Case Report

Calcifying Epithelial Odontogenic Cyst of Maxilla: Report of A Case and Review and Discussion on the Terminology and Classification

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Abstract

A cyst is defined as a pathological cavity which may or may not have an epithelial lining and which has a fluid, semi-fluid, or gaseous contents and is not formed by accumulation of pus. The calcifying epithelial odontogenic cyst (CEOC) was first reported by Gorlin *et al*. in 1962. At that time, it was classified as a cyst related to the odontogenic apparatus. It was later renamed as calcifying cystic odontogenic tumor (CCOT) in the World Health Organization classification devised in 2005 due to its histological complexity, morphological diversity, and aggressive proliferation. CCOT was later recognized by numerous names including Gorlin cyst, calcifying ghost cell odontogenic cyst, and/or dentinogenic ghost cell tumor. It has a peak incidence during the second and third decades of life and does not demonstrate any gender predilection. Radiographically, CEOC may appear as a unilocular or multilocular radiolucent lesion with either well-circumscribed or poorly-defined margins and may also be observed in association with unerupted teeth. Calcification is an important radiographic feature for the interpretation of CEOC/CCOT. The typical histopathological features of CEOC include a fibrous wall and lining of odontogenic epithelium with either columnar or cuboidal basal cells resembling ameloblasts. The treatment of choice for CEOC is conservative surgical enucleation, however, recurrence is also not found to be uncommon. Herein, we are reporting a case of the same in a 21-year-old female which was a great dilemma during the diagnostic work-up.

Keywords: Calcifying cystic odontogenic tumor, calcifying epithelial odontogenic cyst, calcifying ghost cell odontogenic cyst, dentinogenic ghost cell tumor, Gorlin cyst

Introduction

The calcifying epithelial odontogenic cyst (CEOC), which is also recognized by the terms calcifying cystic odontogenic tumor (CCOT), Gorlin cyst, calcifying ghost cell odontogenic cyst, and dentinogenic ghost cell tumor, is a rare developmental lesion that arises from the odontogenic epithelium[1] and represents about 2% of all odontogenic pathological changes in the jaw.[2-5] It is clinically characterized as a painless, slow growing cystic lesion which affects both the maxilla and mandible equally, though, the lesion is said to have a definite predilection for the anterior regions of the jaws and usually arises intra-osseously. It has a peak incidence during the second and third decades of life with a mean age of 30.3 years and does not demonstrate any specific gender predilection.[6] Radiographically, CEOC may appear as a unilocular or multilocular radiolucent lesion with either well-circumscribed or poorly defined margins and may also

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be observed in association with unerupted teeth.[7] Calcification is an important radiographic feature for the interpretation of CEOC and is detected in approximately half of the reported cases.[8] The typical histopathological features of CEOC include a fibrous wall and lining of the odontogenic epithelium with either columnar or cuboidal basal cells resembling ameloblasts. Stellate reticulum-like cells overlay the basal cell layer while ghost cells, which may occasionally become calcified, are also seen in the cystic lining. Melanin deposits are also seen evident in the epithelial lining occasionally.[8,9] The treatment of choice for CEOC is conservative surgical enucleation. Recurrences, though very rare, are common in cases with malignant degenerations seen in relation to the cystic linings.[7]

Case Report

A 21-year-old female reported to the Department of Oral Medicine and Radiology with a chief complaint of swelling in the upper front tooth region of 6-month duration with a history of discomfort due to the swelling while no associated pain was reported. On extraoral examination, slight asymmetry over the left middle third of the face was noted which was diffuse, 3 cm × 3 cm in greatest dimensions, hard in consistency, and nontender on palpation with retained deciduous tooth in relation to #63 while missing tooth in relation to #23. Vestibular obliteration in relation to #22 to #25 region was also noted with eggshell crackling effect on palpation [Figure 1]. On performing fine-needle aspiration cytology, it was found to be positive yielding 3.8 ml of a straw-colored fluid [Figure 2]. Intraoral periapical radiograph [Figure 3] and maxillary left lateral occlusal radiograph [Figure 4] revealed a well-defined periapical radiolucency extending from #22 to #26 region with root resorption in relation to #63, #24, and #25. Orthopantomograph (OPG) revealed a well-defined radiolucent lesion extending from #22 to #26 region associated with impacted #23 and root resorption in relation to #63, #24, and #25 [Figure 5]. Based on the history and clinical and radiographic examination, a provisional diagnosis of dentigerous cyst in the left anterior maxilla was arrived at while the list of differentials included adenomatoid odontogenic tumor, unicystic ameloblastoma, and CEOC in that order of their occurrence. Surgical enucleation of the cyst was performed while the lining of the cyst was sent for histopathological examination. Histopathological examination revealed a cystic epithelial lining of variable thickness backed by a fibrous connective tissue capsule. The basal cell layer of the odontogenic epithelium showed tall columnar cells with palisading arrangement along with focal areas of cells with reverse polarity resembling ameloblast-like cells. The overlaying layer comprised loosely arranged epithelium with cells resembling stellate reticulum-like cells while a variable number of eosinophilic structures resembling ghost cells were also seen. Underlying fibrous connective tissue stroma comprised numerous bundles of collagen fibers with subepithelial hyalinization and with the presence of few odontogenic epithelial islands [Figure 6].

