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CASE REPORT

Histopathologic Diversity of Gorlin's Cyst: A Study of Four Cases and Review of Literature

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ABSTRACT

Aim: The purpose of the present article is to discuss four different case reports of the so-called calcifying odontogenic cyst and highlight the histopathological diversity of the same.

Background: Calcifying odontogenic cyst was first described by Gorlin et al in 1962. Ever since, its identification as a specific odontogenic lesion, controversies and confusions have existed regarding the relationship between cystic lesions and solid tumor masses that share cellular and histomorphologic features. Although several classifications were proposed, dilemma still persists regarding the nature of these lesions as cysts, neoplasms and even malignancies.

Conclusion and clinical significance: The classifications discussed for the so-called calcifying odontogenic cyst by various authors have only added to further confusion rather than enlightening. Though many authors state that classifications remain only an academic exercise, it definitely has significance in treatment planning. Emphasis should, therefore, be laid on a universally accepted classification.

Keywords: Calcifying odontogenic cyst, Histomorphologic features, Neoplasm.

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INTRODUCTION

The calcifying odontogenic cyst (COC) was first recognized by Gorlin, Pindborg, Praetorious-Clausen and Vickers in 1962 and later by Gold.[1-4,6] Ever since, its recognition as a specific odontogenic lesion, controversy and confusion have existed regarding the relationship between nonneoplastic, cystic lesions and solid tumor masses that share the cellular and histomorphologic features which described by authors.[4]

In 1971, the COC gained international recognition when the World Health Organization (WHO) classification of odontogenic tumors defined it as 'a nonneoplastic 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 that may resemble stellate reticulum and masses of ghost epithelial cells that may be in the epithelial cyst lining or in the fibrous capsule. The ghost epithelial cells may become calcified. Dysplastic dentin may be laid down next to the basal cell layer of epithelium'.[4]

With time, it became apparent that not all COCs are cystic. Some solid lesions indeed are apparently neoplastic in nature. Moreover, the COC is frequently found in association with, or contains areas histologically identical to, various types of odontogenic tumors, such as complex/compound odontomas, ameloblastomas, ameloblastic fibromas and so on. The term COC, originally proposed by Gorlin et al, appears to be not altogether appropriate. So, different terms, such as dentinogenic ghost cell tumor, dentinogenic ghost cell ameloblastoma, odontogenic ghost cell ameloblastoma, atypical adamantinoma, epithelial odontogenic ghost cell tumor, odontogenic calcifying ghost cell tumor, calcifying cystic odontogenic tumor, keratinizing and calcifying odontogenic cyst, keratinizing ameloblastoma, calcifying ghost cell odontogenic tumor, were suggested.[5]

Recently, the WHO panel of experts on odontogenic tumors published the 2005 WHO histological classification of odontogenic tumors. In this publication, calcifying cystic odontogenic tumor (CCOT) was defined as 'a benign cystic neoplasm of odontogenic origin characterized by an ameloblastoma, like epithelium with ghost cells, that may calcify and dentinogenic ghost cell tumor (DGCT) was defined as 'locally invasive neoplasm characterized by ameloblastoma, like islands of epithelial cells in a mature connective tissue stroma. Aberrant keratinization may be found in the form of ghost cells in association with varying amounts of dysplastic dentin'.[1]

Over the years, several classifications have been proposed by different authors with the aim of clarifying the nature and grouping of the different histomorphological and clinicopathological features of this set of tumors.[6]

The purpose of the present article is to depict the histopathological diversity of COC seen in four different cases reported to our institution and to review the different classification systems proposed by various authors with an emphasis on the ambiguity persisting in these classification systems.

CASE REPORTS

Case 1

Case 1 was of a 22-year-old female patient with a chief complaint of palatal swelling in 12 region. The lesion was 4 × 2 × 0.1 cm in dimensions and could be completely enucleated *in toto*. The gross specimen was a single gray to grayish-white soft tissue lesion with a cystic lumen.

