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CASE REPORT

Calcifying Cystic Odontogenic Tumor: A Shadow Cell Lesion

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ABSTRACT

Introduction: The calcifying odontogenic cyst (COC) is a rare developmental lesion arising from odontogenic epithelium with or without odontogenic ectomesenchyme. Though recognized as a benign odontogenic tumor, its pathologic entity includes a spectrum of clinical behavior and histopathological features including cystic, solid and aggressive variants. One of the main histopathological findings in COC are ghost cells. Ghost cells still pose a mystery whether made up of keratin, amyloid, apoptotic bodies or enameloid. Immunohistochemistry was done for this particular case to find out the nature of ghost cells.

Case report: Here, we report a case of 25-year-old male patient who presented with a soft, fluctuant, nontender swelling extending from central incisor to canine obliterating the labial vestibule. Histopathological examination revealed the case as calcifying cystic odontogenic tumor (CCOT). Immunohistochemistry for Cytokeratin 19 done, showed weak positivity inside ghost cells but showed uniform positivity in the epithelial lining suggestive of antigenic alterations within the ghost cells.

Management: The lesion was surgically enucleated and the patient was under follow-up for the past 8 months. No recurrence of lesion was noted

Conclusion: There is a controversy whether CCOT is a cyst or neoplasm. The histopathological examination sections showed ameloblastic epithelial cells along with the features of a COC lesion. And, so we present the case as CCOT. This article also gives an insight into the shadow cells of CCOT.

Keywords: Calcifying cystic odontogenic tumor, Calcifying odontogenic cyst, Cytokeratins, Ghost cells.

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INTRODUCTION

The calcifying cystic odontogenic tumor (CCOT) forms part of spectrum of lesions designated as calcifying odontogenic cyst (COC). Gorlin et al was the first to describe it in 1962.[1-3]

The WHO classification (2005) of odontogenic tumors categorized the calcifying odontogenic cystic neoplasms into ghost cell odontogenic tumors, which comprised of:

- Calcifying cystic odontogenic tumors
- Dentinogenic ghost cell tumors and
- Ghost cell odontogenic carcinoma

Calcifying cystic odontogenic tumor is a benign odontogenic origin cystic neoplasm characterized by ameloblastoma like epithelium and ghost cells. The simple COC lesion.[4]

CCOT includes the four subtypes:

1. Simple cystic
2. Odontoma associated
3. Ameloblastomatous proliferating type
4. Calcifying cystic odontogenic tumor associated with other benign tumors other than odontoma

Calcifying cystic odontogenic tumor has a peak incidence in the 2nd decade of life with a predilection to occur in the anterior jaw region. It can present both centrally and peripherally. The radiographic appearance is of an irregular, unilocular, or multilocular radiolucent area containing radiopaque masses of varying size and opacity.[4]

Gorlin et al[1] suggested that the COC might be an oral analog of the "calcifying epithelioma of Malherbe" a well recognized lesion of skin. The lesions have, in common, the peculiar abnormal keratinization of odontogenic and metrical epithelial cells that is termed as ghost cell or shadow cell keratinization.

Ghost cells are called so due to their shadowy appearance in histopathological examination [Hematoxylin and Eosin (H-E)] sections. These are pale, swollen eosinophilic cells without a nucleus but with a clear cell outline. Ghost cells are also present in other odontogenic and nonodontogenic lesions like odontoma, ameloblastic fibrodontoma, pilomatricomas.[5]

CASE REPORT

A 25-year-old male patient reported with an asymptomatic swelling in the left front upper tooth region for the past 1 year. On extra oral examination, there was a swelling in the left anterior maxillary region with obliteration of nasolabial fold. Intraorally, there was a soft,

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fluctuant, nontender swelling extending from left central incisor to canine obliterating the labial vestibule (Fig. 1). Intraoral periapical radiograph showed a radiolucency along with diffuse radiopacity between 22 and 23 (Fig. 2). There was widening of the periodontal ligament space in relation to 22 and 23 but the teeth are vital. Based on the clinical and radiographic findings, a provisional diagnosis of an odontogenic keratocyst/radicular cyst/lateral periodontal cyst was made. The lesion was surgically enucleated and sent for processing. On H-E, there was a cystic cavity lined by a well-defined and prominent basal layer cuboidal and luminar cells that focally resembled ameloblastic epithelium—overlying loosely arranged stellate reticulum like cells. Large number of ghost cells and calcified particles were also seen. Supporting connective tissue capsule was loosely collagenous with moderate vascularity and sparse inflammatory cells. The findings confirmed a diagnosis of a cystic variant of CCOT (Fig. 3). Immunohistochemistry (IHC) for Cytokeratin 19 done, showed weak positivity inside ghost cells but showed uniform positivity in the epithelial lining suggestive of antigenic alterations within the ghost cells (Fig. 4).

