



ODONTOCALCIFYING ODONTOGENIC CYST (COCAO). A SEPARATE ENTITY!!?

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ABSTRACT

The calcifying odontogenic cyst (COC) was first described as a distinct entity by Gorlin in 1962. The lesion is a mixed odontogenic benign tumor, and although most of the cases present cystic characteristics, a few are of the solid type and its rare malignant transformation is well documented. The COC may occur in association with other odontogenic tumors, the most common is odontoma, and occurring in about 24% of the cases for this association the term Odontocalcifying odontogenic cyst has been suggested. Radiographically is a well-defined mixed lesion and histological consists of a large cyst and ghost cells have been regarded as pathognomonic for calcifying odontogenic cyst. A large controversy regarding COC terminology and classification exists, in the latest WHO publication on odontogenic tumors it was classified as a benign odontogenic tumor and was renamed as calcifying cystic odontogenic tumor (CCOT). It seems that the COC has two features of cyst and neoplasm. In spite of several dualistic classifications of COC, confusion about terminology and nature still exists. COC and the odontoma may represent coincidental juxtaposition of COC or odontogenic tumor develops in the wall of the preexisting COC. This review is of a calcifying odontogenic cyst associated with odontoma and its proposed terminology Odontocalcifying Odontogenic cyst (COCAO) a brief pathogenesis is discussed.

INTRODUCTION

The calcifying odontogenic cyst (COC) was first reported as a separate pathologic entity by Gorlin et al in 1962. Because of its histological complexity and morphologic diversity, it is still debated whether COC is a cyst or a neoplasm. The majority of COCs are cystic in architecture but on rare occasions they appear as solid lesions. This lesion can also be found associated with other odontogenic tumors, like ameloblastomas, ameloblastic fibroodontoma, odontoameloblastic tumor, calcifying epithelial odontogenic tumor and adenomatoid odontogenic tumor.

The COC normally appears as a painless, slow - growing tumor, affecting equally the maxilla and mandible, with predilection to the anterior segment (incisor/canine area). It generally affects young adults in the third to fourth decade, without gender predilection [1].

Odontoma is the most common odontogenic tumor; and a mixed odontogenic tumor. It is also considered a self-limiting developmental anomaly or hamartoma representing a disordered mixture of dental hard tissues. Odontoma are usually diagnosed in the second decade of life and are usually asymptomatic and are frequently discovered on routine dental radiographs both forms of odontoma are frequently associated with unerupted teeth [2].

A large controversy regarding COC terminology and classification exists COC is thought to represent a non-neoplastic lesion, but it has a potential for continuous

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growth [3]. The COC may occur in association with other odontogenic tumors, the most common is the odontoma, occurring in about 24% of the cases for this association the term Odontocalcifyingodontogenic cyst has been suggested [4].

COCs are into three groups – cysts, benign tumors and malignant tumors and suggested that the term COC should be used specifically to designate the unicystic lesions with or without an associated odontoma. In the latest WHO publication 2005 on odontogenic tumors it was classified as a benign odontogenic tumor and was renamed calcifying cystic odontogenic tumor (CCOT) [5]. This review is of a calcifying odontogenic cyst associated with odontoma & brief discussion about its terminology and pathogenesis of odontocalcifyingodontogenic cyst (COCaO).

Pathogenesis

Odontogenesis is a complex interplay between epithelial elements and those that are derived from ectomesenchyme. Tooth formation is initially evidenced by proliferation of the dental lamina, an epithelial structure found in the primitive oral mucosal epithelium. This dental lamina can proliferate only in the presence of the underlying ectomesenchyme, which thus has an inductive effect on the dental lamina forming the enamel organ. The enamel organ is a three-dimensional structure that has four components: the inner enamel epithelium, the stratum intermedium, the stellate reticulum, and the outer enamel epithelium. A process called induction begins when the cells of the dental lamina closest to the inner enamel epithelium differentiate into odontoblasts and begin to form dentin. The formation of dentin again reciprocates in the inductive ability to stimulate the preameloblasts of the inner enamel epithelium, differentiating them into ameloblasts, which begin to secrete enamel. The odontogenic tumors thus seem to reproduce in a more or less acquired way the different steps of odontogenesis. The first group of epithelial tumors is thought to be histologically related to remnants of the odontogenic epithelium (dental lamina, enamel organ, root sheath of Hertwig), while the second group of mixed tumors is composed of both epithelial- and mesenchymal-derived tissues. The critical factor in understanding the mixed odontogenic tumors as a group and their relationship with tooth formation is in recognizing the inductive and reciprocally inductive influences of one tissue on another. The present hypothesis is that the tumors included in the last group recapitulate some stages of odontogenesis, ranging from the earliest phase (ameloblastic fibroma) to that in which there is a high degree of histo-differentiation (odontomas). On the other hand, it is thought that the lesions in the first group of epithelial odontogenic tumors arise from residue of cells issued from actively growing dental lamina that are present within the jaws for a considerable time after birth. Although histological criteria