On microscopic examination, the H&E stained tissue showed a cystic lumen lined by a nonproliferating epithelium of 4 to 10 cells thick. The basal cells were tall columnar and resembled ameloblasts. Overlying these ameloblasts, like cells, were loosely arranged epithelium resembling stellate reticulum. Scattered within the epithelial lining were few ghost cells. Based on these histopathological features, a diagnosis of simple unicystic calcifying odontogenic cyst was given (Fig. 1).

Case 2

A 32-year-old male patient had a chief complaint of pain in the left posterior region. Radiographic examination of the region showed mesioangular impaction of 38. Around the impacted 38, a unilocular radiolucency of 1 × 1 cm was seen.

The histopathologic examination of the biopsied specimen showed a characteristic epithelium of 4 to 10 cells thick. The lining showed basal cells resembling ameloblasts, while the superficial cells resembled stellate reticulum. Areas of eosinophilic material resembling dysplastic dentin were also seen adjacent to epithelial component. Compound odontome like calcification was seen within the connective tissue capsule of the lesion. Based on these features, a diagnosis of odontome producing type of calcifying odontogenic cyst was given (Figs 2 and 3).

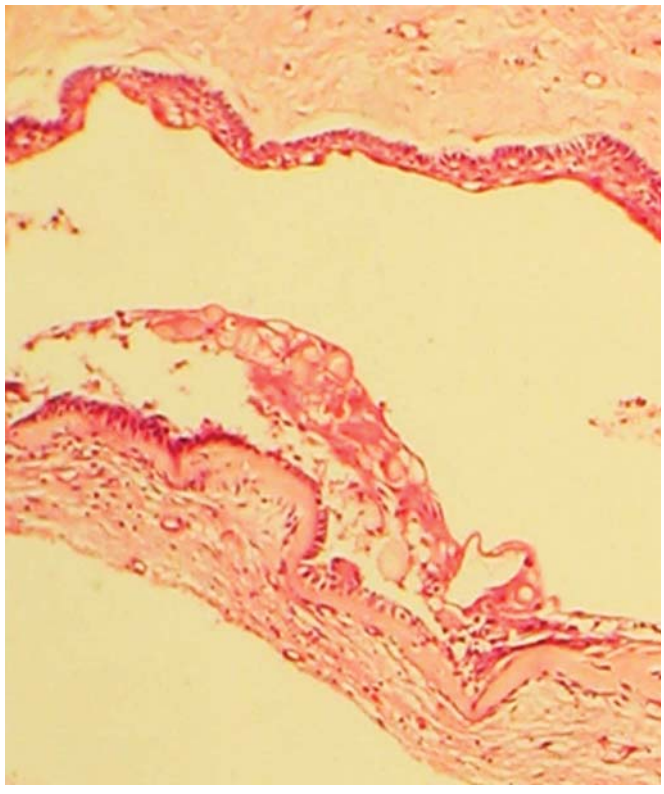

Fig. 2: Photomicrograph showing proliferating cystic epithelium. Ghost cells and juxtaepithelial dentinoid deposition are seen (H&E stain, 4× magnification)

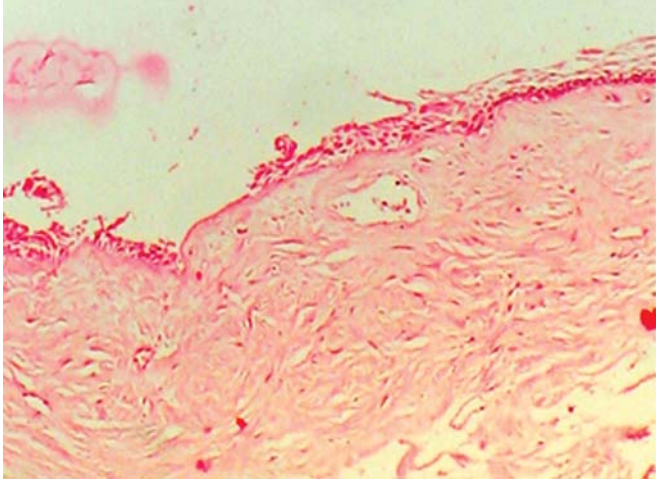

Fig. 1: Photomicrograph showing simple cystic epithelium lining fibrous capsule (H&E stain, 4× magnification)

