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CASE REPORT

Oncocytic variant of central mucoepidermoid carcinoma: a rare case report

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Abstract:

Mucoepidermoid carcinoma constitutes a heterogeneous lesion and may present histological variations that make the diagnosis challenging. This study aims to report a rare diagnosis of central oncocytic mucoepidermoid carcinoma (OMEC). A 45-year-old female patient, presenting a 10-year-old history of increase of volume in the left posterior mandible, with dental displacement and no clinical sign of mucosal involvement. A well-limited hypodense area was observed radiographically, with cortical bone thinning and a discrete area of solution of continuity. Histopathological analysis of incisional biopsy revealed a malignant neoplasia with glandular differentiation, presenting multiple cystic and ductiform spaces and a prominent component of large oncocytic cells, such as cells with squamous, basaloid, and mucous aspects. Histochemical and Immunohistochemical findings contributed to the diagnosis of OMEC. Tumor resection and mandibular reconstruction with microsurgical fibular graft were considered. However, the patient refused the treatment. This is the first report of OMEC with intraosseous occurrence.

Keywords: Carcinoma; Mucoepidermoid Mandibular Neoplasms; Pathology, Oral

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INTRODUCTION

Mucoepidermoid carcinoma (MEC), first described by Masson and Berger in 1924[1] and recognized as a distinct entity by Stewart et al in 1945[2], is the most common primary salivary malignancy in adults and children, comprising 3 - 15% of all salivary gland tumors[3]. MEC occurs mainly in parotid glands, followed by submandibular glands. Palate and buccal mucosa are the most frequent intraoral sites[3,4].

Intraosseous occurrence is uncommon and accounts for 2-3% of all MEC reported. The tumor is often asymptomatic, clinical appearance is atypical (according to the location affected) and radiological patterns are variable. However, central lesions may often present unilocular or multilocular, well-circumscribed radiolucency[5], being detected during routine dental examination.

Histologic grade is a significant predictor of outcome in salivary gland carcinomas. In most cases, MECs are composed by three cell types: mucous cells, epidermoid (squamous) cells, and intermediate cells (undifferentiated). These types may vary in proportions, which sometimes make the histological diagnosis difficult. Several classifications have been proposed in the literature to grade this lesion. The three most known grading schemes (AFIP[6], modified Healey[7] and the Brandwein[8]) although qualitative or semiquantitative, are based on similar parameters, such as cytomorphological and architectural features, in addition to the presence of perineural and/or angiolymphatic invasion. The latest World Health Organization classification of head and neck tumors, in 2017, does not ratify any grading scheme. It only outlines the general features of low, intermediate and high-grade tumors[9–11].

Histological features of CME may be even more heterogeneous. Besides classical MEC, there are other uncommon variants, such as clear cell variant, oncocytic variant and squamous variant[12–14]. Histopathological diagnosis becomes increasingly challenging in face of these variants. This study aims to report a rare diagnosis of a central oncocytic mucoepidermoid carcinoma (OMEC).

CASE REPORT

A 45-year-old female patient was referred to the Stomatology Clinic of the Federal University of Ceara for clinical evaluation, complaining about the existence of an oral lesion, which was noted by the patient 10 years ago. She reported episodes compatible with aggravation and onset of intraoral edema, infectious process with purulent secretion, associated with periods of stress. Anamnesis also revealed a medical history consistent with physical status I, according to American Society of Anesthesiologists (ASA) Physical Status Classification System. At extraoral clinical examination, an increase in volume, was observed in left mandibular angle, encompassing body and ramus regions. However, on intraoral examination, there was no evidence of infection and inflammation. An important, painless, and hardened to palpation cortical swelling in the posterior region of the left mandible, compatible with the alterations seen extraorally, was observed. Additionally, a discrete area of mucosal change was evidenced in the region due to premature contact with the upper tooth (Figure 1).

