Indian Journal of Clinical Dentistry Jan-June 2020
Volume 1; Issue1:Pg. 17-23

Case Report

Ameloblastoma ex COC: An enigma to clinicians and Pathologists

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Abstract

Calcifying odontogenic cyst (COC), though known for more than five decades, is always under constant ambiguity with respect to its nomenclature and classification with extreme diversity in its biologic behavior. It represents a heterogeneous group of lesions that are to be regarded as non-neoplastic, cystic, or solid masses and more frequently found in association with hamartomatous such as odontomas, Adenomatoid odontogenic cyst and other odontogenic tumors such as odontogenic fibroma and Ameloblastoma. Owing to the fewer incidences, uncertain descriptions of the COCs, specific clinical data in the literature is sparse.

Key words: Ameloblastoma, Benign, Calcifying odontogenic cyst, Neoplastic

Introduction

COC of cystic jaw lesions (0.37 – 1.2%) shows extreme assortment in its clinical, radiographic, histopathologic features and in its biologic behavior as well [1]. Two different concepts were attributed in regard to nature of the lesion as monistic and dualistic yet, disagreement still persists. The monistic concept was best exemplified by the WHO postulates that, all COCs are neoplastic in nature, even though the majority are cystic in architecture and appear to be non-neoplastic. In contrast, the dualistic concept, favored by most researchers proposes that COCs contain two different entities, a cyst and a neoplasm [2]. In spite of the diversity that exists in the terminologies, based on its origin , histopathological features, and architectural pattern, controversies still prevail over the usage of terminology pertaining to this lesion. [Table 1]

All the recent classifications have established a category for the variant of COC associated with ameloblastoma. The ameloblastomatous COC and ameloblastoma arising from COC (ameloblastoma ex COC), are the two variants described till date. The ameloblastoma ex COC is very rare, with only three cases have been reported in the literature. This is a case of an ameloblastoma ex COC with special emphasis on its peculiarity, occurrence in the posterior mandibular area.

Case report

A female patient of 22 years old visited a dental practice with a swelling that was insidious in onset, slow growing and painful involving the left angle of the mandible since one week. On extra oral examination, a hard swelling of 1 x 1.5 cm on the left side of the mandible causing mild asymmetry was observed. Intra oral examination revealed a lesion measuring approximately 3 x 2 cm anterioposteriorly that extended from the distal aspect of the lower left first molar to third molar area, causing obliteration of the vestibule. Swelling was soft to firm in consistency, with crepitus being felt on both buccal & lingual vestibular region.

The orthopantomograph (OPG) revealed a well-defined, unilocular radiolucency which extended anterioposteriorly from the left first mandibular molar area to third molar area, superioinferiorly from the superior border of the mandible to 1 cm below the lower border of the man-dible, with root resorption in relation to teeth number 36 to 38 regions with flaring of the roots. Buccal & lingual cortical plate expansion is observed along with the shelling out of lingual cortical plate. [Figure1]. The intra oral radiograph revealed a well-defined unilocular radio -

lucency, involving the periapical area of the distal root of 36 and extending to 38 area causing resorption of three fourth of roots of 37 along with complete root resorption of 38. The radiographic differential diagnosis includes Developmental cysts, Ameloblastoma or CEOT.

A computed tomography (CT) showed a well-defined, expansile, destructive, hypodense mass, with thin residual septae like areas.[Figure 2] On aspiration about 1.5 ml of straw colored fluid was collected and sent for the FNAC analysis. The pro-tein content of the fluid was 3.5g/dl. The Hematoxylin & Eosin (H & E) stained aspirate re-vealed dense acute and chronic inflammatory infiltrate, suggesting an infected cyst. An incisional biopsy was carried out and a gross specimen of single gray to grayish white soft tissue was sent for histopathologic analysis. Microscopic examination of the specimen revealed odontogenic epithelium of 2-3 cell layered in thickness lining the cystic lumen. The periphery of the lesion at one area showed numerous blood vessels & extravasated blood, suggestive of an infected odontogeniccystcyst. Initially, on analyzing clinical & radiographic features of impacted tooth, it was considered as dentigerous cyst and for confirmation excisional biopsy was planned. Under local anesthesia the lesion was enucleated and the excised lesion was sent for histopathological evaluation.

Histopathological examination revealed several pieces of cystic brown lining and soft tissue masses that were brown in colour, with smooth to irregular surface area. The lesional tissue portion of the H&E stained exhibited flat 2-3 cell layered thickness of epithelium and proliferations in some regions of the cystic lumen. Scattered within the epithelial lining, a whorled pattern with few dissipated ghost cells, and juxtaepithelial hyalinized areas were observed.

