Calcifying cystic odontogenic tumor associated with Unicystic Ameloblastoma: A unique entity – A Case report

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ABSTRACT

Calcifying cystic odontogenic tumour (CCOT) is a benign cystic neoplasm of odontogenic origin which involves association of a cyst (COC) with odontogenic tumors. CCOT demonstrates diverse histopathology and variable clinical behaviour. We report a case of CCOT associated with unicystic ameloblastoma in a 15 year old male.

Key Words - odontogenic cyst, tumor, unicystic ameloblastoma.

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INTRODUCTION

Calcifying odontogenic cyst (COC) is considered to be an uncommon cyst and accounts for only 1% of the reported jaw cysts.[1] Because of its diverse histopathology, there has always been confusion about its nature as a cyst, neoplasm or a hamartoma.[2].According to the new World Health Organization (WHO) classification (2005) it has been reclassified as calcifying cystic odontogenic tumors (CCOT). Calcifying cystic odontogenic tumour (CCOT) is a benign cystic neoplasm of odontogenic origin which involves association of a cyst (COC) with odontogenic tumors such as odontome , adenomatoid odontogenic tumor or ameloblastoma.[3]CCOT demonstrates variable clinical behavior and about 65% of cases are found in the incisor and canine areas with the mean age being 33 years.[4] Radiographically, CCOT may present as unilocular or multilocular radiolucency with discrete radiopacities and a well demarcated margin[5] .

In this paper, we report a case of CCOT associated with Unicystic ameloblastoma

CASE REPORT

A 15 year old male patient reported with the chief complaint of pain and swelling in anterior lower jaw since 3 months. There was discomfort during chewing of food. The growth of the swelling was slow and gradual.

Extra orally, the swelling extended from symphysis to left body of mandible (Figure 1). On palpation the swelling was firm and tender. There was no associated lymphadenopathy.

Figure 1: Diffuse extraoral swelling of mandible on the left side of mandible.

Intraoral examination revealed a diffuse intrabony swelling bicortically in the mandible, obliterating left buccal vestibule. It extended from 43 to 36.

The swelling was approximately 3X1 cms in size (Figure 2). There was displacement of 31 and 32 (Figure 3).

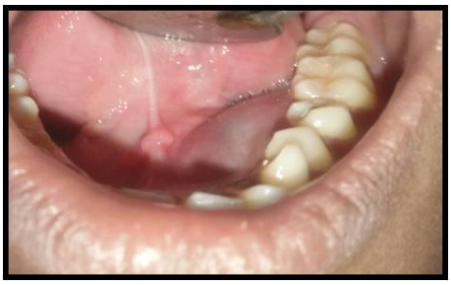

Figure 2: Intrabony swelling on left lingual side of the mandible.

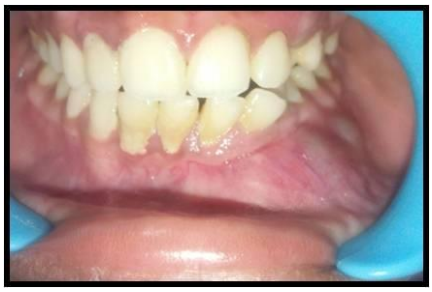

Figure 3: The diffuse intrabony swelling of the mandible obliterated the left buccal vestibule and displaced the anterior teeth on

the left side.

Radiographic examination disclosed a multilocular radiolucency with radio-opaque flecks. Impacted 33, displacement of roots of 31,32, 41, 42 and RCT in relation with 41, 42, 43, 31, 32, 34, 35 were noticed (Figure 4).