Complementary exams, such as panoramic radiography, computed tomography and blood tests were requested. Radiographical findings evidenced a well circumscribed and unilocular radiolucent/hypodense area in left mandibular angle, surrounded by a thin layer of cortical bone (seen in axial, coronal, and sagittal views) with well-defined limits, and a discrete area of solution

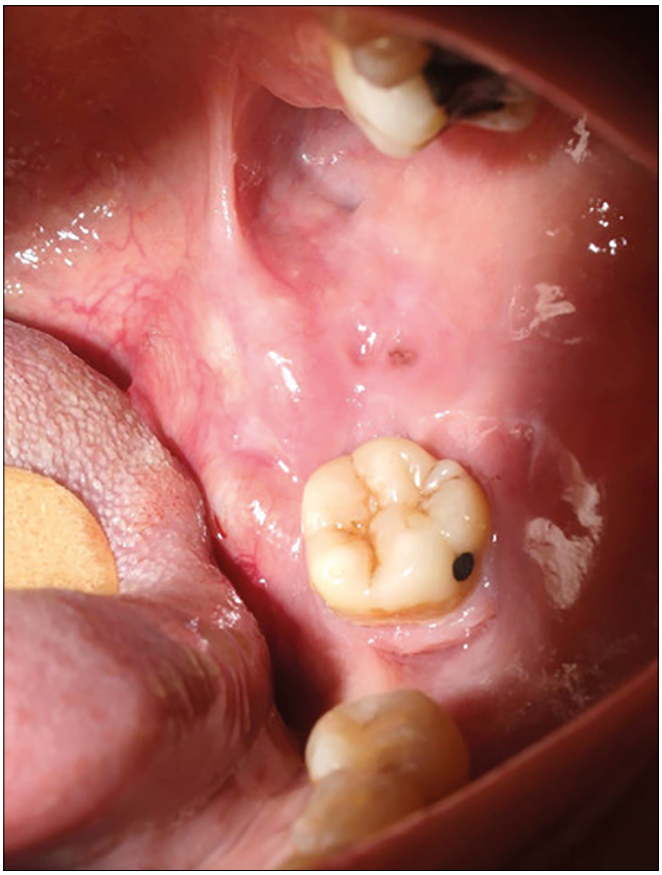

Figure 1. Intraoral clinical aspect of the lesion, evidencing cortical expansion in the mandible left posterior region.

of continuity. Association with a probable displacement of #38 tooth (Figure 2) was also considered. Blood tests did not show any noticeable changes, and an incisional biopsy of the lesion was performed, with a diagnostic hypothesis of dentigerous cyst or ameloblastoma.

Histopathological examination evidenced a malignant neoplasia with glandular differentiation, presenting large oncocytic cells, with a finely granular eosinophilic cytoplasm, as well as vesiculated nuclei with single acidophilic macronuclei. Cells with squamous, basaloid and mucous aspects were also visualized. Multiple cystic and ductiform spaces, sometimes containing basophilic mucoid-like material, were observed. The tumor showed no visible encapsulation, as well as invaded adjacent bone trabeculae, blood vessels, and surface epithelium (Figure 3). Histochemical periodic acid Schiff (PAS) showed positivity in the mucoid material and in oncocytic cells (Figure 4A). After enzymatic diastase action (PAS-D), positivity was seen only in mucoid-like material, while oncocytic component was negative (Figure 4B). Mucicarmine stain also evidenced positivity in the mucoid aspect material (Figure 4, C and D). Immunohistochemical reaction evidenced intense and diffuse positivity for CK7 (Figure 4E) and CK34βe12(Figure 4F), rare focal positivity for CK20, and negativity for GFAP (glial fibrillar acid protein) and S100 markers. The main differential diagnoses of oncocytic carcinoma, glandular odontogenic cyst and metastatic adenocarcinoma were excluded, based on histopathological characteristics and

