

# Calcifying odontogenic cyst: Report of an uncommon entity with a brief literature review

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## Abstract

The aim of this clinical report is to document a rare and unusual case of calcifying odontogenic cyst (COC) in the maxillary anterior region in a 13-year-old girl.

A COC is an extremely uncommon developmental, odontogenic entity and accounts for 0.3%–0.8% of odontogenic cysts. The lesion presents as an array of varied radiographic and clinicopathological characteristics and biological attributes and exists in three histomorphologic patterns – benign cystic, solid (neoplastic) and aggressive (malignant) forms. Thus, several nomenclatures and classifications have been put forth to explain the nature of the clinical entity. However, ambiguities regarding the exact nature of the lesion still prevail. Due to nonspecific clinicoradiographic features, histopathological interpretation remains the key for diagnosis. We report an uncommon occurrence of COC in a 13-year-old female who reported to our Outpatient Department with an asymptomatic right midfacial swelling. The clinical and radiographic findings were suggestive of adenomatoid odontogenic tumor and dentigerous cyst. The decision to enucleate the lesion was considered, and histopathological features were compatible with the diagnosis of COC. Re-ossification with no recurrence was noticed after a 1-year follow-up. COC is an unusual developmental odontogenic cyst that clinically and radiologically simulates other more common jaw entities. Thorough knowledge of the bizarre presentation and biological attributes of such lesions are imperative for an early diagnosis and definitive treatment. Long-term follow-up is advocated to prevent recurrences.

**Keywords:** Calcifying odontogenic cyst, enucleation, ghost cells, odontogenic cyst

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## INTRODUCTION

The calcifying odontogenic cyst (COC) is classically a benign cystic entity lined by odontogenic epithelium and simulates as ameloblastoma. The lesion is categorized under ghost cell lesions as it manifests with distinctive ghost cell keratinization.<sup>[1]</sup> Altini and Farman reported that the entity had been initially documented in the German literature (1932).<sup>[2]</sup> However, Gorlin *et al.* assumed the

condition to be an oral analog of cutaneous calcifying epithelioma of Malherbe.<sup>[3]</sup> Ever since its documentation, there has been disagreement concerning its classification and nomenclature. This ambiguity in the nomenclature and classification has arisen as the entity exists in three histomorphologic distinct forms – benign, cystic lesions, solid tumor (neoplastic) masses and aggressive (malignant) variants.<sup>[4-7]</sup>

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The employed treatment strategies greatly vary and depend on the type of lesion. In general, a conservative approach by enucleation/marsupialization is considered deemed for benign cystic lesions, whereas solid tumor masses and aggressive lesions should be treated by en bloc resection with a vigilant and prolonged follow-up.<sup>[8,9]</sup>

Hereby, we report an uncommon occurrence of COC in the right maxillary anterior region in a 13-year-old female and its surgical management. A 1-year follow-up revealed re-ossification with no evidence of recurrence.

## CASE REPORT

A 13-year-old girl presented to our Outpatient Department with the chief complaint of right midfacial facial swelling for the last 2–3 months. The initial smaller swelling had shown gradual progression to attain the present size. No previous history of trauma with nonrelevant past medical and surgical history was noted. On extraoral examination, gross facial asymmetry involving the right midface region was apparent. The swelling was ovoid-shaped, 5 cm × 4 cm in size, extended supero-inferiorly up to 2 cm inferior to the right infraorbital margin to 3 cm below the inferior border of the upper lip and anteroposteriorly from right nasal alar to about 2 cm anterior to the tragus of the ear. A slight deviation of the nasal tip on the left side with obliteration of the right nasolabial fold was also apparent. Palpation revealed that the swelling was nontender and hard in consistency [Figure 1a]. On intraoral evaluation, a solitary, ovoid-shaped swelling, measuring 4 cm × 3 cm in size, with labial cortical expansion was appreciable in the right maxillary anterior vestibular area. The swelling extended anteroposteriorly from distal margin of 11 to the mesial aspect of 15, superiorly causing obliteration of labial mucobuccal fold and inferiorly to the gingival margins of teeth. The mucosa over the swelling was intact and of the same color as the normal mucosa. Palpatory findings suggested



