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Case Report

Clear cell odontogenic carcinoma: A histopathologic mimicker of intraosseous mucoepidermoid carcinoma; a case report.

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ABSTRACT

Background: Clear cell odontogenic carcinoma is a rare tumour, that is categorized among the malignant groups of odontogenic tumours in the WHO classifications of odontogenic tumour from the 2005 and 2017 classification and to the recent 2022 classifications. This is due to its aggressive clinical behaviour, metastasis to the lungs and lymph nodes and its tendency to recurrence.

Case report: We report a case of a 70-year-old female who presented with a painless mandibular swelling of 5 months duration. Examination revealed a firm jaw swelling that measured 10 by 14 cm in the widest diameter, with hard and fixed submandibular lymph nodes. Radiographic review showed a multilocular radiolucent lesion with hazy boarders. Incisional biopsy was done, and on histopathological examination, sheets, strands, and islands of numerous clear cells with focal peripheral palisaded cells, necrotic foci, mitotic figures, abnormal mitosis, and areas of keratinization were seen in a fibrous stroma. Special staining of the tissue with Periodic acid- Schiff (PAS) and mucicarmine reagents showed positivity for PAS, but negative to mucicarmine.

Conclusion: This report emphasizes that patients with jaw lesions, whose histopathologic report show numerous clear cells, should be evaluated further, at least with special stains, and immunohistochemical staining to exclude other clear cell lesions including central mucoepidermoid carcinoma, which has clear cells (mucous cells) as a histopathological diagnostic feature.

Keywords: Clear cell odontogenic carcinoma, Mucoepidermoid carcinoma, Histopathology.

INTRODUCTION

Benign or malignant tumour of epithelial, mesenchymal, melanocytic, and haematopoeitic derivations may show clear cell changes.[1,2] Clear cell neoplasm of head and neck are rare and presence of clear cells are attributed to various factors, including artifacts, improper cellular preservation, hydropic degeneration of organelles, or due to accumulation of mucopolysaccharides, glycogen, mucin, lipids, phagocytosed foreign materials in the cytoplasm of tumour cells.[1,2]

Diagnosis of clear cell tumours of head and neck may be difficult and challenging due to these numerous factors. While most neoplasms with clear cell components show sufficient original characteristic and histomorphologic features that would enable the pathologist to render a precise and accurate diagnosis, a few others may not[1,2] Mucoepidermoid carcinoma has been reported to be the most common malignant salivary gland tumour.[3] Occurrence of central mucoepidermoid carcinoma in bone due to aberrant salivary glands is rare and accounts for 2-4% of mucoepidermoid carcinoma.[3]

There have been series of classifications of Odontogenic tumours by the WHO, the first being in 1971.[4] The latest edition of the WHO classification of odontogenic tumour was given in 2022, and just like the editions before it, it also adopted the format of the germ cell layer of origin such as epithelial, mesenchymal (ectomesenchyme) and mixed odontogenic tumors. It also divided odontogenic tumors into two categories, based on biologic behavior as malignant and benign.[5] Clear cell odontogenic carcinoma (CCOC) is a subset of the malignant groups of odontogenic tumours as specified in different editions of WHO classification of odontogenic tumours and it is a rare malignant odontogenic tumor with less than 120 cases reported in the jaws since it was first described by Hansen et al. in 1985.[5,6.] CCOC was previously thought to be a benign neoplasm, previously known as clear cell ameloblastoma. However, due to its aggressive clinical behavioural patterns, notable of which are - invasive growth, regional lymph node involvement, local recurrence, and distant metastasis, the WHO reclassified it as a malignant tumor of odontogenic origin from the 2005, 2017 and also in the 2022 classification.[5] CCOC has a preference for females in the 5th decade of life and for the mandible, with 73.8% of reported cases occurring in the mandible.[7]

Here, we report a case of Clear cell Odontogenic Carcinoma (CCOC) affecting the mandible, which mimics a central mucoepidermoid carcinoma in a 70year old female.

