Peripheral Calcifying Odontogenic Cyst

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**Introduction**

The calcifying odontogenic cyst (COC) is a rare odontogenic lesion which was first described as a distinct entity by Gorlin et al. in 1962. Since then, a large controversy regarding its terminology and classification exists in spite of the currently accepted classification by the World Health Organization (WHO) in 1971.

COC is a cystic lesion in which the epithelial lining shows a well-defined basal layer, an overlying layer resembling stellate reticulum, and masses of "ghost" epithelial cells located in the epithelial cyst lining or in the fibrous capsule. COC represents about 1% of jaw cysts, most of which are located anterior to the first permanent molars. Central COC (CCOC) is found most commonly in the second decade of life (more than 40% of cases); while peripheral COC (PCOC) affects individuals most commonly in their sixth decade of life.

COC is thought to represent a non-neoplastic lesion, but it has a potential for continuous growth. A lot of confusion and disagreement is present in the terminology and classification of COC. Some investigators have considered COC as a tumor with a tendency for marked cyst formation. This concept, called "monistic" by Toida has led some researchers to substitute the terms "calcifying ghost cell odontogenic tumor" or "cystic calcifying odontogenic tumor" for that of COC. In addition, a "dualistic" approach has been suggested, that COC can contain two entities: 1) cyst: calcifying ghost cell odontogenic cyst; 2) neoplasm (benign: calcifying ghost cell odontogenic tumor; or malignant: malignant calcifying ghost cell odontogenic tumor); and combined lesion: each of the categories described above associated with odontoma, ameloblastoma, or other odontogenic lesions.

Indeed, Praetorius et al. divided COC to two groups, 1) cystic and 2) neoplastic, considering the different histologic patterns in them. The cystic form can be (1a) simple unicystic, (1b) odontoma producing, and (1c) ameloblastomatous proliferating. The neoplastic form comprises dentinogenic ghost cell tumor. The latter tumor that may have an infiltrative growth pattern is a predominantly solid lesion with features of...
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ameloblastoma, ghost cells, and dentinoid. Other investigators proposed for this neoplastic counterpart the term "epithelial odontogenic ghost cell tumor" and "odontogenic ghost cell tumor".

Subsequently, WHO, which first recognized and defined the COC as a non-neoplastic cystic lesion, classified the entity and its variants as an odontogenic tumor rather than an odontogenic cyst. The neoplastic lesions were subdivided into three subgroups based on location (intraosseous and extraosseous) and histologic features.

Despite its variable clinical characteristics, COC is often referred to as an asymptomatic slow-growing swelling of the jaws or gingival tissues, depending upon whether the lesion is intraosseous or extraosseous. The extraosseous COC is less common, comprising 12% to 20% of the reported cases. By the year 1991, only 54 cases of extraosseous COC had been reported. Seven cases of extraosseous COC were discussed by Buchner et al. in 1991. A MEDLINE (1993 – 2005) search exhibited only 13 new cases of PCOC published in English-language literature. By the year 2008, only one case of extraosseous COC was reported by Cazal et al. in 2005. Clinically, it appears as a localized or pedunculated gingival mass with no distinctive features. And radiographically, it shows no or only superficial bone involvement with surface erosion.

Case Report

An Iranian 55-year-old female patient with a non-contributory medical history was referred to the Oral and Maxillofacial Surgery Clinic, affiliated to Babol University of Medical Sciences in July 2006 with an exophytic, pink to red, soft tissue lesion of the edentulous ridge at the right lower premolars region, with a diameter of 0.8 cm and a four-month duration. The lesion was clinically appeared to be a reactive lesion. It was painless and firm. Premolars had been extracted in the past. No fever, malaise, or lymphadenopathy was present.

The patient denied the history of smoking, alcohol consumption, or any other harmful habits. A periapical radiograph showed that there was no erosion of the underlying bone or the presence of radiolucency. Under local anesthesia, the lesion was completely removed by an oral and maxillofacial surgeon. Clinical diagnosis was peripheral giant cell granuloma. Microscopic examination showed a cyst lined by an epithelium with numerous ghost cells (Figures 1 and 2). The basal cells were cuboidal to columnar that contained darkly staining nuclei, polarized away from the basement membrane, and palisading and similar to ameloblasts (Figure 3). At higher magnification, a foreign-body reaction to herniated ghost cells in connective tissue was present (Figure 4). The definite microscopic diagnosis was PCOC. No recurrence was present at a two-year follow-up.