**Figure 1:** (a) Extraoral swelling in the right midface region, (b) Intraoral swelling with labial cortex expansion in right maxillary anterior region

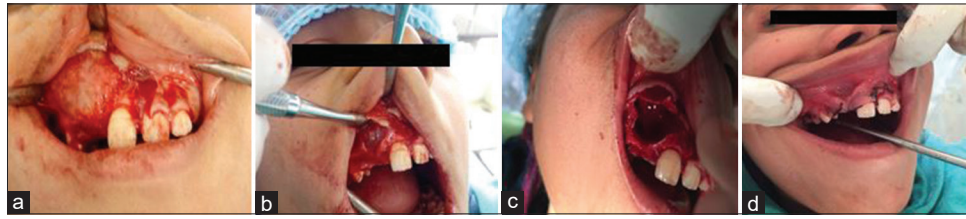
that the swelling was nontender, peripherally bony hard in consistency and fluctuant at the center. The intraoral examination also revealed clinically missing permanent teeth, namely right maxillary lateral incisor, right maxillary canine, right mandibular canine, with mild distal tipping in relation to (i.r.t.) right maxillary central incisor, mesial tipping i.r.t. right maxillary first premolar and retained deciduous right mandibular canine, with no apparent mobility in the associated teeth [Figure 1b].

Based on the location, patient's age and gender, benign clinical nature and association with clinically missing teeth, the condition was provisionally diagnosed as adenomatoid odontogenic tumor (OT). Dentigerous cyst, unicystic ameloblastoma and COC were given a place in the differential diagnosis.

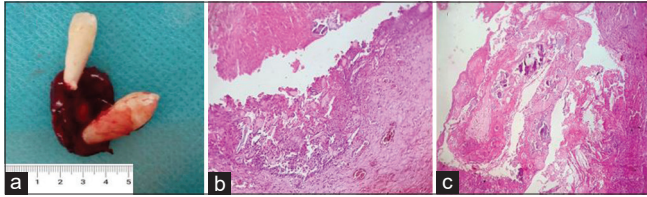
The associated teeth demonstrated a positive response to pulp vitality testing. A yellow-brown, blood-tinged cystic aspirate was obtained on fine-needle aspiration [Figure 2a]. Blood investigations including complete blood count, serum calcium, phosphorus and parathormone levels were within normal limits. Orthopantomogram demonstrated a well-demarcated, ovoid, unilocular radiolucency with thin peripheral sclerotic border in the right maxillary anterior region, extending from mesial margin of right central incisor to the mesial margin of right maxillary first premolar, roughly measuring 3 cm × 2.5 cm in size and encircling the pericoronal region of impacted maxillary right lateral incisor and canine. The internal structure was completely radiolucent. There was a mild distal displacement of the maxillary right central incisor and mesial displacement of maxillary right first premolar with loss of lamina dura of these teeth [Figure 2b].



**Figure 2:** (a) Yellow-brown, blood-tinged cystic aspirate on needle aspiration, (b) Orthopantomogram showing a well-defined radiolucency in maxillary anterior region



**Figure 3:** (a) Intraoperative procedure depicting the crevicular incision, (b and c) Exposed cystic lesion with enucleation, (d) Sutures placed



**Figure 4:** (a) Macroscopic specimen showing the enucleated cyst lesion, (b and c) H&E stain sections reveal nonkeratinized cystic epithelium with palisaded hyperchromatic basal cells. Superficial layers of epithelium resemble stellate reticulum and show the presence of ghost cells (x100)

A decision to enucleate the lesion was considered taking in account the patient’s age, the radiographic appearance and the size of the lesion (after taking written consent from the patient’s parents). A crevicular incision was made under local anesthesia in the maxillary right anterior region. The lesion was exposed and enucleated by careful dissection along with the impacted lateral incisor and canine [Figure 3a-d]. The enucleated specimen was submitted for histopathological examination. On macroscopic examination, the tissue appeared cystic measuring approximately 1 cm × 1.5 cm in size. The roots of the maxillary canine and lateral incisor were firmly adherent to the cystic wall [Figure 4a]. Histological evaluation of the H and E stain, ×100 revealed a cystic lumen lined by nonkeratinized odontogenic epithelium with a distinct basal cell layer of low columnar cells and prominent hyperchromatic nuclei. Few areas showed the presence of stellate reticulum, whereas the remaining showed the presence of squamous metaplasia. Intraluminal proliferations were seen throughout the cystic lining and were composed of epithelial cells interspersed with characteristic ghost cells and Liesegang rings. The cystic wall was composed of fibrous connective tissue [Figure 4b and c]. The histopathological findings were suggestive of a COC. The postoperative healing was unremarkable, and periodic follow-up was advised to the patient. Re-ossification with no recurrence was observed after a 1-year follow-up [Figure 5].