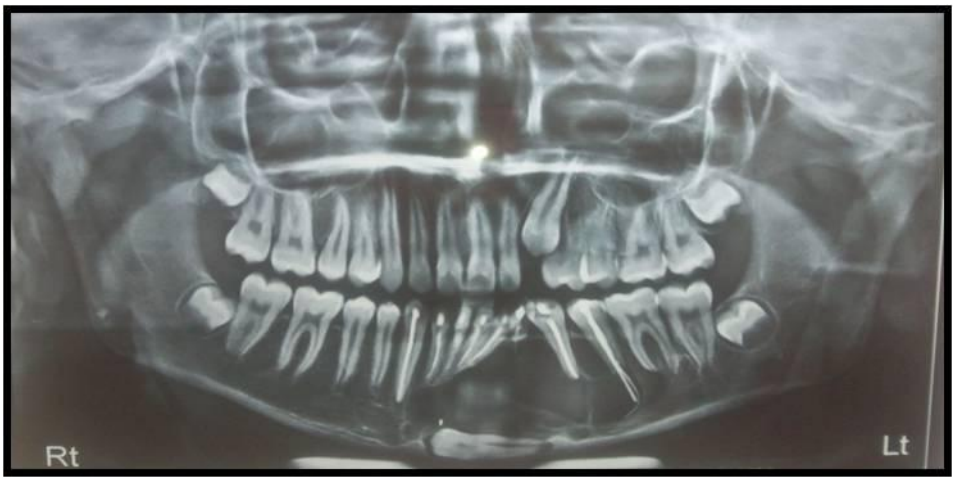

Figure 4: Orthopantamograph showed well defined multilocular radiolucency with radio-opaque flecks extending from lower right canine to lower left first molar. Impacted 33, displaced root of lower anteriors and RCT in relation with 41, 42, 43, 31, 32, 34, 35.

A differential diagnosis of unicystic ameloblastoma and keratocystic odontogenic tumor was made.

An incisional biopsy was done under local anaesthesia and paraffin embedded sections were stained with H and E and analysed for histopathological examination.

Microscopically H & E stained sections showed a cystic cavity lined by thin odontogenic epithelium with a prominent basal layer showing palisaded cells. In areas, epithelium was thicker showing groups of ghost cells towards the cystic lumen (Figure 5).

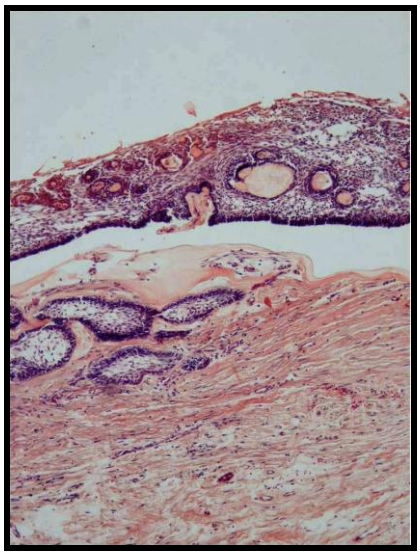

Figure 5: The thicker areas of epithelium with groups of ghost cells towards the cystic lumen

Budding from the basal layer into the adjacent connective tissue, strands of odontogenic epithelium and follicles were seen (Figure 6).

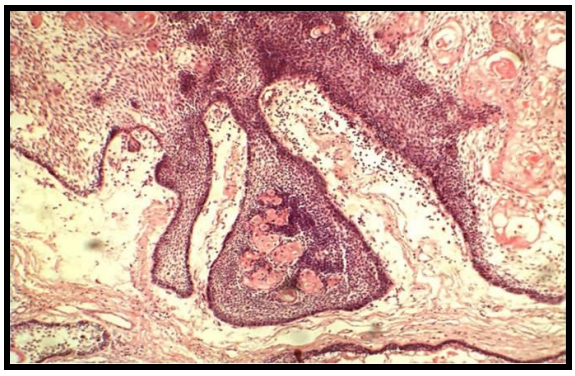

Figure 6 : The presence of ghost cells in the ameloblastomatous epithelial islands

The follicles had peripheral ameloblast- like cells and central stellate reticulum- like cells. Ghost cells were seen in most of the large follicles (Figure 7).