Discussion

COC is usually asymptomatic, and is often an incidental finding on radiographs. Seventy-four percent of the maxillary lesions affected the anterior region while 56% of the lesions located in
the mandible. Radiographically, the lesions appear as unilocular or multilocular well-defined radiolucencies, and may be associated with unerupted teeth. PCOC has been reported to represent less than 25% of cases. There is also the possibility that PCOC is somewhat more common, and that some cases of PCOC have been probably classified as other lesions, such as peripheral ameloblastoma.

They are usually located on the gingiva or edentulous ridge. Their clinical appearance is that of a painless, circumscribed, pink or red, and sometimes papillary nodule. The swelling, which is usually located on the gingival or alveolar ridge, is smooth, with a firm or soft cystic texture, and is about 0.5 – 1 cm in diameter. The incisor-canine or premolar regions of the mandible are most frequently involved. About 55% of PCOC have been found between the canines. In some cases (about 25%), there is an erosion of the underlying alveolar bone. About 30% of PCOC are solid rather than cystic (against 2% of CCOC), which can be related to their small size. PCOC has a less aggressive behavior than the intraosseous counterpart (CCOC) and a simple excision biopsy is curative.

Microscopically, it is possible to find the presence of thick-walled cysts that have a smooth outer surface and a semisolid content. Usually there is a single cystic cavity or multiple smaller cavities. The cysts are lined by an epithelium, which is irregular in structure, variable in thickness, and is composed of a columnar or cuboidal layer of preameloblast-like basal cells with reversed polarity of their nuclei. The epithelial lining of COC sometimes has the capacity to induce the formation of dental tissue in the connective tissue wall, mainly in the form of odontomas. Indeed, COC can be found in association with odontogenic tumors such as odontoameloblastoma, adenomatoid odontogenic tumor, calcifying epithelial odontogenic tumor, and ameloblastoma. The ghost cells forming the suprabasal layers are large and lightly eosinophilic, with a cytoplasm containing diffuse tonofilaments, but not ortho- or para-keratin, and showing a faint outline of the cellular and nuclear membrane. These ghost cells may form small foci within the epithelial lining or fuse into large masses, forming extensive sheets of an amorphous, acellular eosinophilic material, extending or even filling the cyst lumen. Mineralization of the ghost cells may be seen. They may also invade the connective tissue, causing a foreign body reaction. The presence of ghost cells in COC is not pathognomonic, having been described in ameloblastoma, ameloblastic fibroma, ameloblastic fibro-odontoma, and odontomas. The microscopic differential diagnosis must be made with peripheral ameloblastoma.

Like PCOC, peripheral ameloblastoma also occurs at a significantly older age than its counterpart. Both lesions share the presence of prominent elongated basal cells and stellate reticulum zone, but the presence of ghost cells is rare in ameloblastoma.
determine whether an individual lesion having a cystic architecture is truly cystic or neoplastic. Further studies, including immunohistochemical investigation on cell proliferation activity, may help in resolving the question. Proliferating cell nuclear antigen labeling index is a possible parameter for differentiating benign from malignant COC, and the proliferative features in the lining seem to be the main factor influencing the proliferating activity of COC. The presented case, similar to the other reports in the literature, had an asymptomatic localized gingival swelling. Clinical presentation of the PCOC is often described as variable or nonspecific. In the reported case, we believe the neoplastic epithelium arose from the odontogenic remnants of the overlying mucosa due to the lesion intimacy with the oral surface and absence of tooth or bone involvement. But whether the cyst develops as central or peripheral lesion probably depends on the location of odontogenic epithelium, which constitutes the source of the lesion. Nevertheless, the location does not seem to have any relation to either behavior or histologic features of the cyst. Treatment of the extraosseous COC involves surgical excision, and recurrences are unexpected. Generally, cystic COCs have good prognosis, but the neoplastic cases are uncertain. When a COC is associated with other odontogenic tumors, treatment and prognosis must be based on the associated lesion.

**References**