**DISCUSSION**

COC is an uncommon developmental cyst attributing to <1% of odontogenic cysts.<sup>[10,11]</sup> COC exhibits an array of diverse biological attributes and varied clinicopathologic



**Figure 5:** One-year follow-up orthopantomogram revealing re-ossification and no recurrence

presentation, giving rise to uncertainty and ambiguity in the nomenclature and classification.<sup>[2,9,12-15]</sup>

The entity has been described by various terminologies, as documented in Table 1. However, COC is still the favored term.<sup>[10,16]</sup>

COC classification is based on two hypotheses – monistic and dualistic. The “monistic” theory considers COCs to be neoplastic, even though most lesions seem benign and cystic. The “dualistic” theory suggests that the lesion exists in two different forms – a cystic and neoplastic form. The World Health Organization (WHO) (1992) advocated the monistic theory and considered COC as an OT, however, the dualistic theory is recommended nowadays by most researchers.<sup>[17]</sup> Various classifications of COC subtypes have been suggested [Table 2], but most of them do not help differentiate cystic and solid entities.<sup>[12,13]</sup>

**Table 1: various terminologies for calcifying odontogenic cyst**

Author & year	Terminology
Gorlin <i>et al.</i> (1962)	Calcifying odontogenic cyst
Gold M (1963)	Keratinizing calcifying odontogenic cyst (KCOC)
Bhaskar SN (1965)	Keratinizing ameloblastoma (KA)
Fejerskov and Krogh (1972)	Calcifying ghost cell odontogenic tumor (CGCOT)
Freedman <i>et al.</i> (1975)	Cystic calcifying odontogenic tumor (COCT)
Praetorius <i>et al.</i> (1981)	Dentinogenic ghost cell tumor (DGCT)*
Ellis and Shmookler (1986)	Epithelial odontogenic ghost cell tumor (EOGCT)*
Colmenero <i>et al.</i> (1990)	Odontogenic ghost cell tumor (OGCT)*
Shear M (1994)	Odontogenic ghost cell ameloblastoma (OGCA)
Hirshberg <i>et al.</i> (1994)	Odontocalcifying odontogenic tumor (OOT)
WHO Classification (2005)	Calcifying cystic odontogenic tumor (CCOT)



