Case Report

A massive dentinogenic ghost cell tumor that crossed the midline: A rare case report

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Abstract

Dentinogenic ghost cell tumor (DGCT) is a rare tumor of odontogenic origin. A locally invasive lesion can be described by the presence of ameloblast-like epithelial islands, ghost cells, and dentinoid material. It is one of the few lesions with a predilection for the Asian population. The available literature has revealed that only 131 cases to date have been reported and published from 1968 to 2022. The following is a case report of a 25-year-old male with a tumor in the left lower back teeth region for the past 1 month. Orthopantomogram (OPG) reveals a well-defined unilocular radiolucency extending anteroposteriorly and crossing the midline. Histopathology revealed basal ameloblast-like cells and central stellate reticulum-like cells with the characteristic presence of ghost cells. The diagnosis was made based on the clinical, radiographical, and histopathological correlation and was confirmed using immunohistochemical analysis as a DGCT.

Keywords: Benign mixed mesenchymal-epithelial odontogenic tumor, calcifying ghost cell tumor, dentinoameloblastoma, dentinogenic ghost cell tumor, odontogenic ghost cell tumor, odontogenic tumor

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INTRODUCTION

Dentinogenic ghost cell tumor (DGCT) is a locally invasive, extremely rare benign mixed epithelial and mesenchymal odontogenic tumor. It is the rarest of the ghost cell lesions identified and accounts for <3% of all cases ever recorded.[1,2] It is also one of the few lesions with a predilection for the Asian population. The tumor was called by various names such as "calcifying ghost cell tumor," "odontogenic ghost cell tumor," and "dentinoameloblastoma," all of which are obsolete now.[3] World Health Organization (WHO) has classified DGCT under benign mixed epithelial and mesenchymal odontogenic tumors. DGCT is the solid variant of the calcifying odontogenic cyst (COC). The very first description of COC was in 1962 by Gorlin and colleagues and only 2–14% of COCs are of solid variant.[4] Its frequency among the Indian population is 0.4% and 6.8% of all tumors found in the Kancheepuram district, Chennai. The available literature on DGCT is only a mere 131 cases published from 1968 to 2022. Among them, more than half of them were recorded on Asian population.[5] The tumor has a predilection for men with men having twice as much chance of getting the tumor compared to

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women. Peak incidence is seen in patients aged 40–60 years but the age ranges from 11 to 79 years with a mean of 39.7 years. The tumor frequents intraosseous sites with the mandible having a slightly higher predilection.[6] Cases of sporadic peripheral tumors have been documented in the gingiva and alveolar mucosa.[7,8] Radiographically, the tumor is seen as a unilocular mixed radiolucent and radiopaque lesion with well-denied borders. There can also be the presence of root resorption.[9] Histopathologically, the tumor consists of biphasic morphology, showing predominantly ameloblastomatous proliferation and a basaloid to stellate reticulum cells with the presence of ghost cells and dentinoid material.[10] Due to the small number of reported cases, conclusions for an optimal treatment for DGCT cannot be concluded.[11]

The purpose of this article is to report a rare case of massive DGCT that crossed the midline, which was diagnosed based on the clinical, radiographical, and histopathological correlation and was confirmed using immunohistochemical analysis.

CASE REPORT

A 25-year-old male reported to the Department of Oral and Maxillofacial Pathology, Saveetha Dental College, Chennai with a complaint of pain and swelling in the lower left back tooth region for the past 1 month. The patient noticed the swelling before 1 month, which had gradually increased to the present size along with displacement of teeth in the same site. The patient did not have any known systemic disorder and was not under any medication.

Extra oral examination revealed a solitary ill-defined bony swelling on the left side of the face with associated pain. No secondary changes were found in the swelling. Intraoral examination revealed a solitary well-defined bony hard swelling in alveolar mucosa in relation to 33, 34, 35, and 36 measuring 2 × 1 × 0.5 cm. The color of the mucosa over the swelling was similar to the surrounding mucosa and was not associated with any secondary changes. Lingually tilted 33 and 34 were observed [Figure 1].