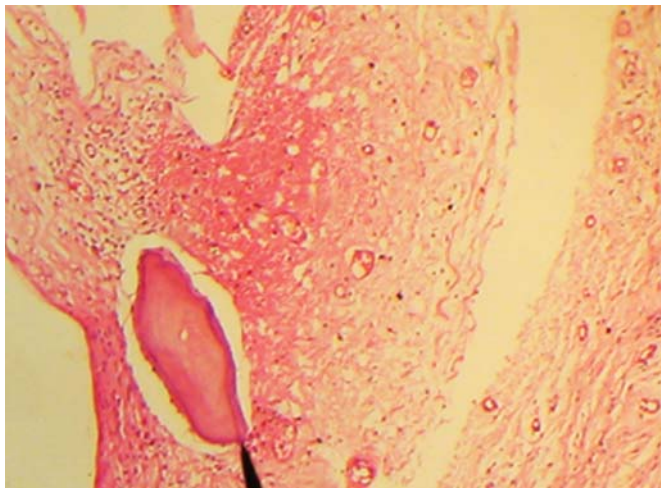

Fig. 3: Photomicrograph showing compound odontome like calcification within fibrous capsule (H&E stain, 10× magnification)

Case 3

A 19-year-old male patient had a swelling over the right side of the maxilla in the anterior region since 3 months. The lesion was associated with an impacted 11 and was 2 × 1 × 1 cm in dimensions. The histopathologic examination revealed cystic lining resembling that of a COC. The cystic lining showed proliferation into fibrous capsule. The proliferating epithelium resembled follicles of solid ameloblastoma. Ghost cells were seen in abundance within the epithelium lining. Histopathologic features suggested a diagnosis of ameloblastomatous proliferation type of COC (Fig. 4).

Case 4

A 45-year-old male patient had a swelling in the mandibular anterior region. The swelling was 4 × 3 × 3 cm in dimension and was crossing the midline, involving 33, 32, 31, 41, 42 and 43. Radiographic examination showed multilocular radiolucency in the mandibular anterior region. The histopathologic examination of the same showed a typical cystic lining of calcifying epithelial odontogenic cyst. The cystic lining showed multifocal intramural and intraluminal proliferation. The proliferating cystic lining resembled solid multicystic ameloblastoma in plexiform pattern. The cystic lining contained numerous ghost cells, whereas solid multicystic ameloblastomatous areas showed little or no ghost cells. These histopathologic features again warranted the diagnosis of ameloblastomatous proliferation type of COC (Figs 5 and 6).

DISCUSSION

The central calcifying odontogenic cyst is a rare lesion. Its clinical and radiological features are not pathognomonic

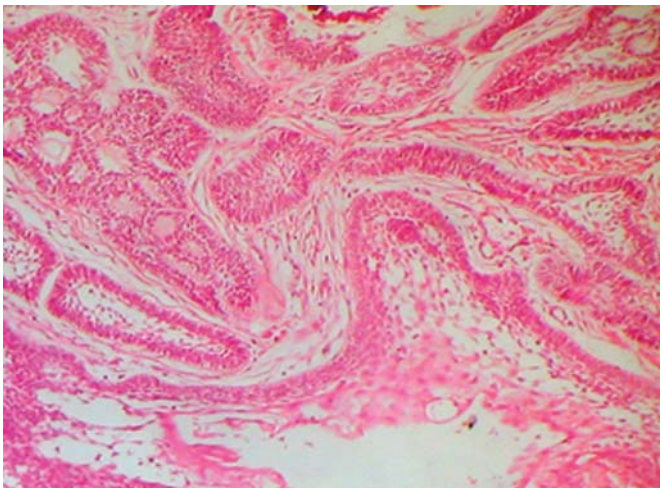

Fig. 4: Photomicrograph showing proliferating cystic epithelium and ameloblastomatous proliferation within cystic capsule (H&E stain, 10× magnification)

