

Dentinogenic Ghost Cell Tumor associated with Odontoma: A unique Histopathological Entity and its Surgical Management

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We report a rare case of dentinogenic ghost cell tumor (DGCT) associated with complex composite odontoma in a 17 years male affecting the posterior segment of the mandible. On radiographic examination, there was a well-defined multilocular radiolucency surrounding the radio opaque mass with respect to 44, 45 and 46. Histopathologically it showed ameloblastomatous proliferation with dentin like areas and ghost cells. It was associated with tooth like structures consisting of dentin, cementum and pulp like areas. DGCT with odontoma is extremely rare with only two cases being reported in literature till date. The management with its rare occurrence is discussed here.

Keywords: Dentinogenic ghost cell tumor, ghost cells ,odontoma.

INTRODUCTION

In 1962, Gorlin and his colleagues first described calcifying odontogenic cysts (COC) and reported it as a distinct odontogenic entity.¹ Classification of COCs have been put forward into a monistic and dualistic nature. According to World Health Organization (WHO) classification, monistic concept hypothesized that all COCs are neoplastic in nature whereas the dualistic concept contain two different entities, a cyst and a neoplasm.² COCs with predominant cyst like areas are termed as “calcifying cystic odontogenic tumors” (CCOT) while the neoplastic entity is termed as a “dentinogenic ghost cell tumor” (DGCT).³ Various terms have been used for description of this lesion such as COC, keratinizing calcifying odontogenic cyst (KCOC), calcifying ghost cell odontogenic tumor (CGCOT), CCOT, DGCT, epithelial odontogenic ghost cell tumor (EOGCT), odontogenic ghost cell tumor (OGCT) and odontocalcifying odontogenic cyst.²

DGCT is the rarest condition among odontogenic ghost cell lesions. It constitutes only 11.5% of all COCs. According to WHO, DGCT can be defined as “locally invasive neoplasm characterized by ameloblastoma like islands of epithelial cells in a mature connective tissue stroma. Ghost cells (aberrant keratinization) can be found in association with varying amounts of dysplastic dentin.” The recent WHO classification (2017) of odontogenic tumors retains the term DGCT for the solid variant.^{4,5}

Odontomas are odontogenic in origin, consisting of enamel, dentin, cementum and pulpal tissue. Some authors describe it as hamartomatous developmental malformation. According to WHO 2017 classification of odontogenic tumors, it is divided into two types: compound and complex odontoma.⁶ The current case focuses on the rarity of occurrence of a DGCT with complex composite odontoma and its surgical management.

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Case report

A 17 year old male patient reported to our department with the complaint of swelling in right lower back tooth region since 8 months. No significant history related to any medical condition was evident. On intra-oral examination, a swelling of size 3x1.5x1.5 cm with bony hard consistency was located in right mandibular posterior region with respect to mid region of 44 to retromolar region. The overlying mucosa appeared to be normal. The examination revealed an un-erupted second molar. The premolars and molars were aligned properly with no evidence of mobility (figure 1A).

On radiographic examination, orthopantomogram (OPG) revealed a radio-opaque mass of size 3x2.5 cm located in right posterior mandibular region. A well-defined multilocular radiolucency was appreciated, surrounding the radio opaque mass with respect to 44,45 and 46. Resorption of roots of 45 and 46 was also observed (figure 1B). Axial view of computed tomography showed multilocular radiolucency in posterior mandible with breach in cortical plates associated with radiopaque mass (figure 1C). A provisional diagnosis of odontoma and a differential diagnosis of calcifying epithelial odontogenic tumor were considered.

The case was planned for excision under local anaesthesia via intra oral approach. A mucoperiosteal flap was raised to expose the

lesion which consisted of a distinct soft tissue lining encapsulating the hard tissue mass. The lining and the hard tissue mass were excised using curette and high-speed rotary instruments and chisels and mallet respectively (figure 2A). The lower border was very thin and an iatrogenic fracture of mandible was encountered during excision. Therefore, transosseous wiring at the lower border was done via extra oral submandibular approach to reduce and stabilize the fracture segments [figure 2B]. Sharp margins were rounded off. The residual bony defect, being large, was obliterated with amalgamated Platelet Rich Fibrin (PRF) and Demineralized freeze-dried bone allogenic graft (DFDBA) and covered with PRF membrane (figure 2C). Extraoral and intraoral wounds were closed primarily. The patient was kept on maxillo-mandibular fixation for 6 weeks. Antibiotics and analgesic were prescribed and the patient was instructed to use 0.2% chlorhexidine gluconate solution as mouth rinse. The specimen was sent for histopathological examination.