DISCUSSION

Calcifying cystic odontogenic tumors are uncommon benign slow-growing cysts of developmental origin partly exhibiting characteristics of a neoplasm. Calcifying ghost cell odontogenic cyst is comparatively rare in occurrence, constituting about 0.37 to 2.1% of all odontogenic tumors. The most notable features of this pathologic entity are histopathological features, which include a cystic lining demonstrating characteristic "ghost" epithelial cells with a propensity to calcify.[4] Calcifying cystic odontogenic tumor epithelium shows positive reactions for keratin-14 and keratin 10\13 in its basal and upper cell layers respectively, which shows the epithelium differentiates to squamous type. The transforming growth factor beta signalling pathway is less activated in CCOT than in ameloblastoma, indicating less cellular proliferation and differentiation

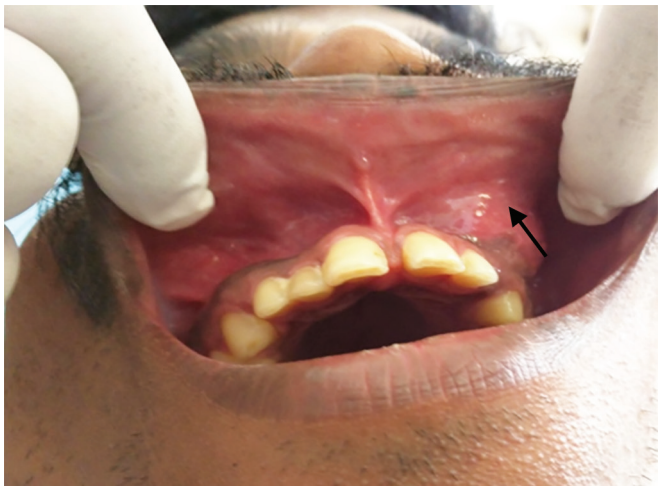

Fig. 1: Swelling extending from left central incisor to canine obliterating the labial vestibule