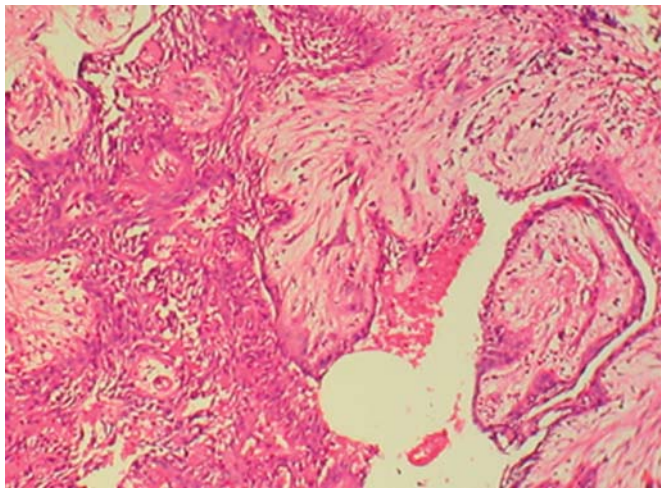

Fig. 5: Photomicrograph showing cystic lining showed multifocal intramural and intraluminal proliferation (H&E stain, 10× magnification)

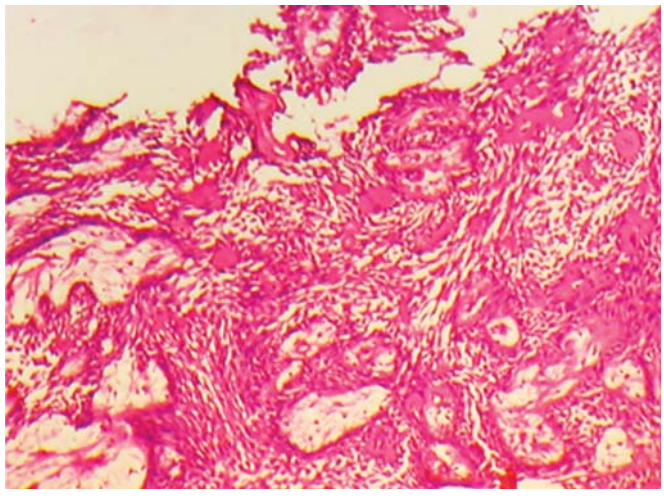

Fig. 6: Photomicrograph showing cystic lining with many ghost cells while solid multicystic ameloblastomatous areas showed little or no ghost cells (H&E stain, 10× magnification)

and characterized by histological diversity. Gorlin et al were the first to describe this entity. They initially regarded it as the oral analog of cutaneous calcifying epithelioma of Malherbe, but later labeled it the COC.[7] Prior to this, Rywkind[8] described it as a variant of the cholesteatoma, while Maitland[9] regarded it as a type of ameloblastoma. Recently, WHO has defined these lesions as CCOT, as a result of its neoplastic behavior.[10]

The odontogenic origin of the COC is widely accepted. Praetorious et al suggested that it develops in the dental follicle, gingival tissue or bone from remnants of either odontogenic epithelium or reduced enamel epithelium.[11]

CCOT constitutes only about 2% of all benign odontogenic lesions. About 78% of them occur in the jaw bones, while the rest of them occur in the soft tissues. These lesions most commonly occur at various ages of 10 and 30 years; however, lesions in maxilla tend to occur in older

patients. These lesions normally appear as a painless slow-growing tumor, equally affecting the maxilla and mandible with predilection to anterior part of the jaws.[12] Radiographically, these lesions appear either as a unilocular or multilocular radiolucent area with either well-circumscribed or poorly-defined margins. Differing amounts of radiopaque materials are observed. These lesions are observed in association with an unerupted tooth in 10 to 32% of cases.[13]