**Table 2: Various classification systems for calcifying odontogenic cyst**

Author & year	Type	Description
Praetorius <i>et al.</i> (1981)	Type 1	Cystic type (a) Simple Unicystic type (b) Odontomaproducing type (c) Ameloblastomatous proliferating type
Buchner <i>et al.</i> (1990)	Type II	Neoplastic type: Dentinogenic ghost cell tumor (DGCT)
	Type 1	Peripheral (Extrasosseous) COC Cystic variant Neoplastic (solid) variant
Hong <i>et al.</i> (1991)	Type II	Central (Intraosseous) COC Cystic variant Simple Unicystic/multicystic Associated with odontomas Associated with odontogenic tumors (other than odontomas) Other variants (clear cells or pigmented variants) Neoplastic variant Malignant COC
	Type 1	COC associated with ameloblastoma The Ameloblastomatous cystic variant (clusters of ghost cells and calcifications) The neoplastic variant associated with ameloblastoma (few or no ghost cells with calcification)
Toida <i>et al.</i> (1998)	Type 1	Cyst: calcifying ghost cell odontogenic cyst (CGCOC)
	Type 2	Neoplasm: A. Benign: calcifying ghost cell odontogenic tumor (CGCOT) a. Cystic variant: cystic calcifying ghost cell odontogenic tumor (CGCOT) b. Solid variant: solid calcifying ghost cell odontogenic tumor (CGCOT) B. Malignant: malignant calcifying ghost cell odontogenic tumor (CGCOT)
Li & Yu <i>et al.</i> (2003)	Type 3	Combined lesion: each of the categories described above associated with the following lesions: a. Odontoma b. Ameloblastoma c. Other odontogenic lesions
	Type 1	Developmental odontogenic cyst: Calcifying odontogenic cyst (COC, Unicystic lesions with or without odontoma)
	Type 2	2. Benign odontogenic neoplasm: a. Odontogenic ghost cell tumor (OGCT, solid tumor with foci of ghost cells and dentinoid) b. combined lesions (odontogenic tumors [other than odontoma] with COC features) *
Barnes <i>et al.</i> (2005)	Type 3	Odontogenic carcinoma: Odontogenic ghost cell carcinoma (OGCC) (malignant counterpart to COC or OGCT)
	Type 1	(1) Nonneoplastic (simple cystic) variant (CGCOC) (a) With non-proliferative epithelial lining (b) With non-proliferative epithelial lining associated with odontomas (c) With proliferative epithelial lining (d) With Unicystic, plexiform Ameloblastomatous proliferation of epithelial lining
Praetorius <i>et al.</i> (2006)	Type 2	Neoplastic variant (a) Benign type (CGCOT) (i) Cystic subtype (cystic CGCOT): (COC turning into Unicystic ameloblastoma) SMA ex epithelial cyst lining (ii) Solid subtype (solid CGCOT) Peripheral ameloblastomalike Solid multicystic ameloblastomalike (b) Malignant type (malignant CGCOT) (i) Cystic subtype (ii) Solid subtype
	Type 1	'Simple' cyst, calcifying odontogenic cyst (COC)
Gorlin <i>et al.</i> <sup>[3]</sup>	Type 2	Cysts associated with odontogenic hamartomas or benign neoplasms: calcifying cystic odontogenic tumours (CCOT)
	Type 3	Solid benign odontogenic neoplasms with similar cell morphology to that in the COC, and with dentinoid formation (Dentinogenic ghost cell tumour)
WHO	Type 4	Malignant odontogenic neoplasms with features like those of the dentinogenic ghost cell tumour (Ghost cell odontogenic carcinoma)

Our case findings were suggestive of simple unicystic type (Type I [a]) of the COC (based on the proposed classification by Praetorius *et al.* [1981]).

Gorlin *et al.*<sup>[3]</sup> were the first to document COC and proposed subclassifications with debatable terminologies.<sup>[13]</sup>

WHO considered it as tumor (1992),<sup>[17]</sup> and later termed the entity as calcifying cystic OT (2005).<sup>[18]</sup> However, the recent WHO Classification of Head and Neck Tumours (2017) considered the entity as the COC. The current WHO classification termed COC for the cystic lesions and dentinogenic ghost cell tumor for the neoplastic entities.<sup>[19]</sup>

The benign or cystic form is most frequently seen (80%–98%).<sup>[15,20]</sup> COC can be associated with OTs, particularly odontomas, but it has also been reported with adenomatoid OT, ameloblastoma, ameloblastic fibroma and ameloblastic fibro-odontoma.<sup>[17,21]</sup> The solid tumor mass/neoplastic variant contributes for 11.5% of cases.<sup>[15,20]</sup>

In general, COCs are central/intraosseous, and peripheral COCs are occasionally seen.<sup>[16,22]</sup> The central lesions frequently exhibit an asymptomatic, expansile bony hard jaw swelling. In general, buccal cortical expansion is seen, sparing the palatal cortex.<sup>[8,9]</sup> The other infrequent features are tooth discoloration and pain if secondarily infected.<sup>[9]</sup> Initial lesions are an incidental finding on a routine radiographic examination.<sup>[11,23]</sup> Extraosseous COC manifests as an asymptomatic, well-defined, smooth surface nodular mass of size 0.5–3.0 cm, on the alveolar mucosa or gingiva.<sup>[8,9,24]</sup>

COC may be seen anywhere in the oral cavity, however, most of the cases are seen in the anterior jaw region.<sup>[4,8,16,21]</sup> COC equally affects both maxilla and mandible,<sup>[2,9,22]</sup> with no gender predilection.<sup>[2,3,9,22]</sup> The lesions are mostly seen in the second decade of life,<sup>[2,4,9]</sup> although few cases may be reported in individual's aged between 1 and 82 years of age. The majority of COC occurs anterior to the first molar region, with more than 75% of cases occurring in the incisor-canine region or intercanine region.<sup>[4,8,9,13,17,24]</sup> Mandibular lesions frequently cross the midline, in contrast to the maxillary lesions.<sup>[1,7]</sup>

In the present case, a 13-year-old female patient reported an asymptomatic bony hard swelling in the maxillary right anterior jaw region. Buccal cortical expansion with clinically missing right maxillary lateral incisor and canine was noticed. Our case was in coherence with the published literature findings.