CASE REPORT

A 70-year-old female presented with a painless mandibular swelling of 5 months duration, which was rapidly increasing in size. She initially resorted to over-the-counter antibiotics and analgesics, with no useful relief, which made her present to us at the Dental center of the University of Benin Teaching Hospital (UBTH), Benin City, Nigeria. On examination, swelling was firm and measured 14 x 10 cm. Intraorally, swelling extended from the first lower left premolar to the retromolar region of the same side, with bucco-lingual expansion of the cortical plates (fig. 1) and mobility of associated teeth. There was no ulceration, however, the ipsilateral submandibular lymph node was hard and fixed to the underlying structures.

Radiographic review showed multilocular radiolucent lesion with hazy boarders (fig. 2). Microscopic examination of the incisional biopsy specimen revealed sheets, strands, and islands of

numerous clear cells in fibrous stroma. There were foci of peripheral palisaded cells, necrotic tissues, mitotic figures, abnormal mitosis, and keratin pearl formations (fig. 3). Provision diagnoses of Clear cell odontogenic carcinoma was made to rule out intraosseous Mucoepidermoid carcinoma. On special staining with Periodic acid- Schiff (PAS), and mucicarmine reagents, the tissue was positive to PAS, but negative to mucicarmine. A successful segmental resection of the mandible and the ipsilateral upper cervical lymph nodes was done and no recurrence seen so far. The histopathological findings of the post operative specimen were consistent with the incisional biopsy. There was no evidence of tumour invasion of the lymph nodes on histopathologic examination.

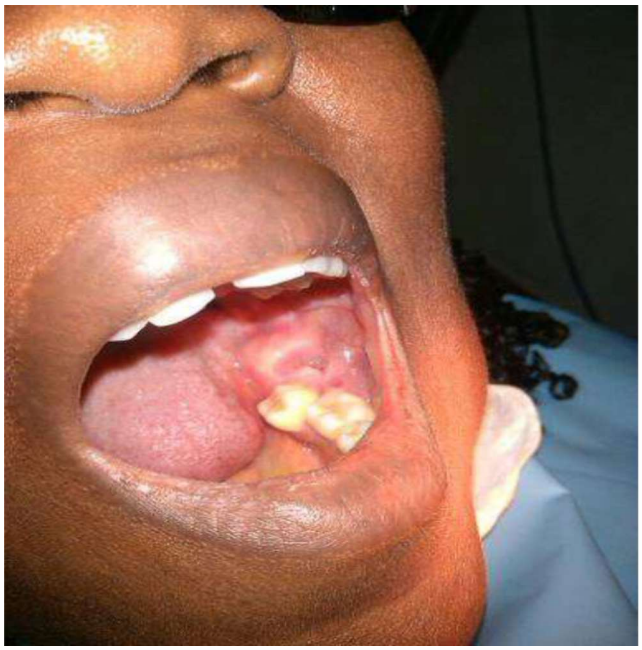

Fig. 1: Swelling in the left posterior mandible with bucco-lingual expansion.

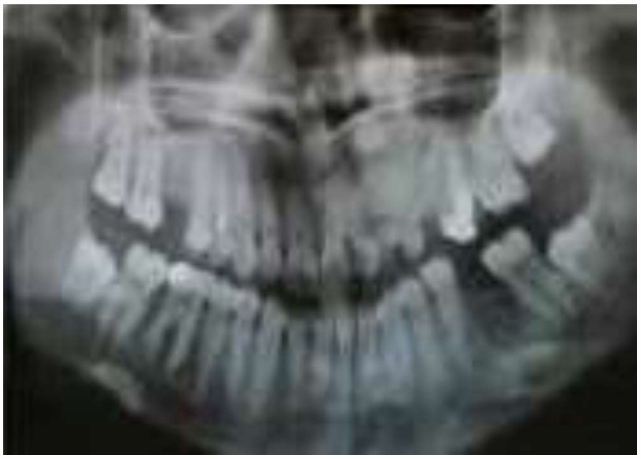

Fig. 2: orthopantomogram showing multilocular radiolucency with hazy boarders in the mandible