COC has been histopathologically defined by the WHO as a nonneoplastic cystic lesion that is lined by enamel organ, like epithelium, containing denucleated eosinophilic ghost cells and calcifications in the epithelium and connective tissue wall, and is sometimes associated with other features.[14]

Ghost cells are swollen and keratinized cells without nuclei, with a clear conservation of basic cellular outlines, endowed with resistance to resorption and tendency to develop foreign body granulomas.[15] However, the nature of the ghost cells is not clear and many hypotheses have been advanced and are under debate. Some of the hypotheses are (1) Ghost cells have been considered as abnormal keratinized bodies,[16] (2) they may represent simple cell degeneration or a form of enamel matrix,[17] (3) ghost cells might derive from the apoptotic process of odontogenic cells or represent different stages of normal and abnormal keratin formation, therefore, deriving from metaplastic transformation of odontogenic tumors.[18]

Lucchese et al analyzed the ghost cells using confocal laser scanning microscope, and depending upon different fluorescence extent, divided the ghost cells into three types or stages: (1) Scarcely detectable, (2) well resolved and (3) cells showing excellent resolution.[19]

Ever since, the lesion was first recognized as a distinct pathologic entity by Gorlin et al, many authors stressed the cystic nature of the lesion and its peculiar histologic features that distinguished it from the calcifying epithelial odontogenic tumor. With time, it became apparent that not all the COCs are cystic. Some solid lesions are apparently neoplastic in nature. Moreover, the COC is frequently found in association with, or contains areas histologically identical to, various types of odontogenic tumors, such as complex/compound odontomas, ameloblastomas, ameloblastic fibromas and so on. Such extreme diversity of these lesions has led to confusion and disagreement in their terminology and classification.

In 1981, Praetorius et al[11] proposed a widely used classification which tried to resolve the question on the cystic or neoplastic nature of COC. They proposed that it could be divided into cystic and neoplastic types. The cystic variety was classified as simple unicystic type (type Ia), odontome producing (type Ib) and ameloblastomatous proliferating type (type Ic) and the neoplastic variant was termed as dentinogenic ghost cell tumor (DGCT) (Table 1). However, this classification was found to be somewhat ambiguous in interpreting the nature of the subdivided variants. So, authors continued to use COC as a general term to include all cystic and neoplastic variants. In addition, this classification included various types of combined lesions, such as 'ameloblastomatous proliferating type' and 'COC associated with odontogenic tumors', in the cystic variant of COC. This added further to the confusion concerning the nature of these lesions.

Table 1: Classification of the so-called COC by Praetorius et al (1981)

Type 1: Cystic type
1. Simple unicystic type
2. Odontomas producing type
3. Ameloblastomatous proliferating type
Type 2: Neoplastic type
Dentinogenic ghost cell tumor

To clarify these confusions, Toida[20] proposed two mutually contradictory concepts regarding the nature of COC: The monistic and dualistic concepts (Table 2). The monistic concept was in keeping with the WHO classification in 1992, which regards COC as a tumor with tendency for marked cystic formation. However, current thinking strongly favors the dualistic concept that COC contains two entities: A cyst and a neoplasm.

Table 2: Classification of the so-called COC by Toida (1998)

1. *Cyst:* Calcifying ghost cell odontogenic cyst
2. *Neoplasm:*
   - A. *Benign:* Calcifying ghost cell odontogenic tumor
     - a. Cystic variant—cystic calcifying ghost cell odontogenic tumor
     - b. Solid variant—solid calcifying ghost cell odontogenic tumor
   - B. *Malignant:* Malignant calcifying ghost cell odontogenic tumor
3. *Combined lesion:* Each of the categories described above associated with the following lesions:
   - (a) Odontoma
   - (b) Ameloblastoma
   - (c) Other odontogenic lesions

Recently, the WHO panel of experts on odontogenic tumors published the 2005 WHO Histological Classification of Odontogenic Tumors,[10] in which COC was renamed as calcifying cystic odontogenic tumor (CCOT) and retained the term DGCT (Table 3).