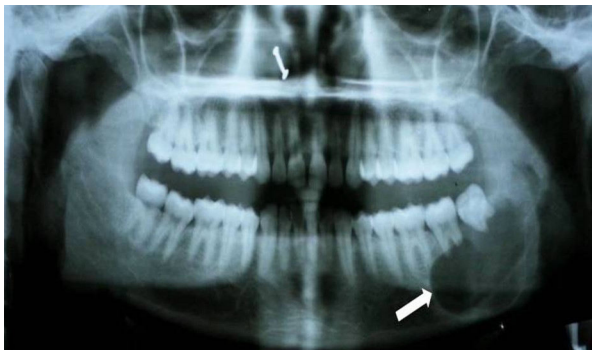

Fig- 1: Preoperative, orthopantomogram (OPG)

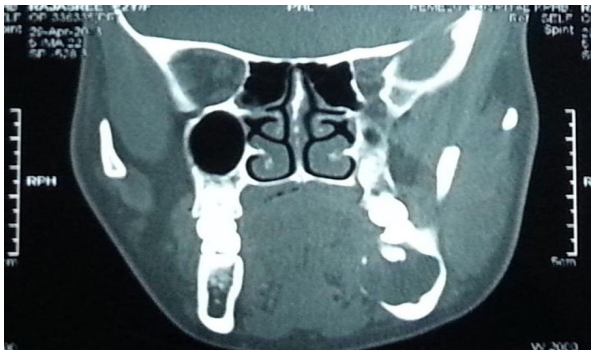

Fig- 2: Axial view of the CT scan

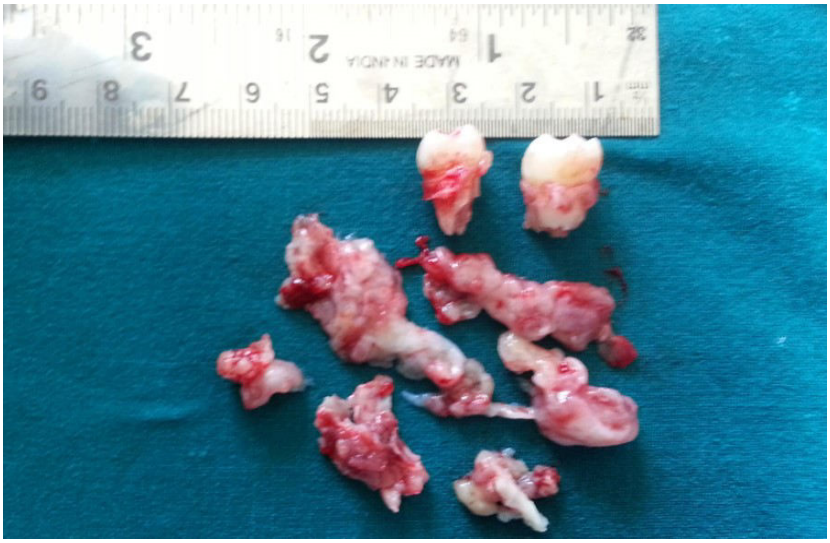

Fig- 3: Excised lesional tissue showing multiple bits of cystic lining and soft tissue masses