On gross examination, the hard-calcified mass was measuring 3.8 x 2.3 x 2 cm in size along with 45 and 46 and one soft tissue bit of size 3 x 2.5 x 1.3 cm [figure 3A]. Cut sections of hard tissue showed periphery of bony hard tissue containing soft tissue within it (figure 3B).

Histopathological examination of the soft tissue revealed cystic wall lined by odontogenic epithelium with many areas showing proliferation of epithelial lining in the form of interconnecting cords and strands, follicles and islands (figure 4A). Peripheral basal cell layer showed tall columnar ameloblast like cells having hyperchromatic nuclei with reversal of polarity and subnuclear vacuolization. Intervening and superficial cells were loosely arranged resembling stellate reticulum, with many areas showing spindle shaped cells. Eosinophilic masses of anucleated ghost cells within the epithelial lining along with juxtaepithelial hyalinization and extensive dentinoid formation was seen (figure 4B and 4C). Scattered odontogenic epithelial islands were seen in connective tissue.

Decalcified H&E stained sections showed tubular dentin with areas showing entrapped basophilic enamel and cementum like material. Many pulp like spaces were seen, showing basophilic calcified masses. Some areas showed ill defined dentinoid like material associated with globules of basophilic calcification (figure 4D).

Ground section shows bulk of tubular dentin attached with agglomerates of atubular dentin at focal areas. At one end, dentin is covered with discontinuous enamel layer while the other end show cementum like layer with entrapped cementocytes (figure 4 E and F).

Based on clinical and histopathologic findings, the final diagnosis of DGCT associated with complex composite odontome was given.

Inter-maxillary fixation was removed after 6 weeks and there was no mobility elicited at the fractured site. Six month's post operative OPG revealed good bone fill at the operated site and complete union of fracture segment (figure 5 A, B). Patient is kept on strict regular follow-up quarterly to check for any complications and recurrence of lesion.

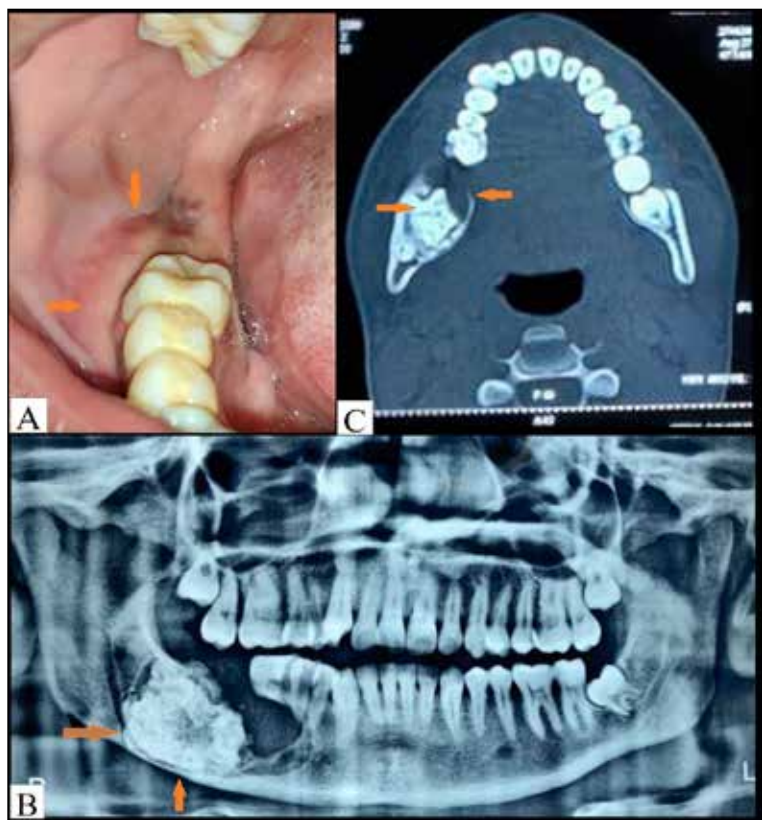


Figure 1. Clinical and radiographic findings:

