

Central mucoepidermoid carcinoma radiographically mimicking an odontogenic tumor: A case report and literature review

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Abstract

Central mucoepidermoid carcinoma (CMC) of the jaw bones is a rare malignant salivary gland tumor of unknown pathogenesis, comprising about 4% of all mucoepidermoid carcinomas (MECs). Most cases are histologically classified as a low-grade tumor and radiographically appear as a well-defined unilocular or multilocular radiolucent lesion. Block resection or wide local excisions are the treatment of choice and patients usually show a good overall prognosis although a long-term follow-up is necessary. This report describes a case of a 28-year-old male with MEC in the posterior region of the mandible and discusses its clinical, radiographic and histopathological findings. Although rare, CMC may be considered a differential diagnosis in cases of proliferative and osteolytic lesions in the oral cavity even when its clinical and/or radiographic findings do not suggest malignancy.

Key Words: Central mucoepidermoid carcinoma, demographic profile, Jaw bones

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INTRODUCTION

Salivary gland tumors account for <3% of all head and neck tumors. Due to their diverse biological behavior and variable histological subtypes, the diagnosis and management of these lesions are a challenge for researchers, surgeons and clinicians.^[1,2]

The World Health Organization^[3] classifies mucoepidermoid carcinoma (MEC) as a malignant neoplasm of epithelial origin that represents 3–15% of all salivary gland tumors. It was first described in 1945 and currently has been considered the most common malignant salivary gland tumor, with most

of them arising within the parotid gland. Histologically, MEC is characterized by three main cell types: Epithelial, mucin-producing and intermediate cells. Central osseous origin of this tumor is rare, representing 2–4% of all MECs. These central mucoepidermoid carcinomas (CMCs) are most common in the mandible, having a female predilection and unknown pathogenesis.^[4-6]

Although rare, due to its diverse clinical presentation, case reports may help in their diagnosis. Therefore, we describe a case of primary CMC in the mandible of a young patient mimicking an odontogenic tumor.

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CASE REPORT

A 28-year-old male patient was referred to a public oral diagnosis center, complaining of severe pain in the right posterior region of the mandible endured for 3 months. No swelling or gross abnormalities were noticed on extraoral physical examination. Intraoral mucosa presented normal color [Figure 1], and palpation revealed obliteration of the right ascending ramus.

Panoramic radiograph showed a well-defined multilocular radiolucent lesion extending from the mesial aspect of the tooth #47 into the ascending ramus. Pulp vitality testing was positive in the referred tooth. Based on the patient's report and clinical aspect of the lesion, the provisional diagnosis considered was solid/multicystic ameloblastoma [Figure 2].

Incisional biopsy was performed and microscopic examination revealed cystic and solid structures predominantly composed of three morphologically distinguished cell patterns: Epidermoid, mucous and intermediate cells [Figure 3]. In view of these findings, the histopathological diagnosis was CMC.

Several human neoplasms may present clear cells, mucous cells and squamous cells. Although the CK7 immunoeexpression is not useful in distinguishing the various types of salivary gland neoplasms, it may facilitate differentiation of primary salivary gland tumor from metastatic tumors, squamous cell carcinoma and odontogenic tumors. Histopathological findings added together with CK7 immunoeexpression confirms the final diagnostic of MEC.^[7] The index of Ki-67 expression can help evaluate the cell proliferation rate.

Immunohistochemical analysis of CK-7 (cytokeratin-glandular epithelial cell marker) and Ki-67 (cell proliferation marker) through EnVision + HRP (Dako, Glostrup, Denmark) technique was made to evaluate the biological behavior of the tumor. Anti-Ki-67 and anti-CK-7 primary monoclonal antibodies (dilution 1:200 and 1:50, respectively; Dako, Glostrup, Denmark) were diluted in phosphate-buffered saline tampon solution with pH 7.4 and incubated for 60 min. Analysis showed low expression of Ki-67 and diffuse expression for CK-7 revealing a low cell proliferation rate and glandular epithelial differentiation of the tumor. This configured CMC, morphologically and molecularly, as a low-grade malignant tumor [Figures 4 and 5].

