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Research Article

UNUSUAL VARIANT OF CALCIFYING CYSTIC ODONTOGENIC TUMORS – REPORT OF 3 CASES AND REVIEW OF DIAGNOSTIC AND THERAPEUTIC APPROACH

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A B S T R A C T

Calcifying cystic odontogenic tumor (CCOT) is defined as a benign cystic neoplasm of odontogenic origin, characterized by ameloblastoma-like epithelium, with ghost cells within the epithelial lining or fibrous capsule that may undergo calcification. The calcifying odontogenic cyst (COC) account nfor only 1%-2% of all odontogenic tumors, and only 2%-14% of all COCs are solid tumors. Dentogenic ghost cell tumor is a solid neoplastic clinicopathological variant of COC and a rare odontogenic tumor. Owing to its rarity, there are few clinical series evaluating the biological behavior of COC and its variant. The aim of this case series is to present the surgical management of calcifying cystic odontogenic tumors and find out whether conservative approach (Enucleation with peripheral osteotomy followed by chemical cauterization) is sufficient for the management of CCOT instead of surgical resection of tumor. In parallel, clinical and radiographic findings as well as histological features are outlined and discussed along with review of the existing literature.

INTRODUCTION

Calcifying cystic odontogenic tumor (CCOT) is defined as a benign cystic neoplasm of odontogenic origin, characterized by ameloblastoma-like epithelium, with ghost cells within the epithelial lining or fibrous capsule that may undergo calcification.[1] The calcifying odontogenic cyst (COC) was first recognized as a distinct clinicopathological entity in 1962 by Gorlin *et al*.[2] COCs account for only 1%-2% of all odontogenic tumors, and only 2%-14% of all COCs are solid tumors. Dentinogenic ghost cell tumor (DGCT) is a solid neoplastic clinicopathological variant of COC and a rare odontogenic tumor.[3]

There are numerous names for calcifying odontogenic cyst (COC), Dentinogenic ghost cell tumor (DGCT), and Ghost cell odontogenic carcinoma (GCOC), depending on the different terminology and classification of this group of lesions.[4] The present case was classified according to the latest criteria proposed by the World Health Organization.[5] This case series include a case of CCOT with odontome, CCOT with ameloblastic proliferation and extremely rare dentinogenic ghost cell carcinoma.he aim of this case series is to present the surgical management of calcifying cystic odontogenic tumors and find out whether conservative approach (Enucleation with peripheral osteotomy followed by chemical cauterization) is sufficient for the management of CCOT instead of surgical resection of tumor. In parallel, clinical and radiographic findings as well as histological features are outlined and discussed along with review of the existing literature.

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Case report 1

A 22-year-old female patient reported to the department with complaint of pain and swelling since 6 months where extraorally pus draining sinus was seen and tenderness was present on left angle region of mandible. Intraorally 38 was impacted and tenderness was present distal to 37. Panoramic radiographs (Fig. 1) revealed a radiopaque mass of approximately 3×3cm distal to 37 suggestive of complex odontoma. Impacted 38 was seen with radiolucency in pericoronal region suggestive of follicular space, dentigerous cyst or CCOT with odontome.

Under local anesthesia, the cyst and odontome were nucleated, third molar was extracted along with peripheral osteotomy and chemical cauterization was done. The specimen was sent for histopathological examination. The microscopic specimen of the cystic lining showed cystic lumen which was partly lined by odontogenic epithelium. Basal cells were columnar to cuboidal with hyperchromatic nuclei (Fig. 2A). Suprabasally ghost cells showed eosinophillic cytoplasm and remnants of nuclear membrane were seen and the specimen of calcified structure which was encapsulated showed mature dentine cut in T.S and L.S. At places, there were empty spaces resembling enamel and denticles consisting of dentine surrounded by rim of basophilic cementum like tissue at the periphery (Fig 2B).

Dentin enclosed loosely arranged connective tissue composed of collagen fibre bundles and endothelial lined blood vessels resembling pulp tissue. All these features are suggestive of CCOT with odontome. On two year of follow up, there weren't any signs of recurrence.

