Case Report

# Clear cell odontogenic carcinoma of maxilla: A diagnostic challenge

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## ABSTRACT

Clear cell odontogenic carcinoma (CCOC) is a rare odontogenic tumor which occurs mostly in the mandible. It is primarily seen in fifth to seventh decades with a female predilection. We report a case of CCOC in the maxillary arch of a 66-year-old woman. Morphologic examination along with histochemical and immunohistochemical markers led to the establishment of the diagnosis. It is important to diagnose this entity and differentiate it from other clear cell tumors in the head and neck region as it is a locally aggressive tumor with a propensity for regional, nodal, and distant metastasis.

**Key words:** Ameloblastoma, clear cell, clear cell odontogenic carcinoma, maxilla

## INTRODUCTION

Odontogenic neoplasms composed predominantly of clear cells are quite unusual and represent a diagnostic challenge. Odontogenic carcinomas are malignant epithelial odontogenic neoplasms which usually arise from the anterior region of the mandible and have a predilection for females.[1] Although initially being thought to be benign, because of their aggressive behavior, a predilection for local recurrence and evidence of distant metastasis, these tumors are now considered malignant.[2] We present a case of clear cell odontogenic carcinoma (CCOC) in the maxilla of a 66-year-old female.

## CASE REPORT

A 66-year-old woman presented with 3 months history of swelling in the right upper jaw which gradually increased in size. Local examination showed an ulcerated lesion in the right maxillary arch which was destroying the underlying bone [Figure 1a]. On computed tomography, a heterogeneous soft tissue mass lesion measuring 3 cm × 3.5 cm was found in the maxilla, causing the destruction of the alveolar process of maxilla and erosion of floor of the right maxillary sinus with dislocation of teeth [Figure 1b]. Cervical lymphadenopathy (Level 2) was also noted. A provisional diagnosis of ameloblastoma/squamous cell carcinoma was made and an incisional biopsy was performed. Microscopic examination revealed a tumor composed of sheets and nests of round to polyhedral cells having centrally placed nucleus with the prominent eosinophilic nucleolus and abundant clear to eosinophilic cytoplasm [Figure 2a and b]. The cells at the periphery of the nests occasionally demonstrated nuclear palisading away from the basement membrane, i.e., reverse nuclear polarity. The differential diagnoses that were considered included clear cell ameloblastoma, CCOC, intraosseous clear cell salivary gland tumors such as epithelial-myoepithelial carcinoma, mucoepidermoid carcinoma, and clear cell myoepithelioma. Tumor cells were periodic acid-Schiff (PAS) positive and diastase sensitive, thus confirming the glycogen content of the cytoplasm. The cells did not show positivity for alcian blue, ruling out mucoepidermoid carcinoma. On immunohistochemistry, tumor cells showed positivity for cytokeratin (CK)

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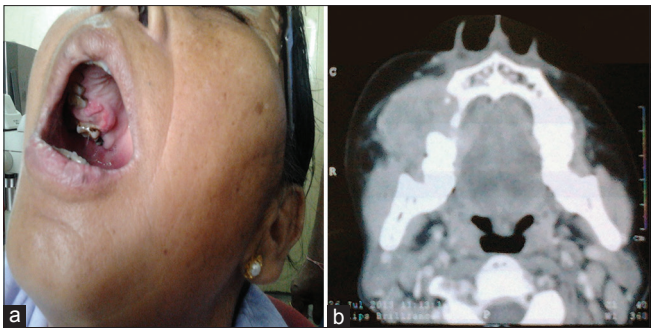

**Figure 1:** (a) Local examination showing an ulcerated lesion in the right maxillary arch. (b) Computed tomography showing a heterogenous soft tissue mass lesion in the maxilla

19 [Figure 2c] and epithelial membrane antigen (EMA). The cells were negative for vimentin and smooth muscle actin (SMA). Thus, epithelial-myoepithelial carcinoma and clear cell myoepithelioma were also ruled out. The possibility of metastasis was not considered as positron emission tomography scan did not reveal any active lesion elsewhere in the body. Based on the radiologic, histopathologic, histochemical, and immunohistochemical findings, a diagnosis of CCOC/clear cell ameloblastoma was rendered.