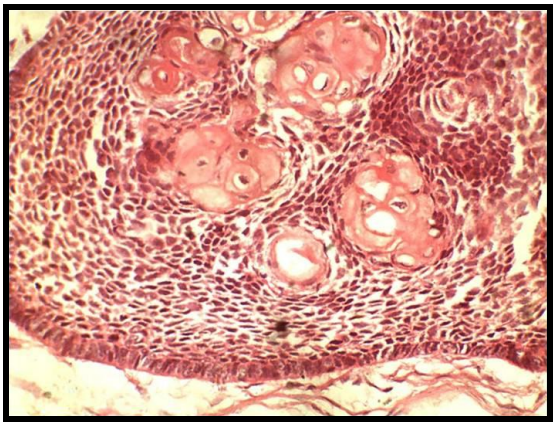

Figure 7: High power showing ameloblastic follicle with ghost cells and lined by preameloblast like cells

The connective tissue showed mild chronic inflammation and extravasated blood elements. Histopathological diagnosis of CCOT associated with Unicystic Ameloblastoma was made. The excisional biopsy of the lesion revealed features consistent with the histopathology of the incisional biopsy and the diagnosis of CCOT associated with Unicystic Ameloblastoma was confirmed.

DISCUSSION

Calcifying odontogenic cyst (COC) was first categorized as a distinct entity by Gorlin *et al.* in 1962.[1] . Since then it has been recognized to include various subtypes that show diversity in clinical and histopathological features as well as in biological behaviour.[6] The pronounced peak frequency of COCs is in the second decade.[7,8] COC usually occurs intraosseously and may also occur extraosseously. COCs are primarily cystic in nature and appear to be non neoplastic. But they can also appear as solid lesions; at least some of which are neoplastic in nature. A rare malignant variant also exists. [6,9,10]

Buchner[7] noted that 24% of reported cases of COCs were associated with odontomas. Other reports have shown that COCs often coexist with other odontogenic tumours, such as ameloblastoma, ameloblastic fibroma, ameloblastic fibro-odontoma and so on[7,10,11] . In the WHO Classification of head and neck tumors published in

2005[12], classification of COC has been given on the same basis.

WHO 2005 CLASSIFICATION

GROUP 1	Simple cysts with or without limited proliferation of odontogenic epithelium on the cyst wall.	Calcifying odontogenic cyst (COC)
GROUP 2	Cysts associated with odontogenic hamartomas or benign neoplasms	The following combinations have been published -
		Solid/multicystic ameloblastoma associated CCOT
		Unicystic ameloblastoma associated CCOT
		Adenomatoid odontogenic tumor associated CCOT
		Ameloblastic fibroma associated CCOT
		Ameloblastic fibro-odontoma associated CCOT
		Odonto-ameloblastoma associated CCOT
		Odontoma associated CCOT
		Odontogenic myxofibroma associated CCOT
GROUP 3	Solid benign odontogenic neoplasm with similar cell morphology to that in the COC, and with dentinoid formation	Dentinogenic ghost cell tumor (DGCT)
GROUP 4	Malignant odontogenic neoplasms with features similar to those of the dentinogenic ghost cell tumor	Ghost cell odontogenic carcinoma (GCOC)

Amongst all neoplasms associated with CCOT, ameloblastoma is the most prominent tumor. A classification advocated by Hong *et al*. has two categories for COC associated with ameloblastoma: the ameloblastomatous cystic and the neoplastic variant. The former is characterized by a unicystic structure in which the lining epithelium shows unifocal or multifocal proliferative activity that resembles ameloblastoma. It also shows the presence of isolated or clustered ghost cells and calcifications.

On the other hand, the latter neoplastic variant is called ameloblastoma arising from CCOT (ameloblastoma ex

CCOT)[13] and is extremely rare. It is characterized by few or no ghost cells with calcification in the transformed ameloblastomatous epithelial portion, while the cyst lining of the epithelium contains considerable number of ghost cells and calcifications.[13,14] . In the study of 92 cases carried out by Hong et al,[13] only 2 were ameloblastoma ex CCOT and 11 were ameloblastomatous CCOTs. Now all these cases are considered as CCOT associated with Unicystic ameloblastomas [15].