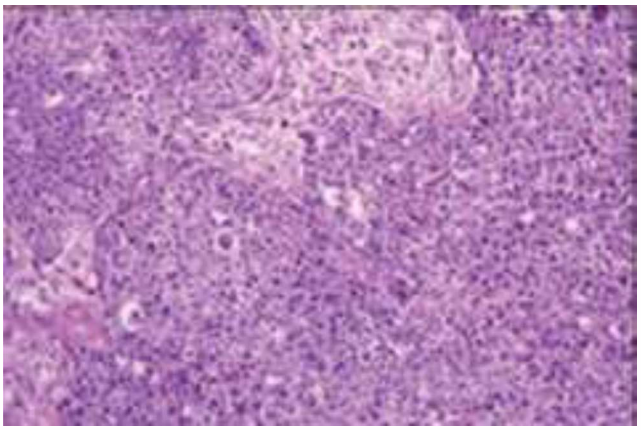

Fig. 3: section of CCOC showing sheets, strands, and islands of numerous clear cells with mitosis in fibrous stroma H&E x100

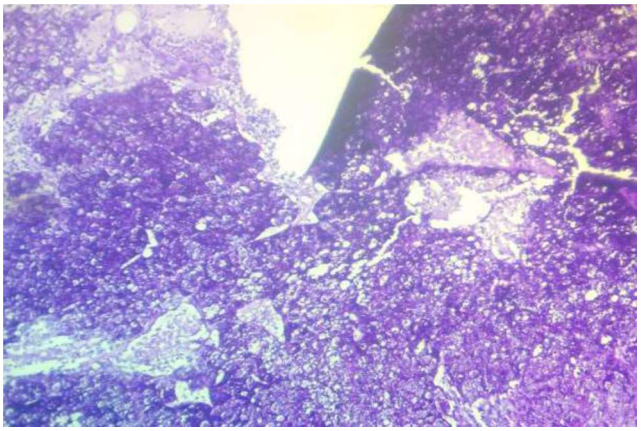

Fig. 4: CCOC showing PAS positivity H&E x100

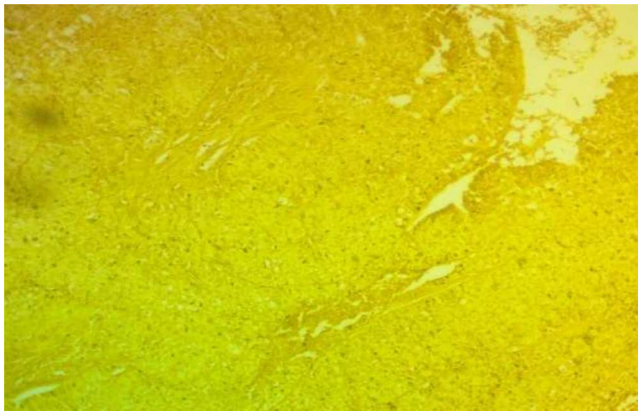

Fig 5: CCOC- mucicarmine negativity

DISCUSSION

Clear cells in a lesion could be from fixation artifacts, cytoplasmic accumulation of water, glycogen, lipids, mucins, hydropic degeneration of organelles and vacuolation of the cytoplasm. When increased number of clear cells are seen on histopathology, the definitive diagnosis may prove to be a challenge.[8] Clear cell odontogenic carcinoma, formally known as Clear cell odontogenic tumour (CCOT) and Clear cell ameloblastoma, was first reported by Hansen et al in 1985.[6] It was initially thought to be a benign neoplasm and since the malignant potential of CCOC had not been recognized at that time, CCOC was included under benign neoplasm arising from odontogenic epithelium without odontogenic ectomesenchyme in the 1992 WHO classification.[6,9]

Hansen et al[6] and Bang et al[9] were the first to employed the use of the term CCOC when they reported cases with pulmonary and lymph node metastasis in 1989. Emphasis was on early therapy due to the aggressive clinical behaviour of this tumour.[9] Patella et al.[10] corroborated with the findings of Bang et al[9], that this tumor could behave in an aggressive way and has true metastatic potential. This entity was hence considered distinct from clear cell variant of ameloblastoma which presents with similar clinical characteristics. Due to the aggressive clinical behaviour, predilection for local recurrence, evidence of distant metastasis and histologically distinct features, CCOT was designated as malignant tumor of odontogenic origin.[5,7,8]