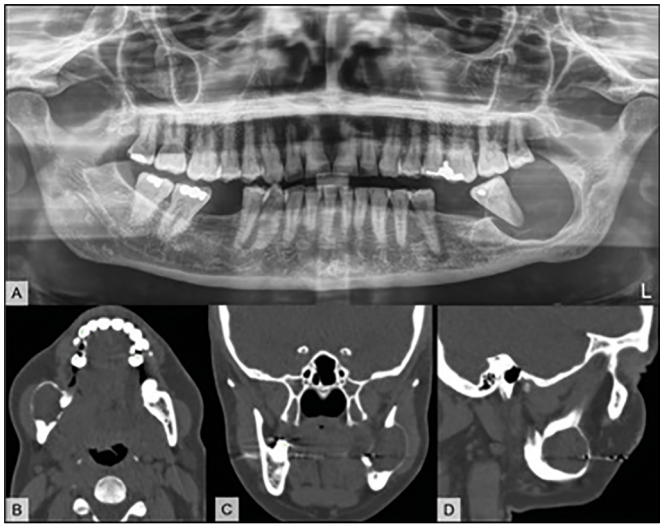

Figure 2. Computed tomography, evidencing, in panoramic reconstruction **(A)**, well delimited hypodense area, associated with tooth # 38. On axial **(B)**, coronal **(C)** and sagittal **(D)** sections, a well delimited hypodense lesion, surrounded by a thin layer of cortical bone can also be seen, associated with a discrete area of solution of continuity.

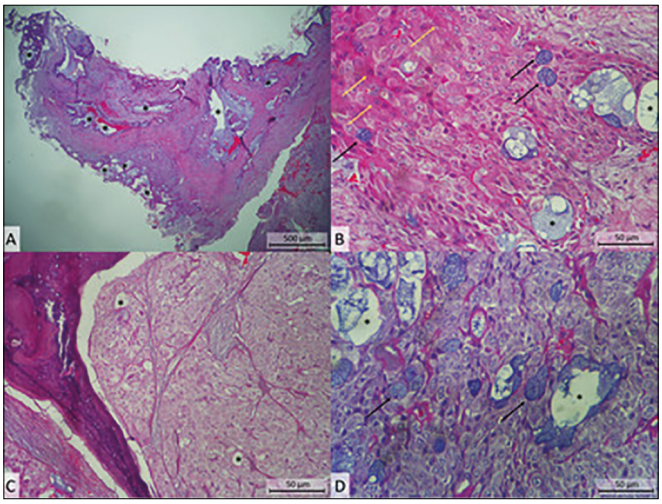

Figure 3. Photomicrographs (hematoxylin and eosin staining), showing, in 40x magnification **(A)**, neoplastic lesion with glandular component, presenting multiple cystic spaces (black asterisks), sometimes filled with mucin-like material and supported by fibrous stroma. At higher magnification (400x), an area composed of epidermoid cells (yellow arrows) and mucous cells (black arrows) **(B)** is visualized. There is also a predominantly oncocytic component, containing some cystic spaces and bordered by trabeculae of cortical bone **(C)**. Areas with higher amounts of mucosal cells are also found, associated with cystic spaces **(D)**.