The patient was referred to a head and neck service in a public hospital for oncological treatment. Tumor node metastasis staging system was T4aN0M0 (tumor larger than 4 cm with mandible invasion and without regional or distant metastasis). A planned treatment of the lesion was done which included hemimandibulectomy and ipsilateral neck dissection of the



Figure 1: Intraoral clinical image revealed normal mucosa



Figure 2: Panoramic image showing multilocular and radiolucent lesion extending from the right posterior body of mandible into the ascending ramus

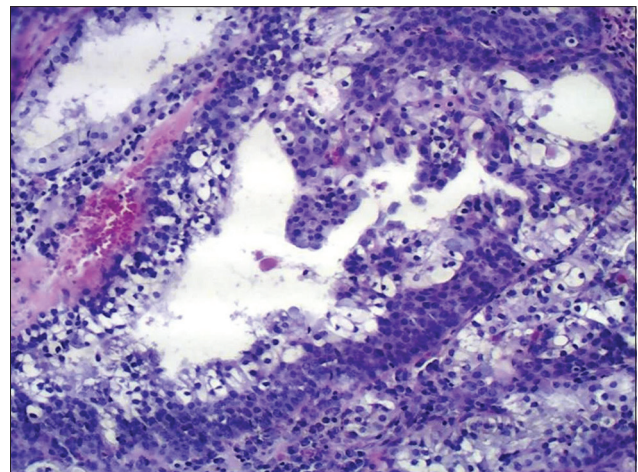


Figure 3: Photomicrograph shows cystic structures formed by epidermoid, mucous and intermediate cells (H&E stain, ×100)

submandibular lymph node chain. The patient has been under clinical follow-up for 1 year and 8 months without any evidence of recurrence.

DISCUSSION

Primary CMC is a rare intraosseous tumor with pathogenesis widely discussed. Various possible origins have been considered

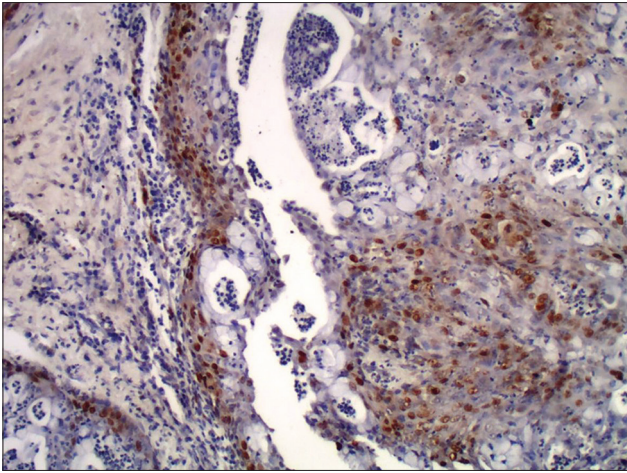


Figure 4: Expression of Ki-67 in neoplastic central mucoepidermoid carcinoma cells (IHC stain, $\times 100$)

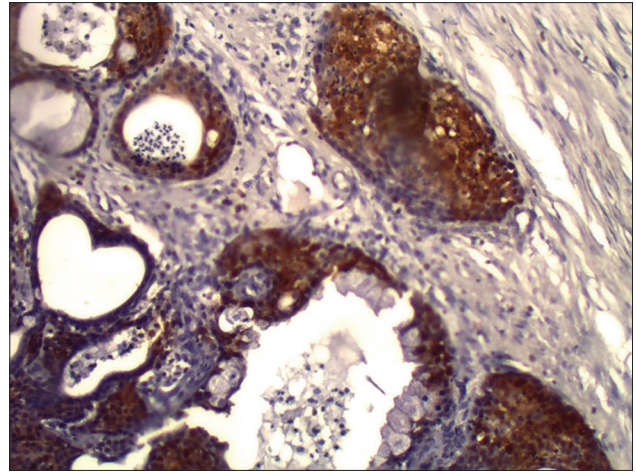


Figure 5: Expression of CK-7 in neoplastic central mucoepidermoid carcinoma cells (IHC stain, $\times 100$)

