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Case Report

Dentistry Section

Central Mucoepidermoid Carcinoma of Maxilla: A Case Report with Immunohistochemical Analysis

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ABSTRACT

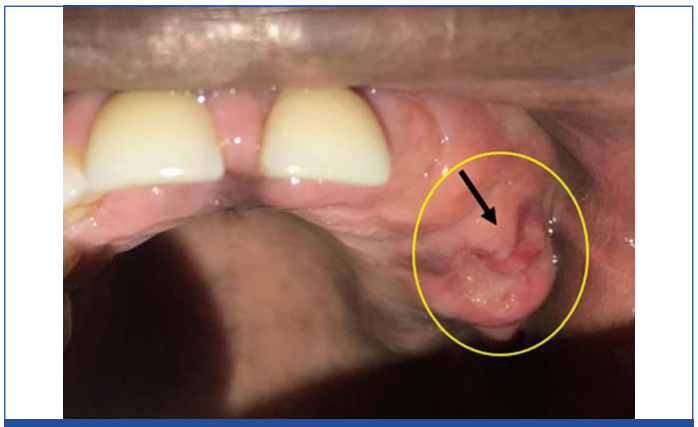
Mucoepidermoid Carcinoma (MEC), which accounts for 3-4% of all cancers of the maxillofacial region, is the most common type of salivary carcinoma. It most commonly occurs in the major salivary glands. The palate, retromolar region, buccal mucosa, tongue, and lips are common sites for tumors arising in minor salivary glands. Central MEC (CMEC) is an infrequent neoplasm of the jaw bones, accounting for 2-4% of MECs and showing varied biological behaviour. The aetiology of this tumour is uncertain, but several concepts have been proposed based on neoplastic transformation of the odontogenic cyst epithelium or ectopic salivary tissue. Most of these lesions occur in the third to fifth decades with a female predilection and are common in the mandible but rare in the maxilla. Radiographically and clinically, CMEC is often misinterpreted as an odontogenic lesion. To confirm the diagnosis, identifying the origin with the aid of immunohistochemistry is crucial. Hereby, the authors present a rare instance of low-grade CMEC in the maxilla of a 51-year-old male patient, which posed a diagnostic challenge and is accompanied by a review of the literature.

Keywords: Immunohistochemistry, Intraosseous mucoepidermoid carcinoma, Neoplasm, Salivary gland malignancy

CASE REPORT

A 51-year-old male presented to the Department of Oral Medicine and Radiology with a chief complaint of swelling on the left side of the face for four months, which had gradually increased in size after extraction of the left maxillary posterior teeth due to mobility at a private dental practice [Table/Fig-1]. No significant medical or family history was noted. On intraoral examination, a diffuse swelling measuring approximately 5×3 cm extended medio-laterally across the left posterior maxilla. A non healing extraction socket with evident pus discharge was seen in the region of tooth 25 [Table/Fig-2]. A palpable, solitary left submandibular lymph node was noted; it was tender, fixed, and hard on palpation. Based on the history and clinical presentation, a provisional diagnosis of osteomyelitis was considered. Carcinoma involving the left maxillary alveolus and deep fungal infection were considered in the differential diagnosis. Orthopantomogram (OPG) showed an ill-defined radiolucency with ragged borders extending from the distal aspect of tooth 21 to the maxillary tuberosity [Table/Fig-3]. Cone-beam Computed Tomography (CBCT) revealed an isodense osteolytic lesion with erosion of the buccal cortex and thinning of the palatal cortical plate. The floor of the maxillary sinus and the left zygomatic arch were eroded [Table/Fig-4a,b]. Based on these features, carcinoma of the left maxillary alveolus and Primary Intraosseous Squamous Cell Carcinoma (PIOSCC) were considered in the differential diagnosis.