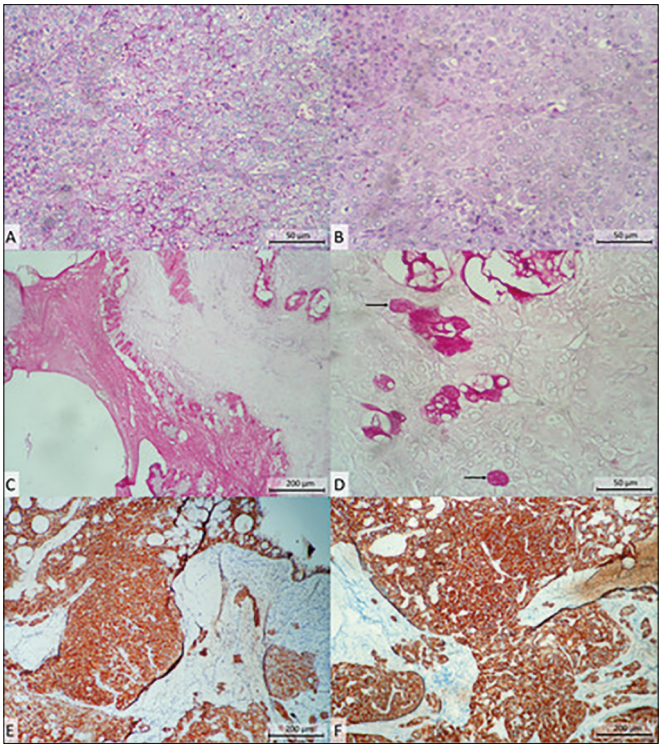

Figure 4. Photomicrographs after histochemical and immunohistochemical analysis, evidencing: **A.** Oncocytic component area after histochemical reaction of PAS (without diastase), showing positivity in cytoplasmic granules of neoplastic cells. **B.** Same microscopic field of A, presenting negativity for PAS-D reaction. **C and D.** Histochemical reaction for mucicarmine, at lower (C) and higher (D) magnifications, showing positivity for mucoid-like material (black arrows). **E and F.** Immunohistochemical reaction for CK7 (E) and CK34βe12 (F), evidencing intense and diffuse positivity in the tumor parenchyma.

immunohistochemical profile. The involvement of other organs was also investigated, but no tumor foci were detected. Therefore, considering clinical, radiographical and atypical microscopical findings, and based on the three most popular MEC grading schemes[6–8], the diagnosis of an oncocytic variant of intraosseous low-grade mucoepidermoid carcinoma was established. The patient was referred to the responsible department (Head and Neck Surgery) for proper treatment. A multispecialized approach was considered, involving Head and Neck, Plastic and Maxillofacial surgery, associating tumor resection to mandibular reconstruction with microsurgical fibular graft. Nevertheless, the patient chose not to perform the treatment, claiming personal reasons, and is in psychological accompaniment.

DISCUSSION

Central MEC is a well-recognized entity, but its etiology and histogenesis is still unclear. Ectopic salivary gland tissue, metaplastic transformation of odontogenic epithelium or intraosseous extension of maxillary sinus/submucosal mucous glands have been reported as possible origins of central MEC[15].

Females are twice more frequently affected than males. It has been reported in all ages (from 1 to 78 years), with the majority occurring in 4th and 5th decades of life[3,16]. Mandible is twice more commonly affected than maxilla, and the most common site of occurrence is the posterior region (from premolar to mandibular angle). Swelling, pain with trismus and paresthesia can be noted occasionally. Metastases are established in 9% of the cases, mainly to the regional lymph nodes and occasionally to the ipsilateral clavicle, lung and brain[5,12]. About 50% of central MEC are associated with dental cysts and impacted teeth, resembling odontogenic lesions (such as inflammatory and development odontogenic cysts and odontogenic tumors), which may contribute to misdiagnosis[3,17,18].

The main differential diagnosis of central MEC (especially low-grade ones) is glandular odontogenic cyst (GOC). The distinction between these two entities based only in morphological findings is occasionally challenging. In addition, the presence of a prominent oncocytic component directs the diagnosis to other lesions, such as oncocytic carcinoma or metastatic adenocarcinomas.

Immunohistochemistry may be helpful in their differentiation, although there is no pathognomonic marker profile. On the other hand, *MAML2* gene rearrangement is specific to identify MEC, no matter the location. Studies evidenced that this method is quite effective when it refers to the diagnosis of the mucoepidermoid oncocytic variant[19,20]considerable progress in salivary gland taxonomy has been reached by the discovery of tumor type-specific fusion oncogenes generated by chromosome translocations. This review describes the clinicopathologic features of a selected group of salivary gland carcinomas with a focus on their distinctive genomic characteristics. Mammary analog secretory carcinoma is a recently described entity characterized by a t(12;15. However, biomolecular approach, despite its benefits, is not a reality of diagnostic routine[21,22].