including: (a) Entrapment of the retromolar mucous glands within the mandible, which later undergo neoplastic transformation, (b) embryonic remnants of the submandibular and sublingual glands trapped within the mandible during development, (c) neoplastic transformation and invasion from the lining of the maxillary sinus, (d) neoplastic transformation of the mucous secreting cells from the epithelial lining of the dentigerous cyst associated with impacted third molars and (e) neoplastic transformation of entrapped minor salivary glands within the maxilla.^[8]

The criteria for diagnosis of CMC are (a) cortical preservation of bone; however, cortical rupture does not exclude the diagnosis, (b) radiographic evidence of bone destruction, (c) exclusion of an histologically resembling metastatic tumor (d) exclusion of odontogenic tumor and (e) histopathological and immunohistochemical confirmation.^[8,9] In the present case, the patient presented all necessary diagnostic criteria. Clinical presentation includes swelling and slow-growing lesion, with pain and altered sensation of the inferior alveolar nerve on long-standing lesion.^[5,6,10] However, these findings are not always necessarily present. In our case, for instance, the patient only complained of pain.

CMC affects mainly females between the first and seventh decades of life though cases occurring in the fourth and fifth decades are most common.^[2,5,10,11] Our case occurred in a male patient with only 28 years which reveals an unpredictable clinical presentation of this tumor.

Radiographic features are diverse and not exclusive of CMC. Usually, it appears as a unilocular or multilocular radiolucent lesion with sclerotic and well-defined margins. These same characteristics are found in some cystic lesions and tumors of odontogenic origin.^[3,5] In this case, the provisional diagnosis

was ameloblastoma, just as the most common diagnostic hypotheses are tumors and odontogenic cysts as observed in Table 1.^[12-23]

The differential diagnosis of unicystic/multicystic lesions in the mandible or maxilla usually includes ameloblastoma and keratocystic odontogenic tumor; however, it should not exclude less common, but more serious conditions, as metastatic tumors; malignant osseous tumors; primary intraosseous carcinoma and malignant salivary glands tumors [Table 1]. Besides that, in many cases of malignant tumors, the outer cortical bone is absent or has been expanded and extended into surrounding soft tissue^[11] as it was observed in our case.

To better characterize this tumor, a literature search was conducted in the PubMed database to survey the published cases reports of CMC in the last 5 years, as described in Table 1. Our findings show CMC affected men and women equally, with age range 8–80 years (mean age = 40.3). The mandible was the most common anatomic site with mandible: maxilla ratio of 1.5:1, and pain was the main symptom. Radiographically, CMC was found to be predominantly radiolucent and multilocular.

Microscopic examination reveals an infiltrative neoplastic lesion characterized by the proliferation of nests, islands and cystic structures that are composed of epidermoid, mucous and intermediate cells. In this case, it was observed that predominance of cystic structures, absence of cellular atypia, necrosis and mitosis characterizes it as a low-grade CMC.^[3,8]

Cellular proliferative index and proteins related to cellular differentiation can infer in the biological behavior of CMC. Ki-67 has been considered the most useful marker for predicting the outcome of several types of cancer, including CMC. Its high expression is directly related to the aggressive

Table 1: Features of central mucoepidermoid carcinomas described worldwide in the last five years (2011-2016)