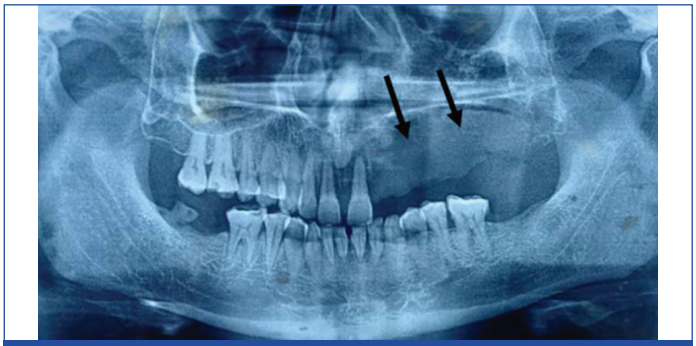
[Table/Fig-1]: Diffuse extraoral swelling on left middle third of face.



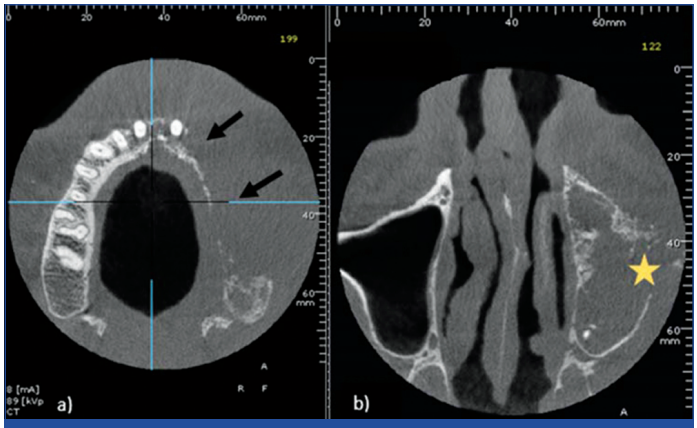
[Table/Fig-2]: Non healing extraction socket in 25 region.

Following the incisional biopsy, the initial histopathological diagnosis was thought to be PIOSCC due to the lack of ulceration of the oral mucosa overlying the tumour, focal areas of histopathological resemblance to keratin pearl formation, and the absence of any other primary tumour on chest radiographs at the time of diagnosis. However, other areas showing glandular features were later identified. Therefore, deeper sections were advised, which revealed glandular epithelium consisting of mucous cells lining cystic spaces [Table/Fig-5a,b]; Haematoxylin and Eosin (H&E) stain, 10× and 40×, respectively. In addition, Periodic Acid-Schiff (PAS) staining demonstrated positive staining [Table/Fig-6a,b]; PAS stain, 4× and 10×, respectively. Immunohistochemistry was performed with a panel of markers: Cytokeratin (CK)14 showed strong positivity, indicating epithelial origin. CK19 was negative, thus odontogenic origin was ruled out. CK7, CK8, and CK18 for glandular and ductal origin revealed strong CK7 positivity with negative expression of CK8 and CK18. Ki-67 assessment of tumour proliferation showed

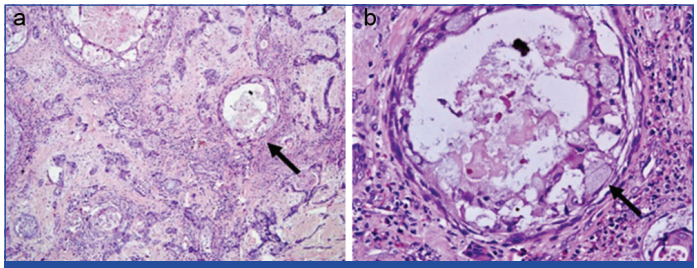
diffuse positivity. Thus, a low-grade CMEC was confirmed [Table/Fig-7a-c]. Unfortunately, the patient was lost to follow-up after being referred to a higher oncology centre for a treatment plan.