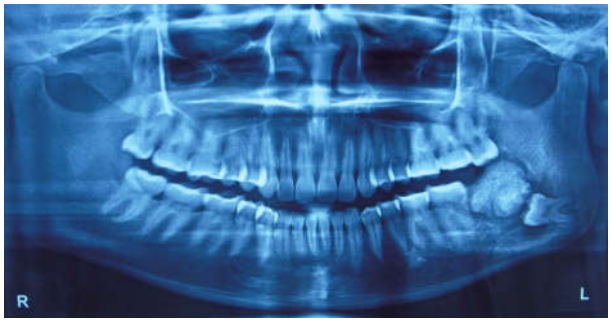

Figure 1 OPG revealed radiopaque mass distal to 37 suggestive of complex odontoma and Impacted 38 with radiolucency in pericoronal region.

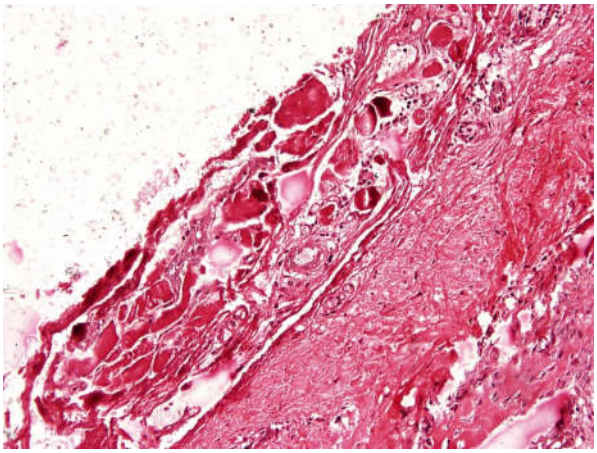

Figure 2A histologic features obtained, revealing cystic lining showed cystic lumen and columnar to cuboidal basal cells with hyperchromatic nuclei (Haematoxylin–eosin (H–E), 10x)

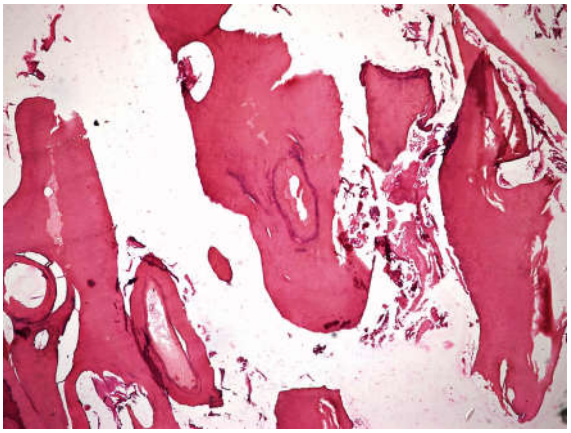

Figure 2B Histologic features obtained, enamel like spaces and denticles consisting of dentine surrounding by rim of basophilic cementum like tissue at the periphery (Haematoxylin–eosin (H–E), 4x)

Case report 2

A 41-year-old male patient reported to Department with complaint of swelling in submental region of mandible since 20 days (Fig. 3). Extraorally, diffuse firm swelling was present on anterior region of mandible. Intraorally, a well-defined swelling present on lower anterior region approximately 3×3cm in size extending from 33 to 43 with obliteration of labial vestibule and expansion of both cortical plates. On palpation, swelling was firm and nontender. Panoramic radiographs (Fig. 4) revealed well defined multilocular radiolucency with corticated border in the anterior region of mandible extending from 36 to 45 with very thin sparsed septa between the radiolucency. Loss of lamina dura with 36. Intraoral incisional biopsy was performed under local anesthesia and sent for histopathological examination. The histopathological features were suggestive of calcifying cystic odontogenic tumor.

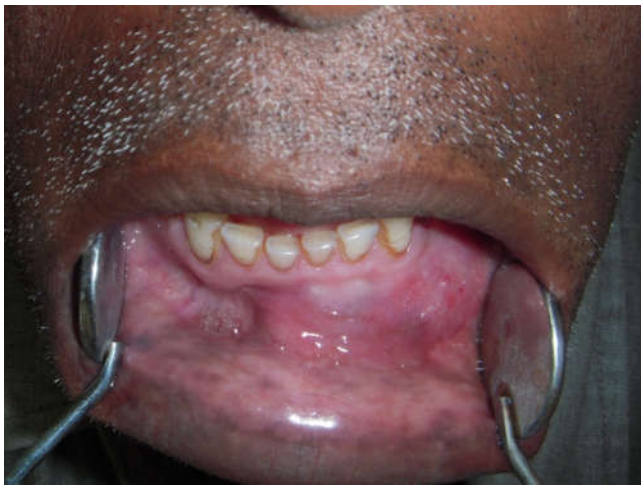

Figure 3 Intraoral photograph showed swelling over submental region.