The universally recognized theory regarding the origin is that COC emanates from the odontogenic derivatives. The dental lamina rests present within the bone/soft tissue are the precursor cells accountable for their origin.<sup>[13,25]</sup>

Radiographically, most of the lesion exhibits a unilocular pattern with a well-demarcated sclerotic border, however, few cases are multilocular (5%–13%). The internal structure may manifest varied presentations – (a) completely radiolucent, (b) mixed pattern - most cases appear as a mixed (radiolucent-radiopaque) lesion, with unevenly distributed calcifications exhibiting an array of radio-opacities and (c) conglomerate of cloudy masses.<sup>[1,2,6,9,17]</sup>

The lesion exhibit three appearances of radiopacities – (a) salt-and-pepper fleck-like pattern, (b) uniform fuzzy amorphous pattern and (c) one aspect of the radiolucent lesion may exhibit a crescent-shaped appearance mimicking a “new moon”-alike pattern.<sup>[13]</sup>

Intraosseous COC has been documented in association with odontomas and impacted teeth (usually canines) in 24%–35% and 35% of cases, respectively.<sup>[20]</sup> Another radiographic finding is that the lesion is frequently associated with unerupted teeth (32% of cases), thus, radiographically simulating dentigerous cyst.<sup>[1,9]</sup> The expansile lesion causes root resorption and divergence of the involved teeth,<sup>[7,11,20]</sup> with thinning and perforation of the cortical bone.<sup>[8,20]</sup>

The differential diagnosis can be established with other lesions of different radiographic aspects, such as ameloblastoma, odontogenic keratocysts, periapical cyst, ameloblastic fibro-odontoma and adenomatoid OT.<sup>[25]</sup>

Our case presented with a unilocular radiolucency with a thin peripheral sclerotic border in the right maxillary anterior region, encircling the pericoronal region of the impacted maxillary right lateral incisor and right maxillary canine. The internal structure was completely radiolucent. The radiolucency caused the mild displacement of the associated teeth. Our case presented with similar radiographic features as previously published in the literature.

The salient microscopic features of the COC are epithelial basal lining arranged in a cuboidal/columnar fashion and simulate that of ameloblasts. A cellular pattern mimicking the stellate reticulum of the enamel organ in the suprabasal layers is also a common feature.<sup>[7,8,26]</sup> Ghost cells are the characteristic histopathological feature of COC, which are eosinophilic cells devoid of a nucleus.<sup>[17]</sup> Eventually, the ghost cells may get calcified, thus, losing the cellular configuration and result in foci of calcified keratin.<sup>[20]</sup>

In addition to the classical features of COC such as cystic epithelial lining with ameloblast-like differentiation and ghost cells, our case also showed many areas with squamous metaplasia of the stellate reticulum.

Enucleation is the preferred treatment for central cystic lesions; however, occasional recurrences have been demonstrated in few cases.<sup>[8,11,16,20]</sup> En bloc resection with a vigilant and prolonged follow-up is the recommended management protocol for neoplastic COC.<sup>[8,9,16]</sup>

The present case was surgically enucleated, and a 1-year follow revealed new bone formation with no recurrence. The patient is still on follow-up.

## CONCLUSION

COC is an unusual developmental odontogenic cyst that clinically and radiologically simulates other more common jaw entities. The lesion has always been a topic of ambiguity concerning the duality of the lesion and has resulted in various nomenclature and classifications. Due to nonspecific clinicoradiographic features, histopathological interpretation remains the key for diagnosis. Long-term follow-up is advocated to prevent recurrences.

## Informed consent

The patient was informed about the nature of disease and treatment protocol. Written informed consent was taken from patient's parents.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published, and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

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