Authors	Age	Gender	Symptoms	Anatomic Site	Radiographic findings	Diagnosis hypotheses
Aggarwal; Saxena (2011) ^[12]	8	Female	Pain	Mandible	Unilocular/radiolucent	DC, KCOT, AMB
Sherin et al. (2011) ^[13]	29	Female	Asymptomatic	Maxilla	Multilocular/Mixed	Fibrous lesion, benign salivary gland neoplasm and vascular lesion
Abu-Karakay et al. (2012) ^[14]	52	Female	Pain	Mandible	Multilocular/radiolucent	Cystic lesion, OT
Chiu et al. (2012) ^[15]	55	Male	Pain	Mandible	Unilocular/radiolucent	Cystic lesion
Varma et al. (2012) ^[16]	50	Male	Asymptomatic	Mandible	Multilocular/radiolucent	AMB
Spoorthi et al. (2013) ^[17]	80	Female	Pain	Mandible	Multilocular/radiolucent	DC, KCOT, AMB
Lakouichm et al. (2013) ^[18]	42	Female	Pain	Maxilla	Multilocular/radiolucent	Cystic lesion
Chan et al. (2013) ^[19]	51	Female	Asymptomatic	Maxilla	Multilocular/Mixed	NI
Chan et al. (2013) ^[19]	73	Female	Asymptomatic	Mandible	Multilocular/radiolucent	NI
Chan et al. (2013) ^[19]	29	Male	Asymptomatic	Mandible	Multilocular/radiolucent	NI
Chan et al. (2013) ^[19]	42	Male	Asymptomatic	Maxilla	Multilocular/radiolucent	NI
Moghadam et al. (2014) ^[5]	44	Female	Asymptomatic	Mandible	Multilocular/radiolucent	OT
Moghadam et al. (2014) ^[5]	56	Female	Asymptomatic	Mandible	Multilocular/radiolucent	AMB
Rathore et al. (2014) ^[11]	18	Male	Pain	Maxilla	Unilocular/radiolucent	Cystic lesion
Sepúlveda et al. (2014) ^[20]	43	Male	Asymptomatic	Mandible	Multilocular/radiolucent	NI
Suresh et al. (2014) ^[21]	52	Male	Asymptomatic	Maxilla	Multilocular/Mixed	Osteosarcoma and osteoblastic metastatic
Chundru et al. (2015) ^[22]	37	Male	Asymptomatic	Mandible	Multilocular/radiolucent	AMB, KCOT
Kechagias et al. (2015) ^[6]	37	Female	Pain	Mandible	Multilocular/radiolucent	AMB
Nallamilli et al. (2015) ^[23]	36	Male	Pain	Maxilla	Unilocular/radiolucent	OT
Present Case - 2016	28	Male	Pain	Mandible	Multilocular/radiolucent	AMB

behavior and worse prognosis of this tumor.^[24-26] In a pioneer study, Skálová and Leivo^[24] reported that recurrences do not occur in CMC and acinar cell carcinoma with low expression of Ki-67. Furthermore, the authors affirmed that the high expression of this protein is related to a worst prognosis.

Although salivary gland tumors have a wide range of histological aspects, they still maintain a salivary gland cell differentiation. The absence of such differentiation may indicate a more aggressive behavior. Usually, the expression of cytokeratins such as CK-7, CK-8 and pan-cytokeratin (AE1/AE3) are high in low-grade malignant tumors. Their presence indicates better overall outcome.^[7,25,26]

Surgery is the main treatment for patients with CMC. As a rule, even as low-grade tumors, CMC should be treated by block resection, hemimandibulectomy or hemimaxillectomy. Neck dissection is usually part of the treatment in cases where metastasis to the cervical nodes is suspected. Radiotherapy indication is controversial but recommended in high-grade CMC cases. Prognosis is usually good, but long-term follow-up is necessary due to the possibility of late recurrence or regional metastasis.^[5,9,10]

CONCLUSION

CMC has a slow and infiltrative growth that invades adjacent structures. Because it can occur within gnathic bones, it may be considered a differential diagnosis in cases of proliferative and osteolytic lesions in the oral cavity even when its clinical and/or radiographic findings do not suggest malignancy.

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Conflicts of interest

There are no conflicts of interest.

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