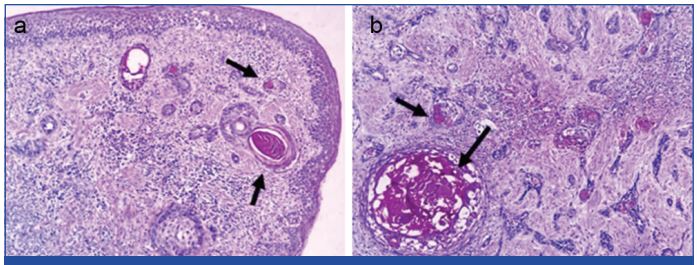
[Table/Fig-3]: Orthopantomogram (OPG) showing an ill-defined radiolucency extending from distal to 21 to maxillary tuberosity with loss of coronal and radicular portions of 22 to 27.



[Table/Fig-4]: a) Axial CBCT showing complete perforation of the buccal cortical plate and thinning of palatal cortex of maxilla; b) Coronal CBCT shows erosion of floor of the maxillary sinus.



[Table/Fig-5]: a,b) Photomicrograph showing macrocysts lined by mucous cells along with intermediate and epidermoid cells (H&E, 10x and 40x, respectively).

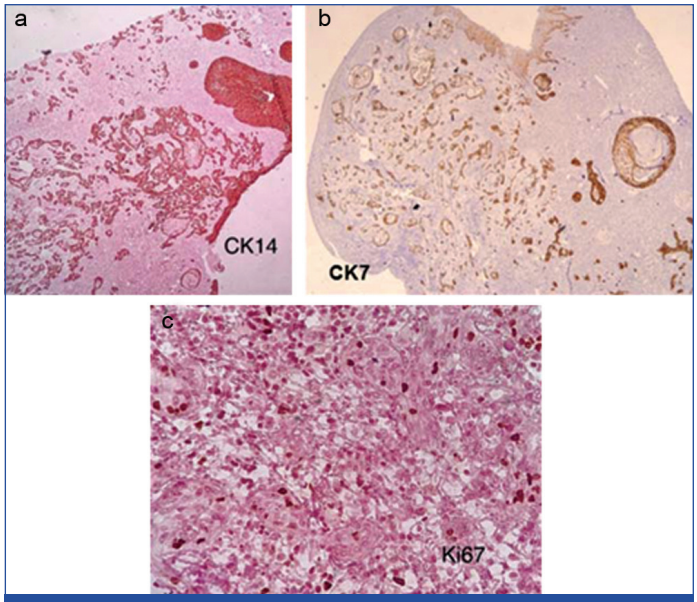


[Table/Fig-6]: a,b) Photomicrograph showing PAS positive material (PAS stain, 4x and 10x, respectively).

DISCUSSION

The CMEC was first described in 1939 by Lepp H [1]. It was included as type 4 in the classification of primary intraosseous carcinomas by Waldron CA and Mustoe TA in 1989 [1,2]. Numerous studies have investigated its aetiology, radiological features, and histology [3,4]. Furthermore, to illustrate the origins of intraosseous salivary carcinomas, Bouquot JE et al., reported that 0.3% of jawbone specimens examined exhibited intraosseous salivary tissue [4].

The pathogenesis of CMEC remains unclear. Four potential origins have been proposed: (1) entrapment of mucous glands in the mandible leading to neoplastic change; (2) developmentally induced submaxillary gland embryonic rests in the mandible; (3) mucous-secreting cells undergoing neoplastic transformation in the pluripotent epithelial lining of dentigerous cysts surrounding an unerupted third molar; (4) tumour development and invasion from the epithelial lining of the maxillary sinus [5].



[Table/Fig-7]: Immunohishtochemical profile: a-b) Strong diffuse positivity for CK14, CK7 (H&E, 4x); c) Mild focal positivity for Ki-67 (H&E, 20x).