The patient underwent right hemimaxillectomy with ipsilateral functional neck dissection (Level 1–5). On gross examination, a tumor measuring 3.5 cm × 3 cm × 3 cm was found in the right maxilla [Figure 2d]. The tumor had an ulcerated surface and was gray white and firm in consistency. It was seen to involve the underlying bone. Postoperative histopathologic examination showed a tumor with morphology similar to that in the incisional biopsy. The diagnosis of CCOC was confirmed. All the resection margins (anterior, posterior, and lateral) were free of tumor. Lymph nodes isolated from the neck dissection specimen were also free from tumor infiltration. The postoperative period was uneventful, and the patient did not show any recurrence of tumor in 1 year of follow-up.

## DISCUSSION

CCOC, formerly known as clear cell odontogenic tumor, was first described by Hansen *et al.* in 1985.[3] According to 1992 WHO classification of odontogenic tumors, it was classified as a benign neoplasm with capacity for local invasion. However, owing to locally destructive and aggressive behavior with propensity for recurrences, nodal and distant metastasis, the latest WHO classification listed it as a malignant tumor of odontogenic origin.[1,2]

The peak incidence of CCOC is in the fifth to a seventh decade with a strong female predilection.[1,4] Most frequent site of occurrence is in the anterior segment of the jaw; with mandible being affected much more commonly than the

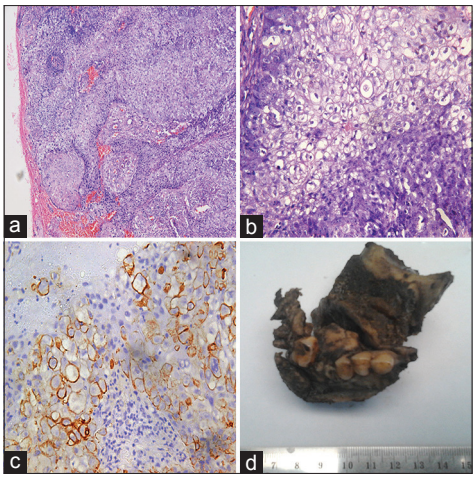

**Figure 2:** (a) Round to polyhedral tumor cells having centrally placed nucleus with prominent eosinophilic nucleolus and abundant clear to eosinophilic cytoplasm (H and E, ×100). (b) High power view of tumor (H and E, ×400). (c) Tumor cells positive for cytokeratin 19 (×400). (d) Gross examination showing a tumor in the right maxillary arch

maxilla. While most of the patients present with gingival swelling and loosening of teeth, other manifestations include delayed healing of wound after extraction of lower incisors, pain, and bleeding.[4,5]

Radiologically, the tumor is manifested as an ill-defined radiolucency with irregular margins. Aggressive tumor growth often results in root resorption.[5]

On histopathologic examination, CCOCs may exhibit the biphasic, monophasic, or ameloblastomatous pattern.[1,5] A biphasic pattern is most frequently seen with islands of epithelial cells in a fibrous stroma. The cells have clear to faintly eosinophilic cytoplasm due to the presence of cytoplasmic glycogen, well-demarcated cell membranes, and irregular nuclei. Mitoses and necrosis are unusual. The monophasic pattern comprises only of clear cells while the ameloblastomatous pattern resembles the growth pattern of ameloblastoma with nests of cells showing central cystic change and squamous differentiation, and peripheral nuclear palisading with reverse polarity.

Histochemically, many of the tumor cells contain abundant diastase degradable PAS-positive granules, but they are negative for mucin. The clear and eosinophilic tumor cells are consistently reactive for CK19 and EMA. They are negative for vimentin, S-100-protein, desmin, SMA, HMB-45, alpha 1-chymotrypsin and CD31.