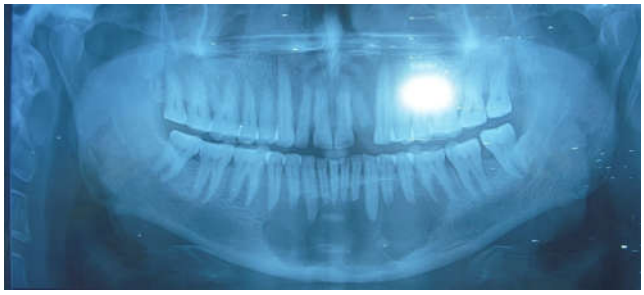

Figure 4 OPG revealed well defined multilocular radiolucency with corticated border in the anterior region of mandible.

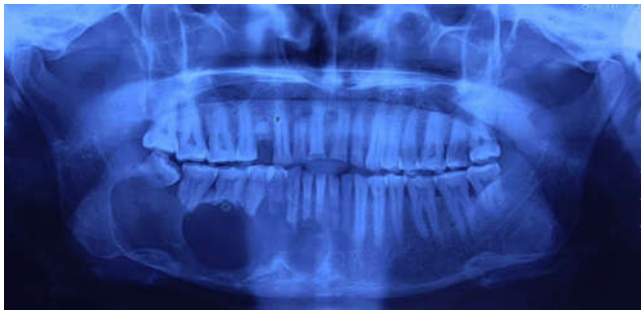

Figure 5 A and B Radiographic views of the initial lesion and after 24 months of enucleation.

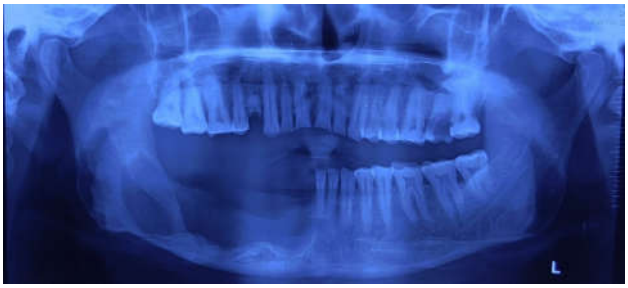

Figure 5 B

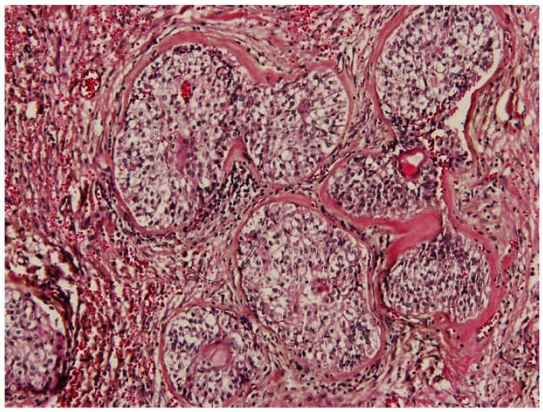

Figure 6A histologic features obtained, revealing irregularly placed ameloblastic follicle some areas showing ghost cell differentiation with nuclear remnant within the follicles

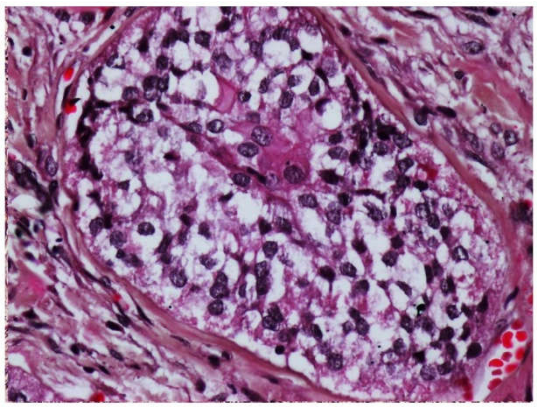

Figure 6 B histologic features obtained, revealing the peripheral cells of these follicles are low cuboidal with hyperchromatic nuclei and the loosely arranged stellate reticulum like cells