Orthopanaramogram (OPG) reveals a well-defined unilocular radiolucency extending antero-posteriorly from 36 to 44 and crossing the midline. Trabeculations were seen within the radiolucency along with resorption of roots of 35, 36, and 37 [Figure 2].

Histopathology showed multiple sections with connective tissue stroma exhibiting numerous cystic odontogenic islands with basal ameloblast-like cells and central stellate

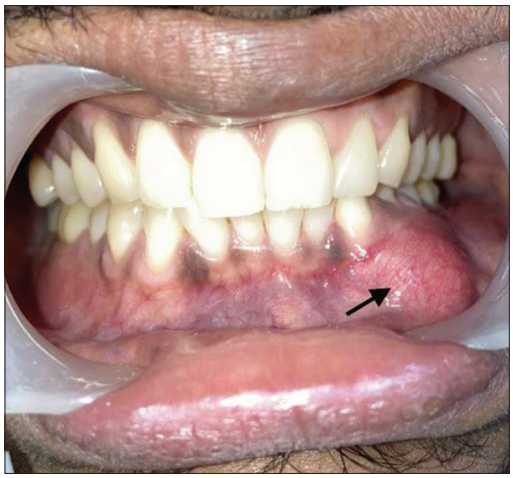

Figure 1: Intraoral image, Arrow mark depicts hard swelling in alveolar mucosa in relation to 33, 34, 35, and 36

reticulum-like cells. Few areas showed odontogenic epithelial lining of variable thickness with budding. Many of the ameloblastomatous islands show eosinophilic ghost cells in the center of the stellate reticulum-like areas with a few undergoing calcification. The ghost cells were more than 1–2% of the tumor. There is evidence of prominent juxta-epithelial hyalinization implicating dentinoid formation. A few islands also show cystic degeneration [Figure 3].

Immunohistochemistry markers calretinin and cytokeratin 8 were applied. Calretinin showed negative expression, thereby excluding ameloblastoma whereas cytokeratin 8 showed positive expression. Based on the clinicopathological and histological findings with the adjuvant immunohistochemical findings, the lesion was diagnosed as a DGCT.

DISCUSSION

DGCT is an extremely rare benign mixed epithelial mesenchymal odontogenic tumor. Various terminologies and classifications of DGCT have been proposed and used in the literature since 1962. The term "calcifying ghost cell odontogenic tumor" was coined by Fejerskov and Krogh in 1972.[12] DGCT, as we know, is a solid variant of COC. COCs were classified by Buchner *et al.* in 1991 as central and peripheral lesions and further subdivided each of them into cystic or neoplastic variants.[13] The rare malignant variant of COC was also included in this classification.[12,14] In the same year, Hong classified COC into cystic and neoplastic lesions and coined the term "epithelial odontogenic ghost cell tumor" for the neoplastic solid variant, which is now known as DGCT.[15] The entire dilemma was solved when WHO in 2005 classified DGCT as a locally invasive neoplasm identified

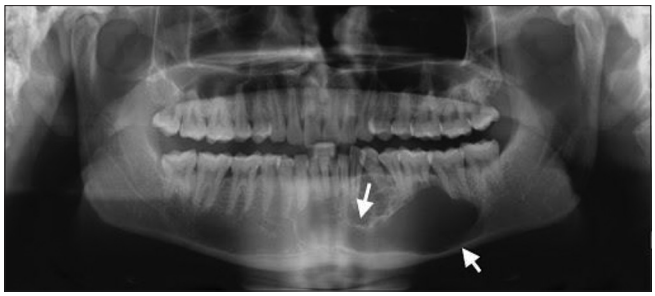

Figure 2: Orthopantomogram depicting unicystic radiolucency extending from 36 to 44. Arrow mark indicating the extent of the radiolucency

with the presence of ameloblast-like islands of epithelial cells with the presence of ghost cells and dentinoid formation and placing them under the benign mixed epithelial mesenchymal odontogenic tumors. The tumor retains its position in the WHO 2022 classification of odontogenic tumors.[16]