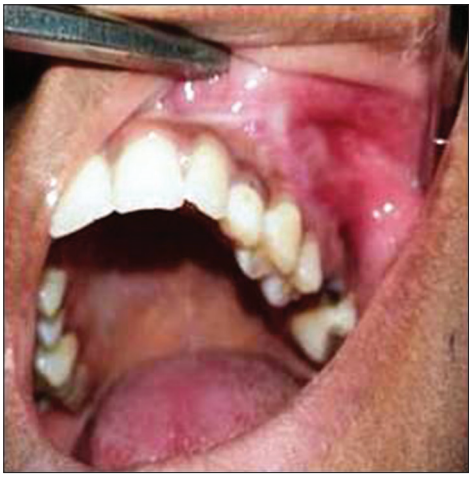

Figure 1: Intraoral examination revealing retained deciduous tooth in relation to #63 with vestibular obliteration in relation to #22 to #25 region

Figure 2: Fine-needle aspiration cytology yielding straw-colored fluid

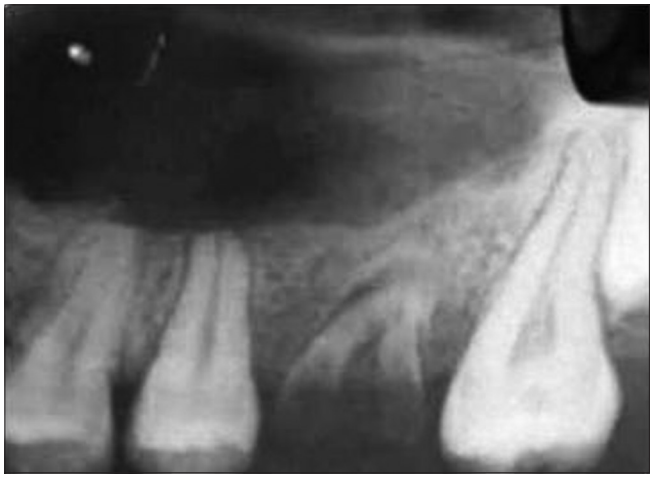

Figure 3: Intraoral periapical radiograph revealing a well-defined periapical radiolucency extending from #22 to #26 region with root resorption in relation to #63, #24, and #25

Discussion

The CEOC was first reported by Gorlin *et al*. in 1962. The lesion has some features of a cyst while some features of a solid neoplasm making the lesion a little controversial and actually comprising two distinct clinicopathologic entities, a cyst and a neoplasm. Although it has commonly been recognized as a benign odontogenic cyst since its original description by Gorlin *et al*. in 1962, this complex pathologic entity encompasses a

spectrum of clinical behaviors and histopathological features including cystic, neoplastic, and aggressive variants.[2] As a result of this diversity, different classification schemes and nomenclatures for this lesion have been suggested at varying times.

According to Altini and Farman, a similar occurring condition had previously been mentioned in German literature in 1932 by Rywkind.[10] It was earlier thought to be an oral presentation of dermal calcifying epithelioma of Malherbe.[2,10,11] In 1971, the World Health Organization (WHO) described CEOC as a nonneoplastic cystic lesion choosing it to be classified as a benign odontogenic cyst while later, in 1992, the WHO classified it as a neoplasm rather than a cyst but confirmed that most of the cases are nonneoplastic.[12] In 2005, the WHO Classification of Head and Neck Tumors reclassified this lesion as an odontogenic tumor and gave it the name of CCOT to emphasize the neoplastic nature of this lesion previously categorized as an odontogenic cyst.[13] Li and Yu have also drawn attention to the dilemma regarding the nature of these ghost cell lesions as cysts, neoplasms, and even, malignancies.[14]

CEOC is now a well-recognized pathological entity, however, it is not very commonly encountered. This lesion manifests either as a central or a peripheral variant, with the central variant being more commonly reported. Praetorius *et al*. suggested bimodal age distribution for the lesion.[15] Several case reports in the literature have described that a greater incidence of the said lesion is seen in the second decade of life, though a plethora of reports have also noticed a specific bimodal distribution as suggested by Praetorius *et al*.[15] with a second peak of incidence in the sixth and seventh decades of life.[16] In the present case, the patient was in her second decade of life. Furthermore, there is a negligible gender predilection with no identified racial predilection either seen for the lesion as has been reported in the literature.[6,15,16]