Radiographically, CMEC appears as well-circumscribed radiolucent lesions, which may be unilocular or multilocular. Erosion of the cortical bone and/or expansion into adjacent soft tissues can indicate aggressive behaviour. Brookstone MS and Huvos AG (1992) proposed a staging system based on cortical bone perforation observed in some cases. Stage I lesions maintain the surrounding cortical bone unaffected and show no signs of clinical enlargement; Stage II lesions show cortical bone expansion with intact periosteum; Stage III lesions show cortical perforation [6]. In the present case, the cortical bone was both perforated and expanded.

The intraosseous site of CMEC makes diagnosis difficult at times. Consequently, CMEC is frequently misdiagnosed as various intraosseous or odontogenic diseases, including Glandular Odontogenic Cyst (GOC), ameloblastoma, dentigerous cyst, and odontogenic keratocystic tumour. The diagnosis of CMEC necessitates the following criteria, first proposed in 1974 by Alexander RW et al., and later refined by Browand BC and Waldron CA: a) radiographic evidence of bone destruction; b) integrity of the cortical plate preserved; c) absence of a primary lesion in the salivary gland; d) exclusion of an odontogenic tumour or metastases; e) histological confirmation of a salivary gland neoplasm [7,8]. Tapia JL et al., state that histological analysis is essential to confirm that MEC manifests as sheets, ribbons, or islands of mucous cells, epidermoid cells, and intermediate cells within a fibrovascular stroma [9]. Three histopathological grades have been described for MECs based on the amount of cystic development, the level of cellular atypia, and the percentage of mucous, epidermoid, and intermediate cells [10].

1. Low-grade: a well-differentiated tumour mostly composed of macro and microcysts; mucin-producing and intermediate cells are present.
2. Intermediate-grade: majority of intermediate cells with a small number of cysts; islands of epidermoid cells and mucin-producing cells are present.
3. High-grade: a poorly differentiated neoplasm in solid blocks largely composed of epidermoid and intermediate cells, with mucin-producing cells present.

An immunohistochemical profile helps distinguish between closely related lesions, such as odontogenic tumours of the jaws, various salivary gland tumours, and GOC. CK7, CK8, and CK18 are positive in the cytokeratin profiles of glandular and central MECs. The CK profile of GOC overlaps with those of MECs (CK7, CK8, CK18) and odontogenic lesions (CK19). Since, CK19 was negative in the present case, odontogenesis was ruled out, and the glandular odontogenic cyst was excluded [11].

The primary surgical management of CMEC includes curettage, enucleation, marsupialisation, and wide local excision. CMEC should typically be treated with extensive local excision, en bloc resection, hemimaxillectomy, or hemi-mandibulectomy, even if they are low-grade tumours. Radiotherapy is recommended for high-grade MEC cases [12].

The review of the literature conducted using the PubMed/MEDLINE database from 2013 to 2023, with the keywords "intraosseous" and/or "CMEC" and "maxilla has been depicted in [Table/Fig-8]." The search yielded 28 case reports involving the maxilla, in which tumours affected males and females with roughly equal gender distribution; the mean age ranged from 15 to 70 years, and swelling was the most common presenting symptom [10,13-34].