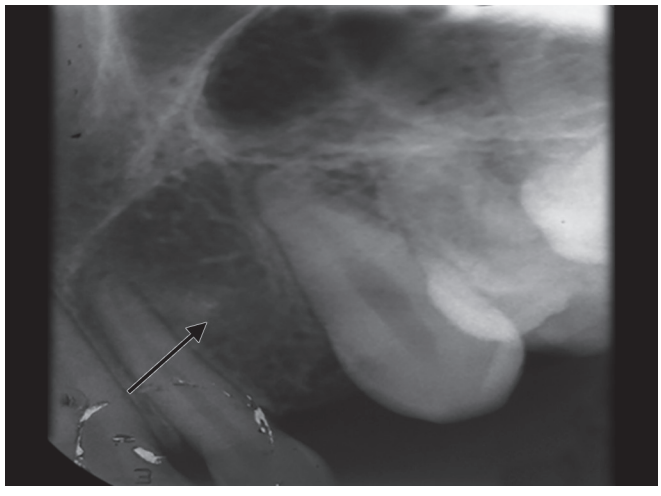

Fig. 2: Radiolucency along with diffuse radiopacity between 22 and 23

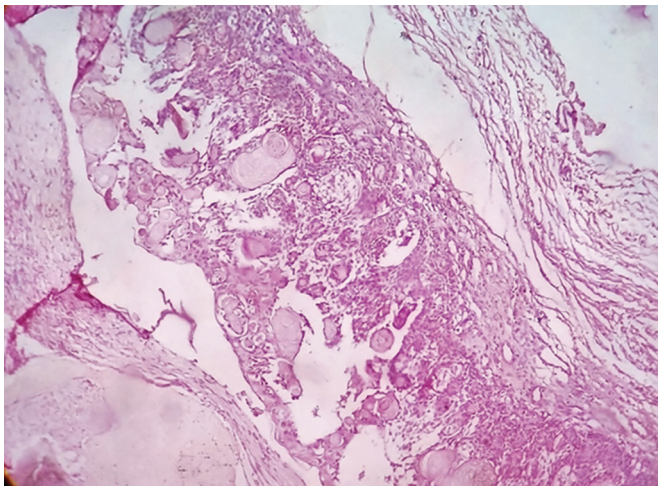

Fig. 3: Cystic appearance of CCOT

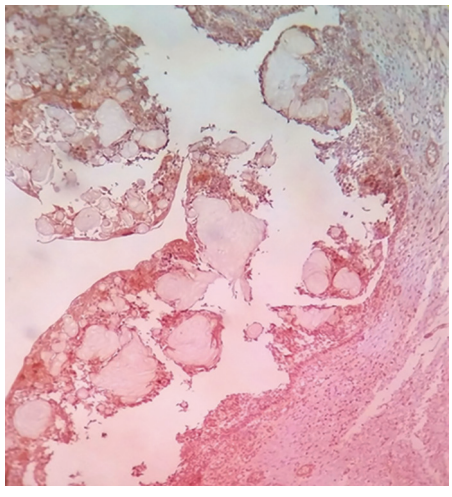

Fig. 4: Ghost cells in CCOT

than ameloblastoma. Ghost cells demonstrate Notch-1 and Jagged-1 overexpression.[5] Notch-1 Jagged-1 signalling subserves the main transduction mechanism responsible for ghost cell fate decision in CCOT. Enucleation is the treatment of choice for most intraosseous CCOTs with few recurrences reported in the literature.[4]

In the early stages of formation, CCOT may have little or no mineralization and therefore, may present as radiolucencies. As the lesion matures, calcifications occur and appear as well-circumscribed, mixed radiolucent-radiopaque masses. Dense opacities are associated with complex odontome. Radiologically, three basic patterns of radiopacities are identified—salt and pepper pattern of flecks, fluffy cloudlike pattern throughout, and a new moon like configuration with crescent-shaped radiopacity on one side of the radiolucency.[6] The differential diagnosis in these instances includes dentigerous cyst, odontogenic keratocyst, and ameloblastoma.

Ghost cells whether odontogenic or nonodontogenic are always epithelial in origin. The mystifying nature of ghost cells can be reflected in forms of true keratinization, prekeratin, stages in the process of ortho, para and aberrant keratin formation, abnormal/aberrant keratinization, highly keratinized epithelial cells, and cells which have lost their developmental and inductive effect.[3] Yamamoto et al found intense staining of ghost cells with high molecular weight keratins and concluded that ghost cell probably has different subclasses of keratins which have a strong tendency to degenerate. Kim et al investigated the expression of the apoptotic and antiapoptotic marker in COC and found that ghost cell was expressing Bax protein while nucleated cells adjacent to ghost cells expressed both Bax and Bcl-XL. Terminal deoxynucleotidyl transferase(TdT) dUTP Nick-End Labeling (TUNEL) assay was positive in nucleated cells adjacent to ghost cells. They suggested that ghost cells are formed during terminal differentiation as an apoptotic process. Günhan et al suggested that ghost cells originate from cells that are programmed for amelogenesis in CCOT through cytoskeletal reorganization.[3]

Several odontogenic and nonodontogenic lesions show the presence of ghost cells. In odontogenic lesions including calcifying CCOT, dentinogenic ghost cell tumor, and ghost cell odontogenic carcinoma, ghost cells are of diagnostic importance. Ghost cells are occasionally seen in odontoma, odontoameloblastoma, ameloblastoma, ameloblastic fibrodontoma, and clear cell odontogenic carcinoma. They are also reported in inner enamel epithelium of developing tooth and in eruption cysts. The role of Wnt-β-catenin-Lef pathway and Notch signaling partially explains the link between tumorigenesis of these lesions and ghost/shadow cell formation and/or calcification.[3] Future molecular studies are required to clarify further genetic and predisposing factors along with types and role of keratins involved in ghost cell transformation.

CONCLUSION

Our case reflects a simple cystic variant of CCOT. The IHC for the case supports the literature as there are some forms of antigenic alterations inside the ghost cells. The presence of ghost cells is not a histopathological finding confined to CCOT only. So, more and more studies are needed to reveal the exact nature of ghost cells and to find out if there is any role for ghost cells in tumorogenesis in those lesions.

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