This report was a case of a 25-year-old patient with a complaint of swelling and pain in the left back tooth region for the past 1 month. There was the presence of a solitary bony lesion with a displacement of a tooth in the said area. According to available literature, DGCT is commonly found in patients over 40 years. The reason for such an early incidence is yet to be understood as only a handful of cases have occurred at a young age.[4] DGCT has a predilection for the posterior mandible, yet this case showed the swelling to be in the anterior mandible. This is a rare site of occurrence for dentinogenic ghost cell tumor. These clinical features made it difficult for the clinician to think of DGCT as a provisional diagnosis and gave the tumor provisionally as unicystic ameloblastoma.[6]

Radiographically the lesion showed a well-defined unilocular radiolucency extending anteroposteriorly from 36 to 44 and crossing the midline. Resorption of roots was seen in relation to 35, 36, and 37. This type of presentation is quite uncommon. Typically, the lesion shows radiolucent, radiopaque, or mixed appearance depending on the amount of calcification. Not only this tumor occurred in the anterior mandible, but it also crossed the midline. Other than the site, the tumor showed radiographically, pathognomonic features of DGCT.[17,18]

Histopathologically, the connective tissue stroma of this lesion showed numerous cystic odontogenic islands with basal ameloblast-like cells and central stellate reticulum-like cells. Few areas showed odontogenic epithelial lining of variable thickness with budding. This is in concordance with the previous literature.[19] Histopathologically, DGCTs are composed of odontogenic epithelium with areas resembling ameloblastoma, ghost cells, dentinoid, or osteodentin-like