On the present case, immunohistochemistry was helpful in distinguishing a primary central MEC from other lesions. CK7 and CK20 immunohistochemical profile favored the differentiation of primary salivary gland neoplasia from metastatic tumor and squamous cell carcinoma. Most mucoepidermoid carcinomas shows a typical CK7+/CK20- profile, although some studies demonstrate that it they present focal positivity for CK20[23]. S100 and GFAP negativity reinforced absence of myoepithelial components, usually present in several other salivary gland tumors[24]. CK34βe12, a high molecular weight cytokeratin, has been described mainly in carcinomas[25], as well as in adenocarcinomas and mucoepidermoid carcinomas[26,27].

A recent study of Souza et al. reviewed thirty-six publications, reporting 147 cases of primary central MEC of jaws. Low-grade histopathological tumor type was mostly observed (54.4%). However, the study doesn't refer to the presence of histological variants, but relates male gender, high grade tumors, conservative treatment and the occurrence of locoregional metastasis to a worse prognosis[20].

Late diagnosis or misdiagnosis of MEC contribute to inappropriate treatment and recurrence. The literature describes some criteria for the diagnosis of this lesion when occurring centrally, including: a) Presence of radiographic distinct osteolytic lesion; b) Positive mucicarmine staining; c) Absence of rupture of one or more cortical plates; however, cortical rupture does not exclude the diagnosis; d) Clinical and histological exclusion of a metastases or an odontogenic lesion; e) Exclusion of origin from a soft tissue salivary gland; f) Histologic confirmation[28]. All criteria, except for the absence of cortical rupture, were found in the case reported (which corroborates to the final diagnosis of central MEC).

The importance of histological confirmation lies in the fact that the heterogeneity of histopathological

features of the lesion may lead to a misdiagnosis. Less frequently variants of MEC include those with oncocytic, psammomatous, sebaceous, spindle cell, sclerosing or goblet cell components. The uncommon occurrence of these variants contribute to diagnostic errors, although do not seem to interfere on tumor prognosis[29].

Most salivary gland lesions with oncocytic change are benign. In fact, all types of salivary gland lesions may have foci of oncocytic cells, although it represents a small portion of the lesion microscopic features (making improbable a diagnostic confusion). However, a prominent content of this component characterizes the histological variant of the lesion, which may resemble other oncocytic malignancies (also are rare in the oral cavity), such as oncocytic carcinoma[30].

Kwon et al. reported a case of OMEC arising from minor salivary glands. Although presenting radiographic characteristics similar to the present case, the granulomatous appearance of the lesion on intraoral examination coupled with soft tissue involvement of the aforementioned study suggests that the lesion was derived from minor retromolar salivary glands[31], which was not found in the present case. In the same study performed by Kwon et al. and published in 2010, the authors listed the occurrence of other 35 Head and Neck OMECs cases in the literature. To date, only three more case reports have been described in the scientific community according our knowledge[32–34] but none of these studies refers to the occurrence of intraosseous lesion.

The lesion described in the present case showed no clinical signs of inflammation or relationship with minor salivary glands of the oral cavity. In addition, the radiographic characteristics met the criteria to classify the lesion as a central mucoepidermoid carcinoma. Immunohistochemical pattern, associated with histomorphological features such as: solid pattern of cell proliferation, with absence of anaplasia and varying degrees of cystic and ductiform formations, invasion of adjacent bone trabeculae and presence of prominent oncocytic cells, as well as epidermoid and mucosal cells, corroborated with the diagnosis of low-grade OMEC. This is the first report describing the rare diagnosis of a central low grade OMEC in oral cavity.

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