- A. A bony hard swelling in the right mandibular posterior region encircling #46 and extending to retromolar region.**
- B. Orthopantomogram (OPG) revealed a well-defined multilocular radiolucency surrounding the radio opaque mass with respect to 44, 45 and 46. Resorption of roots of 45 and 46 also observed.**
- C. Axial view of computed tomography (CT) showed multilocular radiolucency in posterior mandible with breach in cortical plates associated with radiopaque mass.**



Figure 2. Surgical findings: A. Bony defect after excision of lesion.
 B. Transosseous wiring after excision for stabilization of iatrogenic fracture of lower border of mandible.
 C. Placement of Amalgamated Platelet Rich Fibrin (PRF) and Demineralized freeze-dried bone allogenic graft (DFDBA).

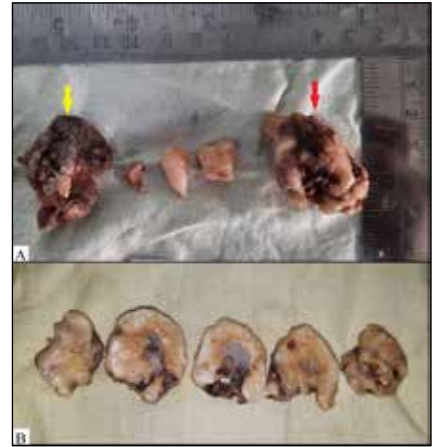


Figure 3. Macroscopic findings: A. A hard-calcified mass (red arrow) and one soft tissue bit (yellow arrow) along with #45 and 46.
 B. Cut sections of hard tissue showed periphery of bony hard tissue containing soft tissue within it.

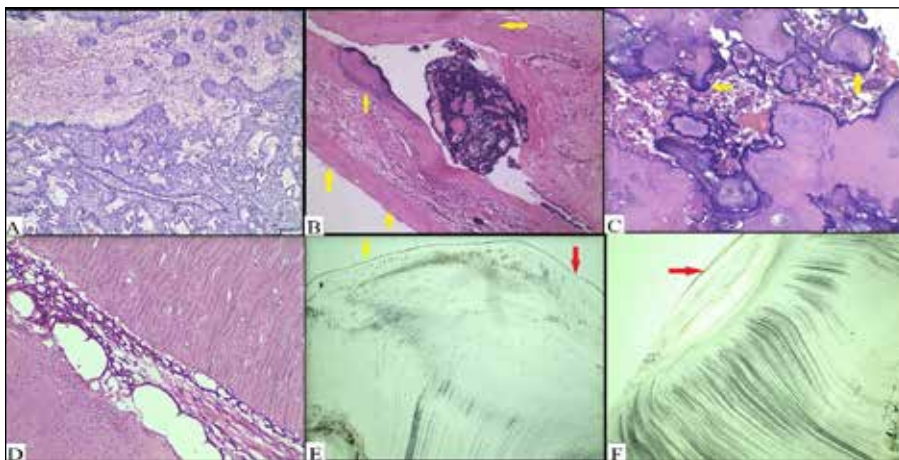


Figure 4. Histopathological findings: A. Odontogenic epithelium showing proliferation of epithelial lining in the form of interconnecting cords and strands, follicles and islands into stromal tissue.(10X)
 B. Tumor tissue with extensive dentinoid material (yellow arrow) is appreciated in juxtaepithelial region.(10X)
 C. Numerous ghost cells undergoing calcification (yellow arrow).(40X)
 D. Tubular dentin with pulp like area. (40X)
 E and F. Ground sections showing bulk of tubular dentin covered with cementum at one end (yellow arrow) and discontinuous enamel at the other end (red arrow). (10X)