The gender, age and site of the lesion in our case agrees with literature.[6,9,7] Okani et al in 2014 reported a case of maxillary CCOC in a 67-year-old woman in Middle Belt region of Nigeria.[11] The gender and the elderly age of their case agrees with our findings however, our case was a mandibular swelling. Histopathologic differentials of CCOC include the following tumours: salivary gland carcinoma such as Mucoepidermoid carcinoma, myoepithelial carcinoma, hyalinizing clear cell carcinoma; Odontogenic tumour such as clear cell variant of Calcifying epithelial odontogenic tumour (CCOT); melanotic tumour such as balloon cell melanoma; and metastatic lesions from renal, prostate, and thyroid carcinoma. Histopathologic findings in our report agrees with the literature,[7,9,10] however there was need to rule out other lesions with clear cell changes mostly intraosseous mucoepidermoid carcinoma which mimics CCOC within the bone This is because some of the cells seen in our case appeared epidermoid along with clear cells resembling mucous cells. We considered CCOC as the diagnosis and intraosseous Mucoepidermoid carcinoma as a differential diagnosis. Therefore, to confirm our diagnosis, there was need to separate one from the other using easy, rapid, reliable and readily available special stains, PAS and mucicarmine. This helped in determining the exact tumour.

The clear cells of the CCOC were negative for mucicarmine and that enabled us exclude intraosseous mucoepidermoid carcinoma in this case. Other salivary gland lesions with clear cell changes were excluded since this case was an

intrabony lesion. Also, there was no evidence of any distant primary lesion, therefore metastasis to the jaw from a distant site was excluded. Melanoma was also excluded because there were no atypical melanocytes seen (Table 1). The role of immunohistochemistry cannot be overemphasized when there is a need to separate a large number of differential diagnoses, as various antibody panels help in delineating the diverse tumours.[14,15] We did not employ immunostaining in our case because the clinical and histopathologic features of the case were enough to restrict our differentials to CCOC and Mucoepidermoid carcinoma.

The histopathological and immunohistochemical differentials of CCOC, and their distinguishing features[14,15] are shown in the table 1 below:

Table 1: Differential diagnoses of CCOC with their respective distinguishing features.

Differential diagnoses of CCOC of the Jaw	Distinguishing features
Odontogenic Tumour • Clear cell variant of Calcifying epithelial odontogenic tumour (CEOT)	• Presence of Liesgang's ring, Amyloid like deposits, and +ve Congo red staining.
Salivary gland Tumors • Mucoepidermoid carcinoma • Myoepithelial carcinoma • Hyalinizing clear cell carcinoma	• Variable presence of intermediate, epidermoid and mucous cells, +ve Mucin staining. • Presence of plasmacytoid, epithelioid and clear cells, and immunopositivity to calponin. • Stromal hyalinization with hyaline or myxoid degeneration, +ve to pancytokeratin and EMA.
Melanotic Tumour • Balloon cell melanoma	• Presence of atypical melanocytes with nodular proliferation of neoplastic balloon cells, +ve Masson-Fontana stain, Melan A and HMB-45.
Metastatic Tumours from: • Renal cell carcinoma • Prostatic carcinoma • Thyroid carcinoma	• Intratumoral hemorrhage and sinusoidal vascularity +ve hepatocyte antigen • High serum PSA • Thyroglobulin +ve

Surgery is the treatment of choice for CCOC although, there is tendency to recurrence after treatment.[14] This patient had surgery done and she is still under follow-up, with no clinical signs of recurrence seen thus far.

CONCLUSION

CCOC has been reported severally as an uncommon tumour that affects the jaws, the mandible more predominantly and in the elderly females mostly. The clinical findings and histopathologic features of our case is in keeping with CCOC. This tumour should always be considered in the differential diagnosis of clear cell lesions as it has the capacity to be aggressive and undergo metastases in cases. A long term follow up after surgery is necessary, since CCOC is notorious for recurrence.

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