have been established for the diagnosis of the COC, its pathogenesis is still speculative, it is proposed that the neoplastic cell is originated from a well-differentiated ameloblast, and its neural crest origin confers to this cell a pluripotential capacity to undergo terminal differentiation. Starting from the postulate that ameloblasts are stem cells, terminal differentiation is not necessarily required to originate the COC neoplastic cell. This fact might justify the ameloblastic like morphology observed in those neoplasms [4,6].

Possibilities of COC associated with odontoma

1. Believed that neoplastic epithelium arise 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 the odontogenic epithelium, which constitutes the source of the lesion [1].
2. Believed that the development of the COC component is a secondary event within the pre-existing odontogenic tumor [7].
3. COC with dental hard tissues in close relation to the lining epithelium as the “odontome producing type” and believed that the odontogenic tumor develops in the wall of the preexisting COC [8].
4. Scholars investigated the histopathologic features of the satellite cysts and epithelial islands in the connective tissue wall of unilocular COC & their results suggest that COC may arise de novo and is not a secondary phenomenon in pre-existing odontogenic tumors [9].
5. It is also argued that the COC is not just a developmental cyst like the dentigerous cyst because it often forms islands of epithelium and dentinoid in the wall; while in some of them, an odontoma forms in the wall [13].
6. COC develops secondarily from odontogenic epithelium that participates in the formation of the odontoma [19].

DISCUSSION

COC was first described as a distinct entity by Gorlin et al in 1962. The review of literature shows that COCs are rare lesions that affect men and women equally, and it appears most frequently in the mandible.^[1] With the available clinical information, the treatments for most of these lesions were also reported to be enucleation or excision. A large controversy regarding its terminology and classification exists 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. The concept, called “monistic” 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 [3].

Microscopically, a cystic lesion which are lined with a basal layer of columnar cells whose nuclei were located next to the basement membrane. Ghost cells have been regarded as pathognomonic for calcifying odontogenic cyst and are recognized by their characteristic eosinophilic appearance, the mass confirmed the presence of denticles with poorly structured/mineralized dentin like structure and fibrous connective tissue, leading to the diagnosis of calcifying odontogenic cyst. The presence of ghost cell keratinization alone is not sufficient enough for the diagnosis nor is it pathognomonic. Ghost cell keratinization may be observed in odontoma, Ameloblastoma, and Ameloblastic fibro-odontoma, ghost cells make the diagnosis of the Gorlin cyst, and however, their presence alone is not sufficient enough to make or dictate the diagnosis [5].

Are new terminologies required?

The COC can also be found associated with other odontogenic tumors, like ameloblastomas [5]. Whether ameloblastoma ex COC should be classified as a subtype of ameloblastoma or as a subtype of COC may be open to discussion. At this present state, it is very difficult to determine whether any individual lesion having a cystic architecture is truly cystic or, in fact, neoplastic in nature [12]. Recognizing the extreme diversity in clinic-pathologic features and biologic behavior among the so called COCs, authors suggest that the term COC should be used to specifically designate the unicystic lesions with or without an associated odontoma, i.e., lesions of the cyst group, and other related lesions identified as benign tumor and malignant tumor should be termed and classified separately. Other authors have reported two cases of an exceptional combination of these tumors combined benign odontogenic tumors calcifying epithelial odontogenic tumors (CEOTs) and calcifying odontogenic cysts (COCs) with either an ameloblastic fibroodontoma or an odontoma. [6]. By studying the 21 intraosseous COCs, the authors suggested that the term COC should be used for unicystic lesions with or without an associated odontoma and other related lesions identified as benign or malignant tumor should be termed separately [13].

Nevertheless, the location does not seem to have any relation to either behavior or histological features of the cyst numerous cases of the Gorlin cyst have been described it has become obvious that it is not one lesion but really two. 1] Cystic lesion 2] Solid neoplastic lesion. 3] Third malignant counterpart of the neoplasm lesion may be added. The calcifying odontogenic cyst may present as

an intraosseous cystic lesion or in association with an odontoma [10].

