International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

Case Report

Calcifying Cystic Odontogenic Tumor Conundrum Continues: A Case Report of Multiple Recurrences in Maxilla

VT Beena[1], Shalu[2], Sabu Paul[3], Jasmin Jose[4]

[1]MDS Oral Pathology. Professor Dept. of Oral Pathology, Govt Dental College, Kottayam, Kerala.
[2]MDS Oral Pathology, Fellow at Head and Neck Pathology, Dharamshila Narayana Super speciality Hospital, Dallupura, New Delhi 110096. (Former Senior Resident, Dept. of Oral Pathology, Govt Dental College, Kottayam, Kerala.)
[3]MDS Oral Pathology. Associate Professor. Dept. of Oral Pathology, Govt Dental College, Kottayam, Kerala.
[4]MDS Oral Pathology. (Former Senior Resident, Dept. of Oral Pathology, Govt Dental College, Kottayam, Kerala.)

Corresponding Author: VT Beena

ABSTRACT

The calcifying cystic odontogenic tumour (CCOT) was first described as a distinct clinicopathological entity by Gorlin et al. in 1962. Ever since then, it has been a controversial lesion because if it's variable presentation and confusion regarding its nomenclature and classification and the confusion still prevails. Here, we have discussed a case report of a 52 year male with the swelling in right side of maxilla with multiple recurrences demonstrating both solid and cystic areas. The lesion has recurred after 12 years from the last recurrence, so we strongly recommend a long term follow up in order to determine the long term recurrence rate, as the currently advised follow up by majority of the authors is 1-3 years. We also want to emphasize on the need of proper categorization of the cases for better understanding of the pathogenesis of each variant, and the need to alter the treatment modality accordingly.

Key words: calcifying; cystic; ghost cells; maxilla; recurrence; tumour.

INTRODUCTION

Calcifying cystic odontogenic tumour (CCOT) is a rare heterogenous group of odontogenic tumours characterized by its diverse presentations clinically, radiographically as well as biologically. The lesion presents in majority of the cases (>85%) as simple cyst alone or with the associated odontogenic lesions. But in 5% cases it presents as a solid/neoplastic variant. Mixed presentations with both solid and cystic areas also exists, contributing to the controversy the lesion has undergone over years, regarding its nomenclature and classification. Clinically it can occur both intraosseously (85%) as well as extraosseously (15%). It can occur at any age, but is usually seen with more frequency in second and third decade. There is an almost even gender predilection and distribution among the jaws. The most common site of occurrence is the anterior part of the jaws. [1,2] In most of the cases CCOT runs a benign course but cases of recurrence as well as malignant transformation to Ghost cell odontogenic carcinoma (GCOC) has been reported. It's very rare in occurrence constituting about 0.37% to 2.1% of all odontogenic tumors, [3] hence current data on the long term recurrence rate is limited and not sufficient to establish the pathological nature of the lesion.

CASE REPORT

A 52-year-old male patient reported to Government Dental College Kottayam with complaint of swelling in the right side of maxilla of eight months duration. His history dated back to 13 years when he initially presented with a swelling associated with the impacted canine, which was diagnosed as dentigerous cyst. Cyst enucleation with removal of impacted canine along with extraction of 12,14,15,16 was done. After a year patient returned with same complaints and then it was diagnosed as calcifying cystic odontogenic tumour. Surgical resection was done for the same. Now, the patient presented third time with a similar swelling on right maxilla; approximately 4 cm × 3 cm in size, extending superoinferiorly from infraorbital rim to angle of the mouth and anteroposteriorly from right ala of the nose to zygomatic bone. Figure 1 shows extra oral clinical features. Swelling was bony hard and slightly tender on palpation. Intraoral examination revealed buccal as well as palatal cortical expansion with obliteration of maxillary vestibule and palatal extension till midpalatine raphe. The swelling was extending anteroposteriorly from midline to maxillary tuberosity. The mucosa over the lesion was intact. Figure 2 shows intra oral features of lesion. Radiographic examination revealed a multilocular radiolucency with flecks of radiopacity. Computed tomographic scan (CT) showed expansile multiloculated cystic lesion in the right maxilla involving posterolateral wall of maxillary sinus, inferiorly upto the alveolar process, medially till the frontal process and the medial wall of maxillary sinus crossing the midline. Maxillary sinus was reduced in volume and cystic lesion in the medial wall of maxillary sinus had caused compression over the nasal turbinate and right nasal cavity with deviated nasal septum to the left. Calcifications and enhancing solid areas were noted within the cyst in the region of nasiolabial fold. Cortical defects were noted at multiple areas. Figure 3 shows CT features of lesion. Excision of the cyst through the midface gloving approach was done.