Name of the author	Year	Age	Gender	Symptoms	Radiographic features	Clinical diagnostic hypothesis	Histopathological grading	Treatment
Lakouichmi M et al., [13]	2013	42	F	Pain	Radiolucent multilocular	Cystic lesion	NA	Broad resection
Velez I et al., [14]	2013	25	F	Pain	Ill-defined radiolucency	Intraosseous tumour	Intermediate to high-grade	en bloc resection
Velez I et al., [14]	2013	70	M	Swelling	Radiolucent multilocular	Ameloblastoma odontogenic keratocyst	Intermediate	Hemi-mandibulectomy
Velez I et al., [14]	2013	56	M	Pain and numbness	Radiolucent and radiopaque	NA	Intermediate	Partial hemi-mandibulectomy
Velez I et al., [14]	2013	52	M	Pain	Radiolucent multilocular	NA	Low-grade	Bloc resection
Velez I et al., [14]	2013	-	F	Pain	Mixed radiolucent/radiopaque	NA	Low-grade	en bloc resection
Chan KC et al., [15]	2013	51	F	Asymptomatic	Multilocular/mixed	NA	Low-grade	NA
Chan KC et al., [15]	2013	42	M	Asymptomatic	Radiolucent multilocular	NA	Low-grade	NA
Rathore AS et al., [16]	2014	18	M	Pain	Radiolucent unilocular	Cystic lesion	Low-grade	Right maxillectomy with neck dissection
Kanmani R et al., [17]	2014	27	F	Swelling	Radiolucent	Odontogenic tumour	Intermediate grade	Left hemimaxillectomy
Suresh D et al., [18]	2014	52	M	Asymptomatic	Multilocular/mixed	Osteosarcoma and metastatic tumor	High-grade	NA
Kullaje S et al., [19]	2014	33	M	Swelling	Radiolucent unilocular	OC	Low-grade	NA
Nallamilli SM et al., [20]	2015	36	M	Pain	Radiolucent unilocular	OT	High-grade	NA
Kim SM et al., [21]	2015	11	M	Swelling	NA	NA	Low-grade	Hemi-maxillectomy
Del Corso G et al., [22]	2016	16	F	Asymptomatic	Multilocular radiolucency	OC	Intermediate grade	Left maxillectomy
Martins TH et al., [23]	2016	17	M	Asymptomatic	Hypodense image with well defined edges involving dental apex of the elements 13, 14, and 15	OC	Low-grade	Right maxillectomy with neck dissection
Purohit S et al., [24]	2016	28	M	Asymptomatic	Mixed radiopaque-radiolucent Lesion	OC	Low-grade	Left hemimaxillectomy
Subramaniam D et al., [25]	2016	30	F	Pain and Swelling	Expansile and lytic lesion with bony erosion	OT	Low-grade	Maxillectomy
Razavi SM et al., [10]	2017	43	F	NA	Radiolucent unilocular	OC and adenomatoid odontogenic tumor	Low-grade	Left hemimaxillectomy
Morais EF et al., [26]	2019	22	F	Pain	Radiolucent unilocular	OC		Left hemimaxillectomy
Başaran B et al.,[27]	2018	48	F	Swelling	Expansile lytic mass	NA	Low-grade	Partial maxillectomy
Świerzy P et al., [28]	2018	53	M	Asymptomatic	Radiolucent unilocular	OC	High-grade	Subtotal maxillectomy
Taghavi N et al., [29]	2020	57	F	Swelling	Radiolucent unilocular	OC	NA	Complete enucleation
Isshiki-Murakami M et al., [30]	2021	18	M	Swelling	Radiolucent multilocular	OC	Low-grade	Cystectomy and partial maxillectomy
Harada F et al., [31]	2021	66	M	Pain	Radiolucent multilocular	NA	Clear cell MEC	Partial osteotomy
Sharma N et al., [32]	2022	35	F	Swelling	Radiolucent multilocular	OC	High-grade	Partial maxillectomy and postoperative radiotherapy
Sibille L et al., [33]	2023	50	M	Swelling	Multilocular radiolucency	OC	Low-grade	Hemimaxillectomy
Howayw Y et al., [34]	2023	18	M	Ulcerative lesion	Radiolucent unilocular	NA	Low-grade	Sub-total maxillectomy

[Table/Fig-8]: Review of literature of similar case reports [10,13-34].
F: Female; M: Male; NA: Non applicable; OC: Odontogenic cyst; OT: Odontogenic tumour

CONCLUSION(S)

The CMEC in the jaws is an infrequent entity. The common site is the posterior region of the mandible; however, maxillary involvement should not be overlooked, as lesions are often misdiagnosed due to varied clinical and radiographic features that resemble odontogenic lesions. The use of CBCT can significantly aid diagnosis and help identify the relationship to surrounding vital structures, which may alter management and prognosis. Thus, prolonged follow-up is necessary in patients treated for CMEC to identify late recurrence and regional metastases.

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