Ledesma-Montes in 2007[1] studied 122 cases of ghost cell odontogenic tumors and devised a comprehensive and

objective classification that would include all the so-called COC subtypes (cystic and solid) and ghost cell odontogenic cyst (GCOC) cases under the 2005 WHO guidelines (Table 4).

In the present compilation, the four cases described earlier were classified according to the classifications proposed by Praetorius et al, Toida et al, WHO and Ledesma-Montes et al. It was observed that case 1 was classified as type Ia according to Praetorius et al classification, type I according to Toida et al classification, type Ia according to WHO classification and CCOT type I according to Ledsma-Montes et al classification. A great deal of agreement was observed between all the four classifications for the case 1. However, for the other three cases, there was no or very little agreement between the classifications used (Table 5). This suggests that there is no uniformity in the different classifications proposed and requires lot more work to be done in this regard.

Table 3: Classification of COC as suggested by WHO in 2005

1. Nonneoplastic (simple cystic) variants (CGCOC[a])
   - A. With nonproliferative epithelial lining
   - B. With nonproliferative (or proliferative) epithelial lining associated with odontoma
     - a. With proliferative epithelial lining
     - b. With unicystic plexiform ameloblastomatous proliferation of epithelial lining
2. Neoplastic variants
   - A. Benign type (CGCOT)
     - a. Cystic subtype (cystic CGCOT)
       (α) SMA ex epithelial cyst lining
     - b. Solid subtype (solid CGCOT)
       (α) Peripheral ameloblastoma like
       (β) SMA like
   - B. Malignant type (malignant CGCOT or OGCC[h])
     - a. Cystic subtype
     - b. Solid subtype

Table 4: Classification of ghost cell odontogenic tumors given by Ledesma-Montes et al in 2008

A. Calcifying cystic odontogenic tumor (CCOT) includes peripheral and central cases
   - CCOT type 1—Simple cystic CCOT includes pigmented and clear cell variants
   - CCOT type 2—Odontoma associated CCOT
   - CCOT type 3—Ameloblastomatous proliferating CCOT
   - CCOT type 4—CCOT associated with benign odontogenic tumors other than odontoma

B. Dentinogenic ghost cell tumor (DGCT)
   - DGCT type 1—Central, solid, aggressive variant
   - DGCT type 2—Peripheral, less aggressive variant

C. Ghost cell odontogenic carcinoma
   - GCOC arising *de novo*—Not associated with a previous DGCT or CCOT but with areas suggesting DGCT
   - GCOC ex-CCOT—GCOC arising from a previous CCOT
   - GCOC ex-DGCT—GCOC arising from a previous DGCT

CONCLUSION

Not only has confusion plagued the terminology used for this complex lesion but also there is a significant source of disagreement which stems from the fact that there appear different concepts or schools of thought when looking at the nature of COC. Therefore, an extensive and more systematic classification is the need of the hour to clear the confusion about COC.

