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CASE REPORT

# Clear Cell Odontogenic Carcinoma: a Diagnostic Dilemma

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**A 26-year-old man presented with a swelling in the right side of face and CT scan revealed a destructive tumor in the right maxilla. Tumor recurred within 5 years of its excision and histopathological examination revealed a clear cell odontogenic carcinoma. The rarity of this tumor, occurrence in maxilla and young age of the patient are some of the rare features which need documentation. The importance of its diagnosis and various differential diagnoses are discussed.** (Pathology Oncology Research Vol 8, No 4, 283–285)

*Keywords:* clear cell odontogenic tumors, clear cell ameloblastoma, maxilla, young age

## *Introduction*

In the current WHO classification of odontogenic tumors, clear cell tumor is classified as a benign but locally invasive tumor.[1] However, high rate of recurrence, local and distant metastasis and tumor related deaths have lead to its reclassification as clear cell odontogenic carcinoma. This is an extremely uncommon entity and mostly reported in the form of case reports. We report a rare case of clear cell odontogenic carcinoma and various differential diagnoses are discussed.

## *Case History*

A 26-year-old man presented with history of loosening of teeth of upper jaw and swelling of right side of the face in July 1995. CT scan revealed an enhancing mass in the right maxilla. Patient underwent infrastructure maxillectomy at another hospital. Based on the histopathological diagnosis of squamous cell carcinoma, he received postoperative radiotherapy. In January 2000, he presented to this hospital with complaints of proptosis and decreased vision of 6 months duration. Examination showed proptosis and loss of vision in the right eye. Computerized tomography revealed a large enhancing mass in right maxillary sinus which was extending into subcutaneous tissue. Floor and medical wall of right orbit were eroded and this mass was extending into the right orbit. Eye ball was displaced upward and tumor was encasing right optic nerve (*Figure 1*). Right completion maxillectomy with orbital exenteration was done and specimen was subjected for histopathological examination.

### *Pathological examination*

Multiple sections examined from the specimen as well as review of the previous biopsy showed islands of cells separated by fibrocollagenous tissue (*Figure 2a*). The peripheral cells were somewhat columnar in shape with nuclear palisading and reverse polarisation resembling those seen in ameloblastoma (*Figure 2b*). The tumor islands were composed of clear cells with well-defined outlines and centrally placed nucleus (*Figure 2c*). Some foci of squamous differentiation were also noted in the central portion and spindling at the periphery of the tumor. Mitoses were rare and no necrosis was seen. In the recurrent tumor, invasion into the peripheral soft tissues and salivary gland was noted. Special stains for mucin were negative but PAS for glycogen was positive. Tumor cells were immunoreactive for cytokeratin (CK), epithelial membrane antigen (EMA) and S-100 protein but negative for vimentin.

The various differential diagnoses considered were squamous cell carcinoma, mucoepidermoid carcinoma, clear cell ameloblastoma and hyalinising squamous cell

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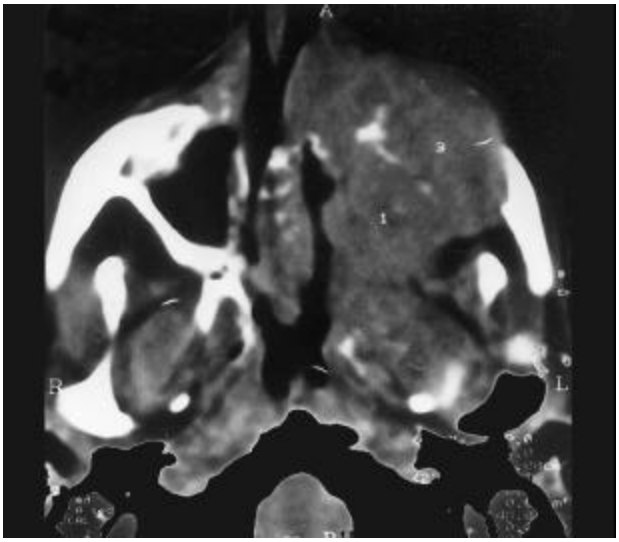

*Figure 1. CT scan head showing an enhancing mass in the right maxillary sinus which is destroying its wall.*

carcinoma. Peripheral palisading of nuclei with reverse polarization,absence of stellate cells, low mitotic activity and negativity for mucin stains ruled out these diagnoses.

### *Discussion*

Clear cell odontogenic tumor with some features of ameloblastoma was first described by Hansen et al[2] and later by Waldron et al.[3] They described an aggressive potential for this tumor. Some authors[3,4] regard clear cell ameloblastoma and this tumor as synonyms. Muramatsu et al[5] in their review of literature of 19 cases (including one new case) concluded that the age ranged from 14 to 89 years (mean 55.6 years) with a peak frequency in the sixth decade of life. Of the 19 patients, 12 were female and 7 were male. Majority of the cases occurred in the anterior region of mandible and the involvement of maxilla was rare. Local recurrence was a common finding and the cytologic atypia appeared to worsen with recurrence[6]. Rarely this tumor can metastasize to regional lymph nodes and lungs,[7,8,9,10,11] and even tumor related deaths have been described.[3,7,8]