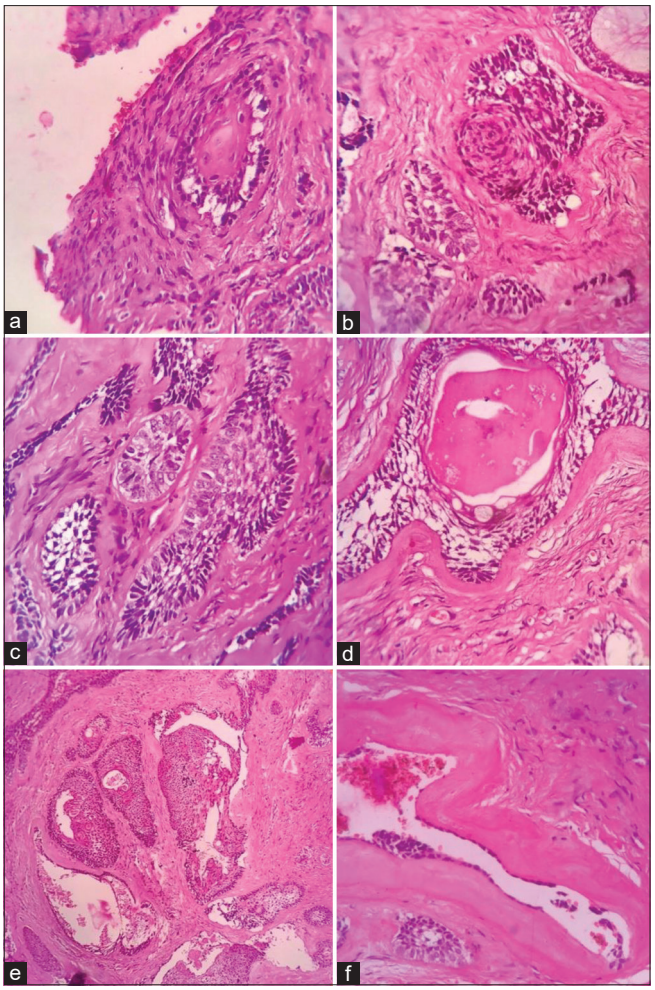

Figure 3: The photomicrograph shows a) ameloblastomatous islands with ghost cell formation, b) ameloblastomatous islands with squamous differentiation in the central lumen, c) ameloblastomatous islands, d) ameloblastomatous islands with stellate reticulum-like cells in the central lumen and juxta-epithelial dentinoid formation. e) and f): ameloblastomatous islands with ghost cell formation in the central lumen and juxta-epithelial dentinoid formation (Photomicrograph, H and E, Mag 4 × and 10×)

material. Aberrant keratinization with occasional calcifications, multinucleated giant cells, mitotic figures, and microcystic spaces are seen.[20] This lesion had evidence of prominent juxta-epithelial dentinoid matrix formation. A few islands also showed cystic degeneration. All of these features directed the diagnosis toward an odontogenic tumor.[21]

Similar features can also be found in other odontogenic lesions like ameloblastoma, ameloblastic fibro-odontoma, and odontoma. The characteristic features that distinguish DGCT from other lesions by WHO is the presence of >1–2% proportion of ghost cells and dentinoid formation.[15]

The striking histological feature that distinguishes DGCT from conventional ameloblastoma and other odontogenic tumors is the presence of ghost cells and dentinoid substances.

Ameloblastic fibro-odontomas can be excluded by the absence of the characteristic cellular primitive ectomesenchyme resembling dental papilla. Compound odontomas are histologically seen as having tooth-like structures which are arranged in a uniform manner similar to the normal tooth. This case did not have such a feature. Hence, based on the above-mentioned findings, ameloblastoma, ameloblastic fibro-odontoma, and odontoma were ruled out.[22,23]

The ameloblastomatous islands in this case showed eosinophilic ghost cells in the center of the stellate reticulum-like areas with a few undergoing calcification. Typically, the ghost cells are enlarged ovoid or polyhedral pale staining epithelial cells with vacuolated nuclear spaces.[24] They are eosinophilic and although the cell outlines are usually well defined, they may sometimes be blurred so that groups of them appear fused. Some of the ghost cells may undergo calcification, starting initially as fine powdery or coarse basophilic granules and later becoming small spherical bodies that ultrastructural studies have shown to represent dystrophic calcification.[10]

Numerous immunohistochemical studies have been reported in concordance with the profiling of this lesion. The odontogenic epithelium is the important component of DGCT where it can express epithelial markers like CK-5, CK-7, CK-8 CK-14, and CK-19. Dentinoid material is positive for the p53 marker while calretinin positivity indicates ameloblastoma. The present case, on immunohistochemical analysis, showed a negative expression of calretinin, which excluded ameloblastoma. Cytokeratin 19 was found positive hence confirming that the lesion is odontogenic in origin.[25,26]

Correlating the clinical, radiographical, histopathological, and immunohistochemical findings, the lesion was diagnosed as DGCT.

Recurrent tumors have the potential to exhibit malignant characteristics such as increased cellular and nuclear pleomorphism with mitotic figures. These malignant features are diagnosed as ghost cell odontogenic carcinoma (GCOC), a rare malignant counterpart of DGCT.[27] About 32.5% of GCOCs are reported from DGCT or COC.[28] Histopathological features and malignant potential of DGCT warrant a long-term review of the patients diagnosed with such a lesion.[29]

CONCLUSION

DGCT shows extensive diversity in its clinical and histopathological behavior. It is important to study DGCTs in their macroscopic, clinical, radiographic, and histopathological behavior. This case report has therefore made us realize that we need to always operate with an index of suspicion at the time of histopathological diagnosis to ensure proper treatment and follow-up. The immunohistochemical analysis has been a valuable aid to understand its behavior further and in-depth.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed

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Conflicts of interest

There are no conflicts of interest.

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