Furthermore, the location of the lesion can be intra- or extraosseous with both the central and peripheral variants seen with an equal frequency in the maxilla and mandible. Most of the lesions, though, have a specific predilection for the anterior regions of the jaws with a majority of the lesions reported in the incisor-canine area of both maxilla and mandible.[17] The reported lesion was of the central variety and was present in the left anterior maxilla. Li and Yu also reported that maxilla was more frequently affected than the mandible while the most common site of occurrence for the lesion was the canine-premolar region of the maxilla. Furthermore, in the mandible, several cases have been seen to cross the midline, but this is less frequently reported in case of the maxilla.[14]

Most of the peripheral lesions reported in the maxilla and mandible involve the gingiva and alveolar mucosa anterior to the first molar while the central lesions are seen in the form of asymptomatic hard swellings as was seen in the present case which presented with a hard bony expansion, however, fairly extensive lingual expansion may also sometimes be observed[18]

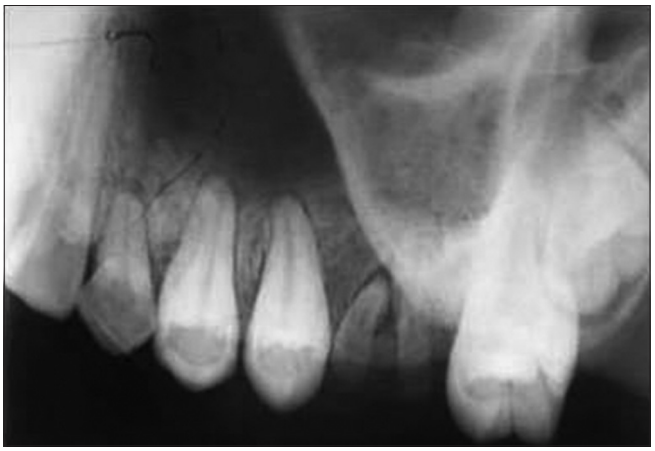

Figure 4: Maxillary left lateral occlusal radiograph revealing a well-defined periapical radiolucency extending from #22 to #26 region with root resorption in relation to #63, #24, and #25

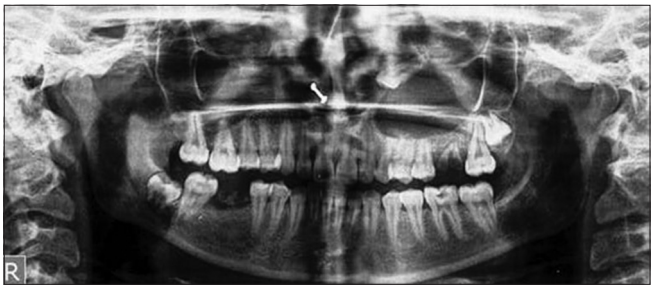

Figure 5: Orthopantomograph revealing a well-defined radiolucent lesion extending from #22 to #26 region associated with impacted #23 and root resorption in relation to #63, #24, and #25

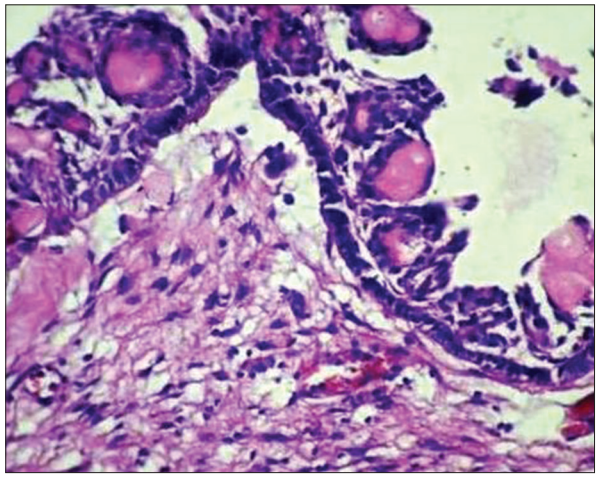

Figure 6: Histopathological examination revealing a cystic epithelium of variable thickness along with a fibrous capsule; the basal cell layer of odontogenic epithelium showing tall columnar cells with palisading arrangement along with focal areas of reverse polarity resembling ameloblast-like cells while the overlaying layer comprising loosely arranged epithelium resembling stellate reticulum-like cells with variable number of eosinophilic structures resembling ghost cells

which was not seen in the present case. Extraosseous lesions often seem to be nonspecific, well-circumscribed, sessile, or

pedunculated masses with a smooth surface and tend to be pink to red in color.[19] Occasionally, CEOC may be seen to perforate the cortical plates and extend into the overlying soft tissues,[17] though this was also not seen in the present case. In the present case, the lesion was relatively well defined and not too invasive as there were no signs of an aggressive behavior when examined clinically, so computed tomography was not advised. The cyst may also displace the adjoining teeth and may lead to resorption of the roots of the teeth in the adjacent area[17] as was seen in the present case too, wherein root resorption in relation to #63, #24, and #25 was evident on maxillary left lateral occlusal radiograph and OPG of the patient.