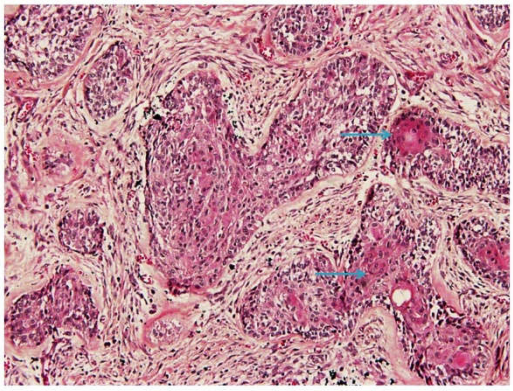

Figure 6C histologic features obtained, revealing areas showing ghost cell differentiation with nuclear remnant within the follicles

Under local anesthesia enucleation of lesion and extraction of 31,32,33,34,35,36,41,42,43,44,45 with peripheral osteotomy followed by chemical cauterization was performed. The specimen was sent for histopathological examination. The microscopic examination showed cystic lumen lined by odontogenic epithelium. Basal cells were columnar to cuboidal with hyperchromatic nuclei and reversed polarity resembling the ameloblasts. Suprabasally loosely arranged epithelial cells resembling stellate reticulum were present. At certain places lining epithelium showed squamous metaplasia and ghost cells. Surrounding connective tissue capsule was well organized. Subepithelially hyalinization was also present. At the periphery irregular bony trabeculae with osteocytes within lacunae and muscle fibers were present. Lining epithelium showed proliferation towards the capsule. Also in the connective tissue capsule, amelobastomatous proliferation was seen at 1-2 sites with dentine like material (dentinoid material) suggestive of CCOT with ameloblastic transformation. On two year of follow-up, no recurrence was seen.

Case report 3

A 35 years old man reported to Department with complaint of pain and rapid expansion of a mass located on the buccal vestibule of the right mandible during the previous four weeks. Extraorally there was a hard immobile mass extending from corner of mouth to mid body region of mandible anteroposteriorly. The overlying skin was smooth and normal. Cervical lymph nodes palpable and enlarged. Intraorally an expansive non-fluctuant mass of 7cm × 4cm in the right mandible with expansion of buccal and lingual cortical plate involving teeth from right lateral incisor to first molar. Mobility of teeth present with first and second premolar with no ulceration of the overlying mucosa and without neurological symptoms. Panoramic radiographs (Fig. 5A) revealed large mixed radiopaque-radiolucent lesion in right body region of mandible extending from 42 to 48 associated with 44, 45 and 46 root resorption. CBCT showed a huge expansive lesion with dimensions of 80 x 32 x 34 mm. Perforation of buccal and lingual cortical plate was seen. Intraoral incisional biopsy was done under local anesthesia. The histopathological examination was suggestive of infected odontogenic cyst.Based on these histopathological diagnosis, but keeping in mind the aggressive nature of the lesion, enucleation and curettage was done under local anesthesia with clear margin by peripheral osteotomy with removal of 0.5cm peripheral bone followed by chemical cauterization with Cornoy's solution. The patient was followed up for 06 months with no evidence of recurrence or distant metastasis.

Entire specimen was sent for histopathological evaluation. The sample measured 5.8 x 5.4 x 4cm which consisted of one of the bits of tissue showed irregularly placed ameloblastic follicle (Fig. 6A). The peripheral cells of these follicles are low cuboidal with hyperchromatic nuclei and the loosely arranged stellate reticulum like cells (Fig. 6B). Certain areas show desmoplastic changes with compressed and highly irregular bizarre ameloblastic follicles. At few sites, deposition of dentinoid surrounding the follicles is also seen, with some areas showing ghost cell differentiation with nuclear remnant within the follicles (Fig. 6C). At places, cells within the follicles show cellular and nuclear pleomorphism with hyperchromatic nuclei and 1-2 bizarre mitosis showing malignant changes. In our case the diagnosis of GCOC was possible only after the resected specimen was carefully examined histologically. On two year of follow up, there weren't any signs of recurrence.