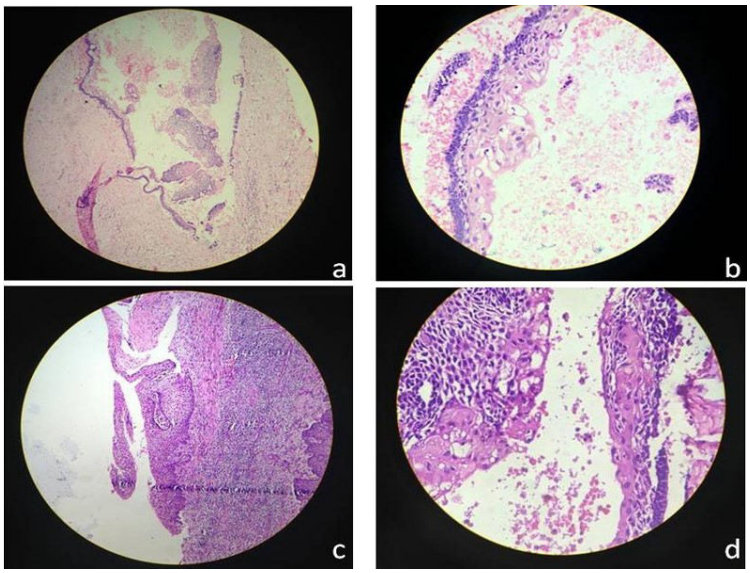

Fig- 4(a): Lesional tissue showing cystic epithelial lining without any ghost cells & calcifications. (H&E- 4X).
Fig- 4(b): Lesional tissue showing areas in whorled pattern, arranged in the discontinuous cystic epithelial lining without any calcification, suggestive of COC. (H&E- 40X).
Fig- 4(c): Lesional tissue showing ameloblastic proliferation within the cystic wall, without any ghost cells & calcifications with the underlying connective tissue showing chronic inflammatory infiltrate (H&E- 10X).
Fig- 4(d): The lesional tissue showing ameloblastic proliferation, with stellate reticulum like areas and epithelial cells showing intercellular spacing on the right side with cystic epithelial lining on the left side showing basal columnar layer showing hyperchromatic nuclei with overlying stellate reticulum like areas. (H&E- 40X).

Tall to columnar with hyperchromatic nuclei which resembled ameloblasts like cells were present. Overlying these ameloblasts were a loosely arranged stellate-shaped cells resembling stellate reticulum. The proliferating cystic epithelial lining resembled plexiform pattern of solid or multicystic ameloblastoma that showed absence of ghost cells or calcifications. Underlying connective tissue showed dentinoid-like material with mature collagen fiber bundles. Ameloblastic follicles and odontogenic islands were present in some regions along with presence of non-keratinized stratified squamous epithelium.

Ameloblastoma with such an epithelial proliferation exhibited the classic Vickers & Gorlin criteria as follows - the basal cuboidal to columnar nuclei showing hyperchromatic polarized nuclei with palisading appearance, sub nuclear cytoplasmic vacuolization with intercellular spacing and sub-epithelial hyalinisation. All the clinical, radiographic and histopathological features were suggestive of ameloblastoma arising from COC or ameloblastoma ex COC [Figure 4]. No history of recurrence of the lesion since 1 year.

Discussion

WHO (1992) described COC as a neoplasm rather than a cyst but confirmed most of the tumors were cystic, non-neoplastic and were in the favor of monistic concept (a tumor but with a tendency for marked cystic formation) [3]. COC is a painless, slow growing tumor in maxilla or anterior part of the mandible have features of a cyst but 15% of them are solid lesions usually affect 3rd & 4th decades of life with combined microscopic features of COC and ameloblastoma in literature [3,4,5].

It is believed that the epithelial lining of the COC has the ability to induce the formation of dental tissues in the adjacent connective tissue wall, which could be reason for the association of COC with ameloblastoma. But the present case is unique in its existence with ameloblastoma ex COC in the posterior part of the mandible. Usually, ameloblastoma ex COC occurs intraosseous appearing as cyst-like, radiolucent lesions. The association of COC with ameloblastoma gained wide acceptance after Hong et al described two well documented cases of ameloblastoma ex COC, describing the rarity of ameloblastoma arising from COC. Ameloblastoma ex COC exhibited unifocal

Table 1: Various terminologies proposed

Terminology	Author
COC was first described as " cholestoma of jaws"	Rywkind (1932)
COC associated with areas resembling ameloblastoma	Thoma and Goldman(1946)
COC associated with areas resembling ameloblastoma –"Atypical adamatinoma"	Maitland (1947)
Calcifying odontogenic cyst (COC) resembles oral analog of "cutaneous calcifying epithelioma of Malherbe"	Gorlin et al (1962)
keratinizing Calcifying odontogenic cyst (KCOC)	Gold et al.(1963)
Keratinizing ameloblastoma	Bhaskar (1965)
Non-neoplastic cystic lesion	WHO (1971)
Calcifying ghost cell odontogenic tumour(CGOT)	Fejerskov and krogh(1972)
Cystic Calcifying odontogenic tumour(CCOT)	Freedman et al.(1975)
Dentinogenic ghost cell tumour(DGCT)	Praetorius et al.(1981)
Epithelial odontogenic ghost cell tumor(EOGCT)	Ellis and shmooker(1986)
Odontogenic ghost cell tumor(OGCT)	Colmenero et al.(1990)
Benign odontogenic tumor	WHO (1992)
Odontogenic ghost cell ameloblastoma(OGCA)	Shear(1994)
Odontocalcifying odontogenic tumor(OOT)	Wirshberg et al.(1994)
Calcifying ghost cell odontogenic cyst(CGCOC)	Toida (1998)
Calcifying cystic odontogenic tumor (CCOT)	WHO classification (2005)

intraluminal and intramural ameloblastoma proliferating from the COC-lining epithelium. The present case showed all the histological features described by Hong et al [4], since it is associated with a neoplastic lesion, it needs to be treated with a regular follow-up [5].