REFERENCES

1. Ledsma-Montes Constantino, Gorlin Robert J, Shear Mervyn, Praetorius Finn, Mosqueda-Taylor Adalberto, Altini Mario, et al. International collaborative study on ghost cell odontogenic tumors: Calcifying cystic odontogenic tumor, dentinogenic ghost cell tumor and ghost cell odontogenic carcinoma. J Oral Pathol Med 2008;37;302-08.
2. Tie-Jun Li, Shi-Feng Yu. Clinicopathologic spectrum of the so-called calcifying odontogenic cysts. The American Journal of Surgical Pathology 2003;27(3);372-84.
3. Buchner Amos, Merrell Philip W, Hansen Louis S, Leider Alan S. Pheripheral (extraosseous) calcifying odontogenic cyst. Oral Surg Oral Med Oral Pathol 1991;72:65-70.
4. Reichart Peter A , Philipsen Odont Hans P. Odontogenic tumors and allied lesions. London: Quintessence Publishing Co Ltd.
5. Hong Sam Pyo, Ellis Gary L, Hartman Kenton S. Calcifying odontogenic cyst—a review of ninty-two cases with reevaluation of their nature as cysts or neoplasms, the nature of ghost cells and subclassification. Oral Surg Oral Med Oral Pathol 1991; 72;56-64.
6. Folpe AL, Tsue T, Rogerson L, Weymuller E, Oda D, True LD. Odontogenic ghost cell carcinoma: A case report with immunohistochemical and ultrastructural characterization. J Oral Pathol Med 1998;27;185-89.
7. Gorlin RJ, Pindborg JJ, Clausen FP, Vickers RA. The calcifying odontogenic cyst: A possible analogue of the cutaneous calcifying epithelioma of Malherbe. Oral Surg 1962;15:1235-43.
8. Rywkind AW. Beitrag Zur pathologic der cholesteatome. Virchow, S Arch Path Anat 1932;283;13-28.
9. Maitland GR. Atypical adamantinoma of maxilla: A case report. J Oral Surg 1947;5:351-55.
10. Kleihues P, Sobin LH. Odontogenic tumors. In: Barnes L, Everson J, Reichart P, Sidaransky D (Eds). World Health Organization classification of tumors. Pathologic and genetics of tumors of the head and neck. Lyon: IARC press 2005:313.

Table 5: Classification of the four cases according to different systems

Cases	*Praetorius et al (1981)*	*Toida et al (1995)*	*WHO (2005)*	*Ledesma-Montes et al (2008)*
Case 1	Type Ia	Type I	Type Ia	CCOT type I
Case 2	Type Ib	Type IIIa	Type Ib	CCOT type II
Case 3	Type Ic	Type IIIb	Type IIAaα	CCOT type III
Case 4	Type Ic	Type IIIb	Type IIAaα/type IIAβ?	CCOT type III

11. Praetorius F, Hjorting-Hansen E, Gorlin RJ, Vickers RA. Calcifying odontogenic cyst: Range, variations and neoplastic potential. Acta Odontol Scand 1981;39:227-40.
12. Buchner A. The central (intraosseous) calcifying odontogenic cyst: An analysis of 215 cases. J Oral Maxillofac Surg 1991;49: 330-39.
13. Tanimoto K, Tomita S, AoyamavM, Furuki Y, Fujita M, Wada T. Radiographic characteristics of the calcifying odontogenic cyst. Int J Oral Maxillofac Surg 1988;17;29-32.
14. Pindborg JJ, Kramer IRH, Torloni H. Histologic typing of odontogenic tumors, jaw cysts and allied lesions. Geneva: World Health Organization 1972:28.
15. Ebling H, Wagner JE. Calcifying odontogenic cyst. Oral Surg Oral Med, Oral Pathol 1967;24:537-39.
16. Gunhan O, Celasum B, Can C, Finci R. The nature of ghost cells in calcifying odontogenic cyst: An immunohistochemical study. Ann Dent 1993;52:30-33.
17. Mori M, Yamada K, Kasai T, Yamada T, Shimokawa H, Sasaki S. Immunohistochemical expression of amelogenins in odontogenic epithelial tumors and cysts. Virchows Arch A Pathol Anat Histopathol 1991;418:319-25.
18. Kim J, Lee EH, Yook JI, Han JY, Yoon JH, Ellis GL. Odontogenic ghost cell carcinoma: A case report with reference to the relation between apoptosis and ghost cells. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000;90:630-35.
19. Alberta Lucchese, Michele Scivetti, Giovanni Pietro Pilolli, Gianfranco Favia. Analysis of ghost cells in calcifying cystic odontogenic tumors by confocal laser scanning microscopy. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;104:391-94.
20. Ariyoshi Y, Shimahara M, Miyauchi M, et al. Clear cell odontogenic carcinoma with ghost cells and inductive dentin formation: Report of a case in the mandible. J Oral pathol Med 2002;31:181-83.

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