcinoma

The adenoid cystic carcinoma, the third most common type of the intraoral salivary gland malignancies, affects older individuals, where the mean age of occurrence is 53 years with a male-to-female ratio of 3:2. Fifty percent of these tumors occur in the parotid gland, whereas the other 50% occur in the minor gland of the palate. These present as slow-growing, ulcerated masses, with an associated chronic dull pain.39

Hybrid tumors are very rare salivary gland lesions composed of two or more different tumoral entities in a single neoplasm. In most cases, adenoid cystic carcinoma has been the predominant component in these lesions. Ruiz-Godoy et al.46 described two patients with hybrid tumors located in the palate, one involved adenoid cystic carcinoma and MEC.

Clear cells tumor

Clear cell tumors are observed in several malignant salivary gland tumors including MEC.33 Occasionally,
mucin material from structural MEC’s cysts leak into the surrounding stroma, resulting in an inflammatory reaction and a nonrepresentative biopsy may mislead the physician to a diagnosis of chronic sialadenitis, which is painful. On some occasions, the inflammatory response may lead to extensive fibrosis, so-called sclerosing MEC. Information concerning calcifications in clear cell MEC of the salivary gland is very scarce. Yang and Chen concluded that clear cell MEC should be considered in the differential diagnosis of salivary gland tumors with calcification.

**Acinic cell carcinoma**

Acinic cell carcinoma (ACC) is an infrequent malignant salivary gland tumor. Approximately 16% of all ACCs occur in the mouth; it accounts for 6% of all primary salivary gland neoplasms and 17% of all primary malignant salivary gland tumors. Omlie and Coutlas found 28.6% of 21 ACC’s cases in the palate. In general, intraoral ACCs are more common in the buccal mucosa, upper lip and palate; more frequent in women; usually asymptomatic and slow-growing, and treated with local excision; much less aggressive in the minor salivary glands, and patients rarely die of disease, and tumors seldom metastasize. Triantafillidou et al. concluded that ACCs are characterized by an indolent clinical course with the potential for both local recurrence and distant metastases. Hystologically, microcystic, papillary cystic, loculated, multicystic neoplasms that can exhibit intracystic papillations. The relative rarity of such lesions is reflected by their exclusion from many principal surgical pathology texts and major review articles.

**Cystadenoma**

Papillary oncocytic cystadenoma of palatal minor salivary glands is a very rare lesion but is important in the differential diagnosis on a palate. Cystadenomas of salivary gland origin are benign, well-circumscribed or encapsulated, multicystic neoplasms that can exhibit intracystic papillations. The relative rarity of such lesions is reflected by their exclusion from many principal surgical pathology texts and major review articles. Cystadenoma of the minor salivary gland occurs very rarely and presents as a painless mass beneath the mucosa of the hard palate, cheek or posterior tongue. Occurrence of oncocytic carcinoma (or malignant oncocytoma) arising from minor salivary glands of the sinonasal tract is an unusual event. As oncocytic metaplasia and oncocytomas are most often observed in older individuals, the oncocyte was previously regarded as a «functional exhaustion» of a normal cell. Most reported cases were treated by simple excision without recurrence. Recurrences are attributable to incomplete excision or due to the mistaken diagnosis of a low-grade cystadenocarcinoma.

**Angiosarcoma**

Angiosarcomas of the oral and salivary gland region are extremely rare, often with relatively good outcome. Fanburg-Smith et al. reported 22 primary and 7 secondary angiosarcomas; one palatal out of 18 intraoral angiosarcomas. Symptoms included a mass with recent enlargement and bleeding. Histologically all tumors were vasoformative (commonly spindled); most of them had solid rather than distinctive papillary areas; almost one third of oral and salivary gland angiosarcomas are the rare epithelioid angiosarcoma variant.

**Metastatic tumors**

Metastatic disease of the oral cavity is uncommon, representing 1% of all oral malignancies, however, the mandibular molar and premolar regions are the most frequently (61%) affected sites. The most common primary sites are lungs, prostate, kidney, bone, adrenal glands and breast, colorectal, genital tract and thyroid in females. Lim et al. found the liver being the most common primary site. The lung was the most common primary site for the jawbone metastases, whereas the liver was for those of oral soft tissue. They concluded this discrepancy might be caused by a relatively high incidence of hepatocellular carcinoma in Koreans. They reported one palatal out of 18 oral soft tissue metastases. Van der Waal et al. reported three palatal out of 24 intraoral metastatic tumors. Primary sites were kidney (clear cell carcinoma), colon and oesophagus (both adenocarcinoma). The majority of these malignancies are poorly defined radiographically with occasional mixed or radiopaque lesions.

**Lymphoma**

Lymphoma and plasmacytoma of the jaws usually occurs in older adult patients and presents as an asymptomatic, ill-defined area of radiolucency. Langerhans cell hystiocytosis and squamous odontogenic tumor can produce bony destruction that mimics focal periodontal disease. The former condition is often associated with radiographic appearance of «float teeth»; the latter often results in a wedge-shaped radiolucent defect between the teeth. Lymphomas of the palate are rare lesions and those arising from the mucosa-associated lymphoid tissue (MALT) located in the hard palate were first reported in 2006.

**Intraosseous tumors**

Primary intraosseous squamous cell carcinoma is more common in older adult men than MEC, but both can result from malignant transformation of pre-existing dentigerous cysts, periapical cysts, odontogenic keratocysts and residual cysts.

Primary central mucoepidermoid carcinoma (CMEC) is an uncommon lesion that was first described by Leep in 1939, with a high predilection for a mandibular location with an average age of onset in the mid-30s. It represents less than 1% of all salivary gland MECs. The fact that 30–50% of CMEC cases are associated with impacted teeth has even led some authors to classify CMEC as odontogenic. Occasionally, it is difficult to distinguish between central and peripheral salivary gland origin. The criteria for diagnosis of intraosseous MEC are the following: presence of intact cortical plate; radiographic...
evidence of bone destruction; histologic transformation; positive mucin staining; absence of primary lesion in the salivary gland and exclusion of an odontogenic tumor63.

Biswas and Crank64 presented findings regarding the relative distribution of various conditions causing maxillary swelling and found 20.8% of palatal bulge. Clinically they found 5 infected/carious teeth and 10.4% dental and dentigerous cysts among 48 patients and 45.4% among 11 non-neoplastic lesions.

It has been suggested that residual odontogenic cysts are the most common form of odontogenic cysts to undergo carcinomatous transformation, which is a rare complication65. It is also not unusual to misdiagnose the non-ulcerative form of necrotizing sialometaplasia as squamous cell carcinoma or MEC. Patients with intraoral MEC had a reduced survival expectation if they were of a male gender, with regional metastasis, high grade of malignancy, strong expression of PCNA and weak expression of c-erbB-2, which plays an important role in the development, differentiation and mitogenic signalization in normal cells65.

Conclusion

Considering the extensive list of differential diagnoses on the hard palate, unfortunately, acute odontogenic infection, as we previously reported50, can now be added to that extensive list. However, the most important factors for presumptive diagnosis of tumorous lesions on the hard palate are time of presence, relation to the mid-palatal line, presence of pain and the nature of bone destruction.

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References

MUKOEPIDERMOIDNI KARCINOM POGREŠNO DJIAGNOSTICIRAN KAO ODONTOGENA UPALA. PREGLED DIFERENCIJALNE DJIAGNOZE NEPČANIH LEZIJA

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