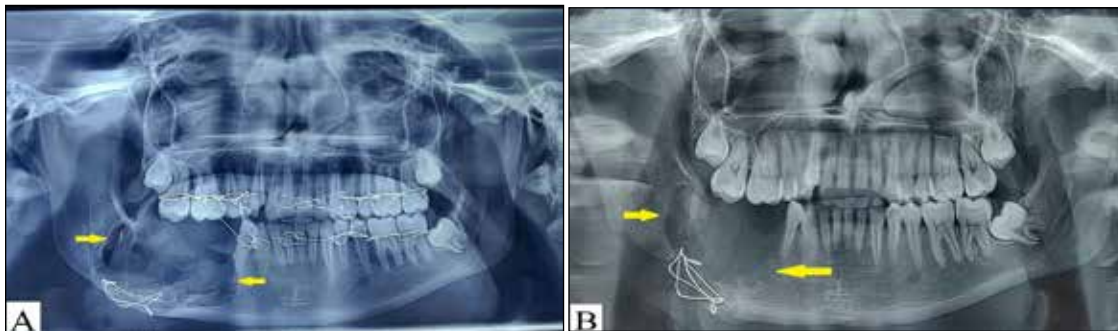


Figure 5. Post operative OPG: A.Immediate post operative OPG revealed large bony defect filled with graft and maxillo-mandibular fixation.
 B. Six month's post operative OPG revealed good bone fill at the operated site and consolidation at fracture site.

DISCUSSION

DGCT is the tumor counterpart of COCs and represents about 0.3–0.8% of all odontogenic tumors. Occasionally, dysplastic dentin and an area of dental hard tissue formation resembling odontoma can be found.⁷ Oliveira *et al* reported a case of COC associated with compound odontoma in a 10 year old child.⁸ Clinically, DGCT appears as a painless slow growing mass and affects the maxilla and mandible equally, with a predilection for the posterior region.⁹ It occurs in second to the ninth decade of life and has a strong male predilection.¹⁰

Radiographically, DGCT appears as a well-defined multilocular radiolucent lesion with varying opacity levels and may be associated with impacted teeth. Occasionally it is found associated with odontomas. In some cases, root resorption and divergence can be found.¹⁰ In our case, we found a large radiopaque mass surrounded by radiolucent cystic cavity. From a clinical and radiographic perspective, the differential diagnosis includes benign radiolucent lesions such as ameloblastic fibro-odontoma, and calcifying epithelial odontogenic tumor. To our best knowledge, there are only two case reports of DGCT with odontoma reported in literature till date. In the current case, the mandibular posterior region was involved in a 17 year old male. Contrary to our case, Bavle RM *et al*¹¹ and Santos OS *et al*¹² have reported a similar case in maxillary posterior region and maxillary anterior region respectively.

Histopathologically, DGCT may show ameloblastomatous proliferations along with dentin formation and agglomerates of ghost cells. The mesenchymal component shows induction of dentinoid, and dentin-like tissue with ghost cells being a significant part of the tumor.⁷ Ghost cells represents the large agglomerates of eosinophilic masses with central empty space which was previously occupied by nucleus. True nature of ghost cells is still unclear as there are various theories suggesting the nature of ghost cells. These theories propose that it may represent the aberrant keratinization, enamel proteins, coagulative necrosis or presence of hard keratins.¹³

In current case, we observed numerous ameloblastic islands and nests in connective tissue stroma along with abundant dentinoid material and ghost cells undergoing calcifications. Beta-catenin plays an important role in the pathogenesis of DGCT and odontoma. An aberrant activation of Wnt signaling pathway can stimulate the tumorigenesis of both tumors.¹³ As there is presence of ghost cells in both tumors, Wnt β catenin signalling pathway may be responsible for the pathogenesis. It could be hypothesized that DGCT and odontoma represent two ends of a spectrum.

Patient was treated surgically followed by graft placement in the bony defect. Recurrence is found in some cases of DGCT after excision. Bavle *et al* reported recurrence in a case of DGCT with odontoma 11 months posttreatment.¹¹ Even though the current lesion was aggressive in nature and causing thinning of the lower border of the mandible, there is no recurrence till date.

CONCLUSION

We report a rare case of DGCT associated with a complex composite odontoma occurring in the posterior mandible. As there is a possibility of recurrence, a long term follow up is recommended as a standard treatment protocol.

Conflict of Interest

Nil

Acknowledgement

Nil

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