The presence of clear cells in the tumors of oral cavity can be due to the cytoplasmic accumulation of water, glycogen, intermediate filaments, or immature zymogen granules.[6] Many benign and malignant tumors may present in the maxillofacial region with clear cell component on histopathologic examination [Table 1]. Odontogenic

**Table 1: Differential diagnoses of malignant clear cell tumors of the oral cavity**

| Differential diagnosis | Histopathologic features | Special stains/immunohistochemical features |
|---|---|---|
| Clear cell variant of calcifying epithelial odontogenic tumour (pindborg tumour) | Prominent amyloid deposition and calcifications in the stroma | PAS<br>Stains for amyloid |
| Mucoepidermoid carcinoma | Intermediate cells, squamous differentiation, and mucin production | Alcian blue |
| Epithelial-myoepithelial carcinoma | Biphasic tubular structure- outer clear and inner cuboidal cells | SMA in nonluminal cells<br>Calponin |
| Hyalinizing clear cell carcinoma of salivary glands | Hyalinising stroma | PAS |
| Metastatic renal cell carcinoma | Typical sinusoidal vascularity | Vimentin, EMA, CD10 and RCC |
| Metastatic liver, prostate, and thyroid carcinomas | Histopathological features characteristic of the primary tumour | Metatstasis from liver - HepPar, AFP<br>From prostate - PSA, PSAP, AMACR<br>From thyroid - TTF-1, CK19, thyroglobulin |
| Malignant melanoma | Prominent eosinophilic nucleoli | S-100, HMB-45, Melan A |
| Clear cell odontogenic carcinoma | Nests of clear cells, cells with eosinophilic cytoplasm and ameloblastoma like pattern | PAS<br>CK14 and CK19<br>EMA<br>Calretinin |

PAS: Periodic acid Schiff, SMA: Smooth muscle actin, EMA: Epithelial membrane antigen, RCC: Renal cell carcinoma, PSA: Prostate specific antigen, PSAP: Prostate specific acid phosphatase, AMACR: Alpha-methylacyl-CoA racemase, TTF-1: Thyroid transcription factor-1, CK: Cytokeratin

neoplasms composed entirely or predominantly of clear cells are rare and include odontogenic cysts, clear cell variants of calcifying epithelial odontogenic tumor (CEOT), ameloblastoma, and CCOC.[7] The diagnosis of CEOT showing clearing of cytoplasm can be made by the identification of psammomatous calcification and amyloid deposits. On the other hand, clear cell ameloblastoma might be difficult to distinguish from CCOC. Indeed, clear cell ameloblastomas and CCOCs have been thought to represent a clinicopathologic continuum of a single neoplastic entity by many authors.[3] Apart from tumors of odontogenic origin, the differential diagnoses of CCOC include salivary gland tumors with clear cell component, melanoma and metastatic tumors. In epithelial-myoepithelial carcinoma and myoepithelioma, the clear myoepithelial cells are immunoreactive for S-100 protein, vimentin, SMA, and calponin. Hyalinizing clear cell carcinoma of salivary gland has a characteristic hyalinized stroma, not seen in CCOC. In acinic cell carcinoma, clear cells usually do not comprise a significant proportion of the tumor. Mucoepidermoid carcinoma can be distinguished by its triphasic architecture comprised of mucin-positive mucous cells, squamoid cells, and intermediate cells. Metastatic tumors such as clear cell renal cell carcinoma can be identified by its characteristically rich vascular pattern and its immunoreactivity for CKs and vimentin. Melanoma reacts for HMB-45, S-100 protein, and other melanoma markers.

CCOC has been shown to exhibit aggressive behavior in terms of recurrence or metastases to regional nodes and distant sites.[3,8] Treatment strategies depend on size of lesion, location, soft tissue involvement and nodal or distant metastasis. Surgical control of CCOC with an en bloc resection of bone and any soft tissue involvement decreases the risk of recurrence. Adjuvant radiationtherapy helps in achieving local control in patients with extensive soft tissue or perineural invasion, and in cases with positive margins or positive nodes and/or extracapsular spread. Because of the potential for locoregional recurrence and/or late metastatic spread, long-term surveillance has been recommended.[8]

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### Conflicts of interest
There are no conflicts of interest.

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