Three histomorphologic patterns are described.[12] The commonest pattern is a biphasic tumor characterized by oval and linear nests of clear cells intermixed with smaller islands of polygonal cells with eosinophilic cytoplasm. Occasionally these two cell-types co-exist in a tumor nest yielding a “glomeruloid” appearance. The second variant is represented by islands that show only the clear cell phenotype whereas the third and least common variant is comprised of clear cell nests with a tendency for ameloblastoid palisading around the periphery. The tumor under discussion belongs to the latter category. The stroma of CCOC is destructive; fibroblastic cellularity is high and the collagen is mature, wrapping around the tumor cells.[12]

The immunohistochemical profile of this tumor suggests that this is of odontogenic epithelial origin. In addition the presence of eosinophilic hyaline fibrillar dentin/bone like structures between tumor cell nests and fibrous stroma

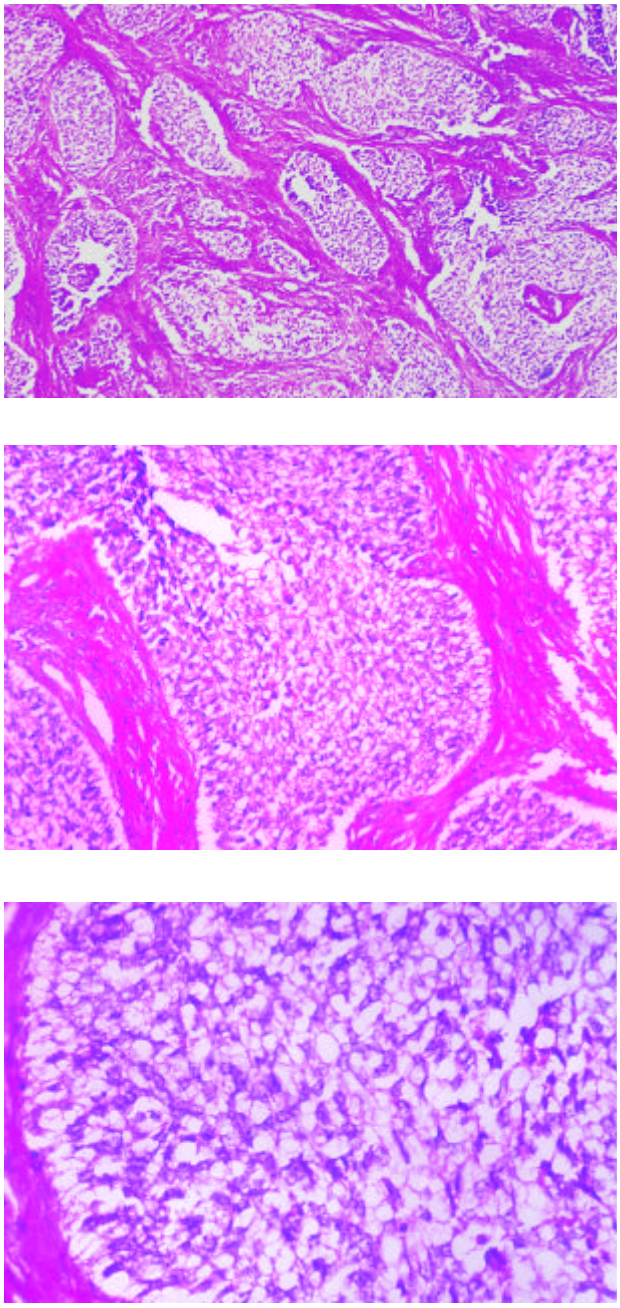


*Figure 2. Photomicrographs showing islands of tumor cells separated by fibrocollagenous fibrous septae (a) (HE X40). Higher magnification showing reverse polarisation of nuclei near the fibrous septa (b) (HE X100). Higher magnification of the same showing sheets of cells with clearing of the cytoplasm (c) (HE X200).*

also suggests that some of the tumors possess epithelial – mesenchymal inductive capacity, a feature shared by many odontogenic epithelial tumors.

Tumors with a conspicuous clear cell component in the head and neck region can impose serious problems with respect to differential diagnoses. They can originate from other other structures like odontogenic epithelium, salivary–glands and melanocytes. Some metastatic tumors especially renal cell carcinoma should be considered in the differential diagnosis.

Intraosseous mucoepidermoid carcinomas of the jaws are unusual but are not rare and selected tumors that are almost exclusively composed of clear cell elements may be encountered. Careful search for intermediate cells, demonstration of mucin and immunohistochemical staining (positivity for smooth muscle actin, S-100 protein and vimentin in addition to cytokeratin) help in arriving at a definite diagnosis. CCOC can be distinguished from the clear cell variant of calcifying epithelial odontogenic tumor because it lacks the characteristic calcification and amyloid deposition. Occasionally, melanocytic tumors may show a predominant clear cell component, but most of these tumors arise in the soft tissue and they have been described only rarely in the head and neck. In addition they show positivity for S-100 protein and melanoma associated antigen (HMB-45). Typical ameloblastomas containing clear cells but not showing features of malignancy or an unusual degree of aggressiveness may arise both centrally and peripherally.[13,14] It is uncertain whether these tumors are related to CCOC, many of which also show a degree of ameloblastomatous differentiation.[3] It is always appropriate to rule out metastasizing disease when clear cell tumors of the jaws are encountered. Renal cell carcinoma has a rich vascular pattern, areas of haemorrhage and the tumor cells are positive for cytokeratin and vimentin.

To conclude,CCOC is a low grade malignancy with frequent recurrences and has the potential of regional and distant metastases. It should be differentiated from squamous cell carcinoma and other clear cell tumors of the head and neck region.

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