Table 1 Cases of Unicystic ameloblastoma associated CCOTs

Author	Year	No. of cases	Age/Sex	Site
1. Hong et al.	1991	11	10-30 /M-F both	Posterior mandible
2. D.Aithal et al.	2003	1	28/F	Left posterior region of mandible
3. S.Iida et al.	2004	1	17/F	Right body of mandible
4. Mashhadi et al.	2009	1	13/F	Left ramus of mandible
5. N.Kamran et al.	2009	1	22/F	Right molar region of mandible

Ghost cells are epithelial cells which are swollen, pale eosinophilic cells. They are seen either singly or in sheets with a clear conservation of basic cellular outline (if not fully coalesced), generally with apparent clear areas or with some remnants indicative of the site previously occupied by the nucleus. These cells lack nuclear and cytoplasmic details and are characteristically seen in calcifying cystic odontogenic tumors (CCOT), craniopharyngiomas and pilomatricomas. Ghost cells have a shadowy appearance in hematoxylin‑eosin stained sections and hence the name. Whether odontogenic or non odontogenic pathology, ghost cells are always epithelial in origin without exceptions.

Gorlin, *et al.* Gold and others believed that these can originate from any layer of epithelium i.e., basal, intermediate or superficial. On the basis of differentiation of epithelium, it can arise from squamoid or stellate reticulum‑like cells, as seen in CCOT. Ghost cells do not show intercellular junctions. The

transformation of epithelial cells into more resistant terminally differentiated apoptotic cells i.e., ghost cells are responsible for the banal behaviour of neoplasms and they also help in relieving the stress of the forming neoplasm.[16]

Because of the rarity of CCOTs associated with Unicystic ameloblastoma, determination of the most common age, sex and location of this lesion is difficult. According to case reports in the literature, as shown in Table 1., it is seen that most of the patients are between 10 to 30 years of age, and the tumor tends to involve the posterior region of the mandible.

No sex predilection has been noted.[2,11,12] Radiographically, CCOTs generally appear as a unilocular lesion with a well-defined margin. The presence of calcifications, which are observed in about half of them,[2,7] is the most important radiographic feature for the diagnosis of CCOTs.

In the present case, radiograph revealed a multilocular radiolucency with radiopaque flecks extending from mesial aspect of 43 to distal aspect of 36. This is consistent with the reports noted in literature so far with respect to site and age of patient. Histopathologically, the present case was diagnosed as CCOT associated with Unicystic Ameloblastoma due to the presence of ghost cells in the ameloblastomatous epithelial proliferations [15].

It is very difficult to determine whether any lesion having a cystic architecture is truly cystic or neoplastic in nature. Hence perhaps the most important consideration regarding ameloblastomatous CCOT is the biological behaviour. Whether these tumours have the same destructive potential and propensity for recurrence as a typical ameloblastoma is unknown. However Buchner [7] suggested that if the CCOT was associated with an ameloblastoma, its behaviour and prognosis would be that of an ameloblastoma, not that of COC. In some cases of ameloblastomatous CCOT, special diagnostic techniques like an IHC study was performed.

Immunohistochemically, there was no difference in amelogenin or CK19 expression among COC with various histological features; there was only a slight difference in bcl-2 and Ki-67 expression. [17,18,19] Bcl-2 positivity was

found to be more in CCOT with an odontoma than in those without an odontoma. CCOT with ameloblastomatous, proliferative type and odontoma associated CCOTs had higher expression of Ki-67.[20,21]An extensive and systematic analysis of many more cases including immunohistochemical investigations on cell proliferation activity may help resolve this problem.

After surgery our case was followed up for a period of 6 months until which there was no evidence of any recurrence. After this the patient did not report for follow-up. There is no doubt that long-term follow-up is mandatory and careful postoperative observations are necessary in such cases.

CONCLUSION

COC is a cyst lined by odontogenic epithelium exhibiting ghost cell keratinization and calcification, with or without areas of epithelial-mediated induction of dental hard tissues. According to Basile et al, the constitutive activation of beta-catenin/TCF-mediated transcription is known to play a role in human oncogenesis and may be important in the development of COCs as well. It is therefore possible that the COC is a "cystic neoplasm". And hence WHO 2005 classifies it as CCOT. Very few cases of CCOT associated with Unicystic Ameloblastoma have been documented in literature; previously these were reported as ameloblastomatous CCOT. Since this case describes CCOT with Unicystic ameloblastoma it could also be considered as a hybrid odontogenic tumor.

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