In addition, the COC may be associated with other recognized odontogenic tumors, adenomatoid odontogenic tumors and ameloblastoma, the most common is the odontoma, occurring in about 24% of the cases for this association the term odontocalcifyingodontogenic cyst(COCaO) has been suggested[4,8]. The COCaO presents a female predominance (2:1) with a mean age of 16 years, most frequently occurring in the maxilla, Radio graphically appears as a mixed radiolucent-radiopaque lesion microscopically the epithelial components in COCaO were identical to those described for simple COC, but the former present's tooth-like structures that appear to be an integral part of the lesion [11].

Several possibilities are suggested regarding the pathogenesis of COCaO. One possibility is that the COC and the odontoma may represent coincidental juxtaposition of COC and an odontoma, because other odontogenic tumors like Ameloblastoma have been reported to be associated with COC. Other investigators suggest that the COC develops secondarily from odontogenic epithelium that participates in the formation of the odontoma. However, it also has been suggested that the odontoma develops secondarily from lining epithelium of the COC and finally few authors think that the COCaO should be regarded as a separate entity, characterized by the clinical differences in location and in age distribution between simple COC and COCaO, In addition to the unique histologic features, differences in gender and in distribution were found between the cases of COCaO and those of simple COC. Hirshberg suggested when COC associated with odontoma it's a separate entity and sorted as a benign, mixed odontogenic tumor termed as odontocalcifying odontogenic cyst (COCaO) [4, 11,16].

Various researchers have published the COC association with odontoma

Hirshberg A, reported occurring in about 24% of the cases [11] Buchner showed this association in 35% of his cases, Nagao et al. in 22% and Shamaskin et al. in 47%. Radiographically COCaO appears as a mixed radiolucent-radiopaque lesion (80%) occasionally calcifications cannot be observed on OPG but can be visualized in CT scan [11,14-17]. Recently Mohtasham [18] has reported a COC associated with odontoma & used the term of odontocal cifyingodontogenic cyst.

But as defined in the WHO classification of 1992, it is: 'A cystic lesion in which the epithelial lining shows a well-defined basal layer of columnar cells, an overlying layer that is often many cells thick and that may resemble stellate reticulum, and masses of "ghost" epithelial cell that may be in the epithelial lining or in the fibrous capsule. The "ghost" epithelial cells may become calcified dysplastic dentine may be laid down adjacent to the basal layer of the epithelium, and in some instances the



cyst is associated with an area of more extensive dental hard tissue formation resembling that of a complex or compound odontoma.' So associated with odontoma is not unusual, the cytokeratin expression in the COCaO has been studied by several authors confirming its odontogenic origin. The COCaO should be treated conservatively by surgical enucleation because recurrences are very uncommon [4]. In the last WHO publication [2005] on odontogenic tumors it was classified as a benign odontogenic tumor and was renamed calcifying cystic odontogenic tumor (CCOT) and defined a benign cystic neoplasm of odontogenic origin, characterized by an ameloblastoma-like epithelium with ghost cells that may calcify [5].

CONCLUSION

It seems that the COC has two features of cyst and neoplasm. In spite of several dualistic classifications of COC, confusion about terminology and nature still exists. COC and the odontoma may represent coincidental juxtaposition of COC or odontogenic tumor develops in the wall of the preexisting COC. COC should be used to specifically designate the unicystic lesions with or without an associated odontoma, i.e., lesions of the cyst group, and

other related lesions identified as benign tumor and malignant tumor should be termed and classified separately, with surgical conservative treatment and a follow-up. As COC may be associated with an ameloblastoma, AOT, Odontoma naming ameloblastoma ex COC, AOT ex COC, or when associated with other combined odontogenic tumors as hybrid COC! COC associated with an odontoma (COCaO) may not be renamed, until or otherwise its behavior and prognosis are altered, for better determination of histopathologic and biologic nature of COC associated with odontoma, An extensive and systematic analysis of many more cases including immunohistochemical investigations on cell proliferation activity may help resolve this problem.

It's rightly said the confusion regarding the terminologies and classification of calcifying odontogenic cyst should remain as academic exercise and more emphasis should be laid on the biological behavior of the lesion [20].

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CONFLICT OF INTEREST:

The authors declare that they have no conflict of interest.

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