Occasionally, few cysts have been completely asymptomatic and discovered during routine radiographic examinations, though, in the present case, the patient reported with a chief complaint of swelling in the upper front tooth region of 6-month duration with a history of discomfort due to the swelling while no associated pain was reported. On extraoral examination, a gross asymmetry over the left middle third of the face was noted while the swelling was found to be diffuse, 3 cm × 3 cm in greatest dimensions, hard in consistency, and nontender on palpation.

Because these lesions arise in the tooth-bearing areas of the jaws, radiographically, they appear as unilocular or multilocular radiolucencies with calcifications of variable density in one-third to one half of the cases reported.[7,8,17] The radiolucent lesions often show regular outline while may be irregular and have poorly defined margins. Root resorption and divergency are the common radiological findings and association with an impacted tooth occurs approximately in one-third of the cases[17] as was seen in the present case which was associated with retained deciduous tooth in relation to #63 while missing tooth in relation to #23. However, the present case did not show radiopacities as an evidence of calcification with the conventional radiography as was suggested by McGowan and Browne who also found that the presence of mineralization was approximately twice as frequently seen on microscopic examination compared to radiographic analysis.[20]

As defined in the WHO classification of 1992, CEOC is a cystic lesion in which the epithelial lining shows a well-defined basal cell layer of columnar cells with stellate reticulum-like cells overlaying the basal cell layer while ghost cells are seen occasionally in the lining of the cyst or in the fibrous connective tissue capsule backing the cystic lining. The ghost cells may occasionally become calcified while a layer of dysplastic dentin may be laid down adjacent to the basal cell layer of the epithelium.[8,9,15,21,22] The present case also showed the presence of ameloblast-like cells, stellate reticulum-like cells, and ghost cells along with numerous bundles of collagen fibers associated with subepithelial hyalinization, though no evidence of calcification was found in the present case.

The epithelial lining of CEOC appears to have the ability to induce the formation of dental tissues in the adjacent connective tissue wall. The ghost cells represent an abnormal type of keratinization and have an affinity for calcification. The formation of dentinoid or osteoid which is frequently described as being present in connection with masses of ghost cells is a characteristic finding of CEOCs. Gorlin *et al*. considered the appearance of dentinoid material in CEOCs to represent an inflammatory response of the body tissues toward ghost cells.[2] Abrams and Howell, however, stated that masses of ghost cells induce granulation tissue to lay down juxta-epithelial osteoid which may then get calcified.[23] Ghost cells have also been hypothesized to be due to the effect of coagulative necrosis and subsequent dystrophic calcification, or they may be seen in the process of an abnormal keratinization of the odontogenic epithelium. Ghost cells are not unique to CEOCs, though, and are seen in a plethora of lesions including the odontomes, ameloblastomas, craniopharyngiomas, and numerous other odontogenic tumors[24,25] and can undergo calcification which is believed to be dystrophic in nature.[11,26,27]

The cytoplasm of ghost cells in CEOCs is also said to demonstrate the distinct immune localization of enamel-related proteins including amelogenin and enamelysin. Fejershow and Krogh also demonstrated fine tonofilaments separated by small empty spaces in the cytoplasm of some ghost cells while most of the cells showed very thick, electron-dense, fiber bundles of relatively uniform size, sharply defined against the large empty spaces in the cytoplasm. Endoplasmic reticulum, mitochondria, Golgi apparatus, and ribosomes, though, could not be identified in these cells while the cell membranes were seen to be intact with junctional complexes of various types.[28]

Enucleation is the treatment of choice for most of the intraosseous lesions of CEOCs as was done in the present case. Recurrences, though uncommon, are frequently seen, especially in relation to neoplastic cases such as dentinogenic ghost cell tumors.[7,29,30]

Conclusion

Although rare, CEOC should be considered in the differential diagnosis of the swellings of intraosseous origin in the maxillofacial region and anterior maxilla, in particular. A thorough clinical, radiological and histological work-up thus becomes mandatory for arriving at a correct diagnosis and an effective plan for the treatment of the said lesion accordingly. A regular follow-up protocol also is important in such cases, especially when a particular histological work-up dictates that to rule out any future recurrence of the lesion as well as to rule out any possibility for malignant transformation of the persisting or recurring pathology.

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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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