Tajima et al have reported a case of ameloblastoma arising in COC [6]. Toida et al stated that though these tumors are rare, they were solid with cystic areas typical of COC were evident within the tumor [7]. Although the delineations between the entities are rather lissome the histopathologic diagnosis that stands as a gold standard for the ultimate diagnosis of the lesion goes in favor of Ameloblastoma ex COC. The differentiating features between ameloblastomatous COC, ameloblastoma ex COC, and odontogenic ghost cell tumor are described in detail [Table 2]. The cases reported in the literature along with their clinical, radiographic and histological features in relation to Ameloblastoma ex COC with the features exhibited by the present case [8,9,10,11]. [Table 3]

Wong et al documented a case with a gingival mass at an extraction site which was initially thought to be a peripheral ameloblastoma. On incisional biopsy it was diagnosed as dentinogenic ghost cell tumour/ CEOT after excision with a margin of sound bone with no recurrence till 2 years [12].

Kasahara et al described an OGCT/COC/CEOT that recurred after segmental resection of the mandible. Histopathological examination revealed tumour invasion of the surrounding cortical bone with areas containing numerous calcifying flaky cell nests, and dentinoid matrix near epithelial cell nests. No atypical mitosis was found. There has been no evidence of recurrence or metastasis in the 4 years [13].Regarding the treatment and prognosis of Ameloblastoma ex COC, it has to be treated similar to ameloblastoma with care and periodic follow up are mandatory [3,5,7].

Buchner has reported that only nine cases have recurred out of ninety two during 8 year follow up however, Philipsen & Reichart stated that recurrences of

Table 2: Differentiating features between ameloblastomatous calcifying odontogenic cyst, ameloblastoma ex calcifying odontogenic cyst, and odontogenic ghost cell tumor.

	Ameloblastomatous calcifying odontogenic cyst	Ameloblastoma ex calcifying odontogenic cyst	Odontogenic ghost cell tumor
Clinical features	Age -2nd and 6th decades Sex-no predilection Site-mandible Painless swelling causing hard bony expansion Displacement of teeth	Age -2nd and 6th decades Sex-no predilection Site-mandible Painless swelling of jaws	Age-older than 50 years Sex –male predilection. Site-mandible. Jaw expansion Obliteration of maxillary sinus
Radiographic features	Unilocular or multilocular radiolucent lesion but flecks of opacity can be seen	Unilocular or multilocular or mixed radiolucent lesion	Multilocular radiolucent or mixed radiolucent lesion.
Histopathological features	Cystic lining lined by columnar cell with an overlying layer of stellate reticulum-like cells with ghost cell that may or may not show calcification. Cystic lining shows intramural and intraluminal ameloblastomatous proliferation which are usually plexiform in pattern but can be follicular. Ghost cells and calcification within the proliferations are seen. Ameloblastoma-like cells are not present. (Vickers and Gorlin criteria	Cystic lining lined by columnar cell with an overlying layer of stellate reticulum-like cells with ghost cell that may or may not show calcification. Ameloblastic proliferation within the cystic wall without ghost cells and calcification Ameloblastoma-like cells can be easily identified. (Vickers and Gorlin criteria)	Ameloblastoma-like areas and odontogenic epithelial islands with ghost cells showing keratinization and calcification. Presence of dentinoid deposition around the proliferation categorizes the tumor as odontogenic ghost cell tumor.

COCs are rare and recommended that a follow up of 10 yrs seems to be beneficial [3,5].

Shah et al described a cystic variant of COC which was asymptomatic with a higher propensity toward the posterior region of the mandible. A wide surgical excision of the lesion with normal margins followed by chemical cauterization of Carnoy's solution was done and no recurrence was seen during a 6 year follow-up [14]. Inadvertent use of the term COC for the lesion carries the possibility of masking the real biological behavior of the solid neoplastic variant and neoplastic with cystic architecture, which has high proliferating index, On the other hand use of the term CCOT (WHO 2005) for the lesion may result in unwanted extensive surgical procedure for the cystic subtypes [7,15,16].