DISCUSSION

The calcifying odontogenic cyst (COC), described separately by Gorlin *et al*' in 1962[2] and by Gold in 1963, is derived from odontogenic epithelial remnants within the mandible or maxilla, or from the gingiva.[6] With time, it became apparent that not all COCs are cysts, and that some, in fact, appeared as a solid neoplasm. In 1981, Praetorius[7] *et al* tried to resolve the

enigma of the proper classification of COC by dividing it into 2 types, cystic and solid neoplastic. The cystic type was further classified into 3 subtypes: simple, associated with odontoma and associated with ameloblastomatous proliferation. They proposed the term "dentinogenic ghost cell tumor" (DGCT) for the neoplastic type. In 2005, the WHO panel on odontogenic tumors decided to consider both types of COC as tumors and divided them into 2 separate entities, renaming COC as a calcifying cystic odontogenic tumor (CCOT) and retaining the term DGCT for the neoplastic type .[8]

CCOT usually occurs in adults for which mean age was 34 years with no gender predilection.[9] Odontogenic ghost cell tumors are the rare solid neoplastic variant of the calcifying odontogenic epithelial cyst (COC). The clinical features of OGCC are not specific. This differs from benign CCOT, which has the mean age of patients with DGCT was 39.7 years and the highest frequency was between the 3rd to 5th decades with male predilection. Moreover, DGCT showed no particular predilection for either the mandible or the maxilla, similarly to CCOT[10]. However, while the posterior region of the jaws was the most common site for DGCT, the anterior region was the most common site for simple CCOT[9].

Radiographically, most DGCTs appeared as unilocular radiolucent-radiopaque with well-defined borders. However, there were also some radiolucent lesions and some multilocular lesions, and about one-third showed partially defined or poorly defined borders. These radiographic features are similar to those of simple CCOT[9], except that DGCT exhibits relatively more lesions with partially defined or ill-defined borders.[10] The histological features include an epithelial lining showing a basal layer of columnar cells and an overlying layer of stratified cells resembling stellate reticulum; there are also masses of ghost cells in the cyst lining, within the cyst or both. The ghost cells may also show calcification. The surrounding stroma is composed of an irregular mass of 'dentinoid' eosinophilic collagenous matrix that lacks the tubular structure of normal dentin.[11,12] With time, it was shown that these lesions might in addition have a solid neoplastic component. These areas are characterized by solid islands and trabeculae of odontogenic epithelial cell proliferation.[4] Odontogenic ghost cell tumors histologically also show proliferating Odontogenic epithelium with formation of dentinoid ground substance and characteristic small groups or large masses of 'ghost cells'. These ghost cells are pale eosinophilic plump polygonal keratinized epithelial cells that have lost their nuclei; they contain a distinct intracytoplasmic keratin that preserves the outline of the cell and the corresponding previous site of the nucleus.[11,13,14] It has been suggested that ghost cells are degenerating or even metaplastic epithelial cells induced by ischemia, but the cause of transformation is unknown.[12]

From the previous reports[15], 3 different pathogenic mechanisms are suggested. The first is GCOC arising de novo. This was characteristic of 40% of the reported cases, in which GCOC is not associated with preceding DGCT or CCOT. The second mechanism is GCOC arising secondary to a benign CCOT. This was characteristic of 36.7% of the reported cases. The third is that arising from DGCT, a recurrent malignant neoplasm with the previously mentioned characteristics, previously diagnosed as benign DGCT and in which occasional areas of dentin-like materials are demonstrated. This type was characteristic of 3.3% of the reported cases. Of the remaining cases, 13.3% were the result of a secondary malignant counterpart of an ameloblastoma, calcifying epithelial odontogenic tumor, or odontogenic cyst after initial treatment.

The treatment of choice for CCOT is surgery. Some surgeons have advocated conservative surgery, whereas others have suggested radical treatment due to recurrences. Surgical treatment ranges from simple enucleation or curettage to hemimandibulectomy or hemimaxillectomy. Although mutations of the tumor suppressor gene PTCH are described in odontogenic keratocysts[16], marsupialization is found to be effective as a preliminary treatment for large lesions.[17] Recently, mutations on the beta-catenin gene have been reported in COC.[18]It is interesting to observe that both genes are related to the WNT pathway and that both cysts seem to respond to decompression . The CCOT is considered a less aggressive tumor than the ameloblastoma and responds well to conservative surgery.[19]

In our all cases, CCOT and its variants undergo for conservative treatment which includes enucleation followed by peripheral osteotomy and chemical cauterization with the Cornoy's solution which means enucleation followed by removal of 3 to 5mm layer of bone around the periphery of the cystic cavity with a sharp curette or a bone bur. The objective of this procedure is to remove epithelial remnants that could originate from a recurrent lesion. No recurrence was seen in all cases.

CONCLUSION

We advocate trying initial conservative treatment of enucleation and meticulous curettage of the surrounding bony wall (3 to 5 mm) with chemical cauterization as the choice of treatment for small to moderate intrabony mandibular and maxillary lesions.

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