Upon considering the facts, authors would like to suggest that, use of nomenclature should emphasize on biological behavior of the lesion rather than familiar or older terms, so that lesion can be approached and treated accordingly. Generally, nomenclature carrying a phrase "cystic" is approached conservatively (enucleation or marsupialization), than nomenclature carrying a phrase "tumor", which are treated more aggressively (en bloc resection) and followed -up precautiously for a longer period.

Conclusion

An inimitable lesion, COC is considered as a monistic tumor form with a tendency for marked cystic formation has evolved as a dualistic concept as cystic and neoplastic forms shows miscellany in all diagonals that include classification, clinical, radiographic and histopathological perspectives. This lesion has further taken

Table 3: Clinical, Radiographic and Histological features of ameloblastoma ex COC reported till now in the literature

Authors	Clinical features	Histopathological features
Aithal et al. (2003)	Age:28 yrs/F Clinical presentation: painless swelling in the left posterior region of the mandible. On palpation well–defined hard, non tender swelling of 2.5X2.0 cm with smooth surface in relation to mandibular 1st and 2nd premolars extending till floor of the mouth with intact overlying mucosa. Radiographic findings: Multilocular radiolucency in the left mandibular posterior region extending from the mesial surface of the canine to second molar was seen.	Ghost cells in the cystic epithelium and juxta epithelial hyalinization in some areas. Odontogenic epithelium in the form of rosettes and acanthomatous ameloblastomic islands in the connective tissue lining of the cyst.
Lida et al. (2004)	Age:17 yrs/M Clinical presentation: Facial asymmetry at right mandibular region is seen. On palpation swelling is hard and tender in consistency. Radiographic findings: Well-defined multilocular radiolucency from lower right second molar involving entire ramus and coronoid process on both the buccal and lingual sides is seen. Presence of an unerupted lower second molar dislocated inferiorly to a position below the first molar is noticed.	Presence of odontogenic epithelium with many masses of ghost cells with calcification, and solid parts showing ghost cells and ameloblastomatous proliferations seen in the connective tissue of the cyst wall
Kamboj M et al (2007)	Age: 58 yrs/F Clinical presentation; Pain on the right side of the mandible for the past five years, and swelling in the associated region since last two years. Intraorally, a large swelling was extending from the canine up to the ramus causing bucco-lingual expansion. On palpation, a hard, but fluctuant and cystic lesion was felt near the angle and retromolar region of the mandible Radiographic findings; multilocular radilolucency on thje right side of the mandible extending from the canine region up to the condyle and coronoid areas.	Cystic spaces lined by odontogenic epithelium comprising of darkly stained basal cells, stellated reticulum like areas with masses of ghost cells. With no calcification. Occasional areas showed juxtaepithelial dentinoid formation. Ameloblatic proliferative activity was seen both intraluminally and intramurally with no histopathologic criteria as suggested by Vickers and gorlin. These proliferations were mainly of follicular pattern with few follicles showing ghost cells. The juxtaepithelial dentinoid formation around the ameloblastomatous proliferations were not seen.
Present case	Age:22 yrs/F Clinical presentation: slow growing painful swelling in the left angle of the mandible. Intraorally, well–defined soft to firm , non tender swelling of 3X2.0 cm with smooth surface in relation to left mandibular first to third molar area with crepitus been on buccal & lingual vestibular area is seen. Radiographic findings: well-defined multilocular radiolucency in the left mandibular posterior region extending from the distal surface of the first molar area to the third molar.	Odontogenic epithelium comprising of darkly stained basal cells that resembled ameloblasts, stellated reticulum like areas with presence of ghost cells at very few areas in whorled pattern, without any calcifications are seen. Ameloblastomatous proliferative activity of plexiform pattern, were seen both intraluminally and intramurally, without ghost cells in the cystic wall.

shape into a tetrad concept of a simple cyst, cyst associated with hamartoma, benign and malignant neoplasms. Histologically whether it represents as two unrelated lesions, COC and ameloblastoma developing simultaneously is a question open to semantics. If a variant of COC has to be diagnosed, it has to include complete information on its clinical, radiographic and histopathological aspects that may act as an aid for future generations from its cataloguing to treatment modalities. Further case reports and long term follow up are required to illustrate its behavior as there is paucity of well documented data pertaining to this lesion.

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How to cite: *Sumanth G, Kalyani T, Saritha K, Swetha P Ameloblastoma ex COC: An enigma to clinicians and Pathologists. Ind J Clin Dent 2020;1(1):17-23*