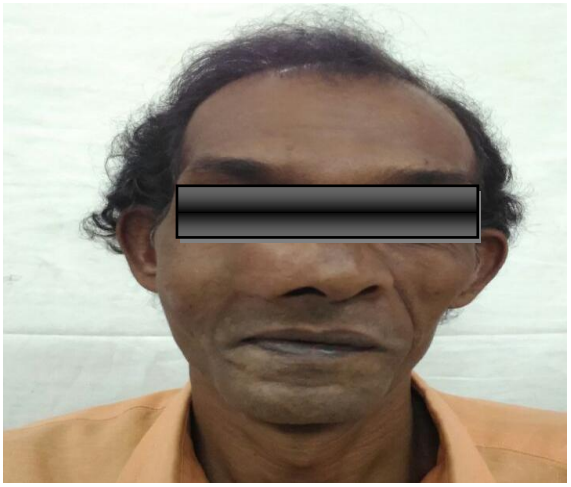

Figure 1: Clinical photographs showing appearance of swelling.

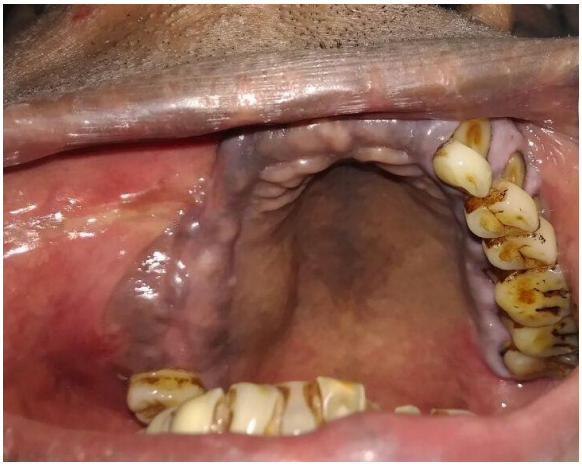

Figure 2: Intraoral swelling showing both buccal and palatal cortical plate expansion.

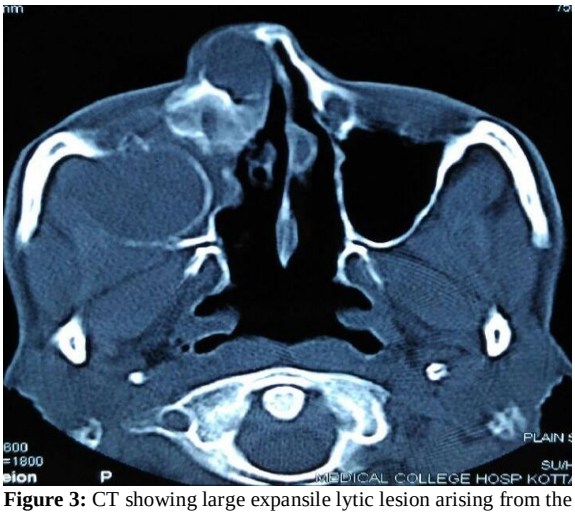

Figure 3: CT showing large expansile lytic lesion arising from the right maxilla extending into the right maxillary antrum and anterior portion of the right nasal cavity.

Histopathology of tissue revealed moderate to densely collagenous cyst wall with a discontinuous odontogenic epithelial lining. The cystic lining demonstrated a basal layer composed of cuboidal to columnar cells; stellate reticulum like suprabasal layer admixed with "ghost epithelial cells", few of which appeared to have undergone calcification. Homogenous eosinophilic deposits (dysplastic dentin/ osteodentin) were identified in an area in juxtaposition to the proliferative epithelial lining. Figure 4 shows histopathological features of the lesion.

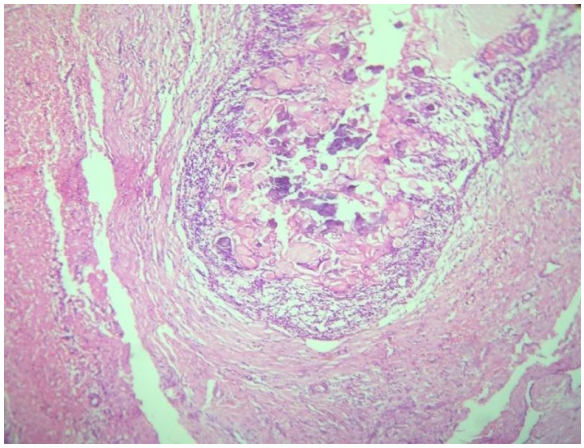

Figure 4: Cystic lumen lined by odontogenic epithelium and areas of "Ghost" epithelial cells projecting into the lumen with areas showing calcification (H and E Stained ×100).

Islands with a cellular morphology similar to that of the lining epithelium were noted within the connective tissue stroma, accounting for the solid component of the lesion. Two possible conclusions drawn were that the tumor could either be a cyst with mural tumoral proliferations or a solid tumor with a tendency towards cyst formation. Tumor recurrence was confirmed by histopathologic evaluation. However, in contrast to the earlier lesion, clinically the lesion had led to more apparent facial disfigurement and microscopically the recurrent cystic lesion had tumoral proliferations in the cyst wall which were not present in the previous lesion. Figure 5 shows the solid areas within the tumor.

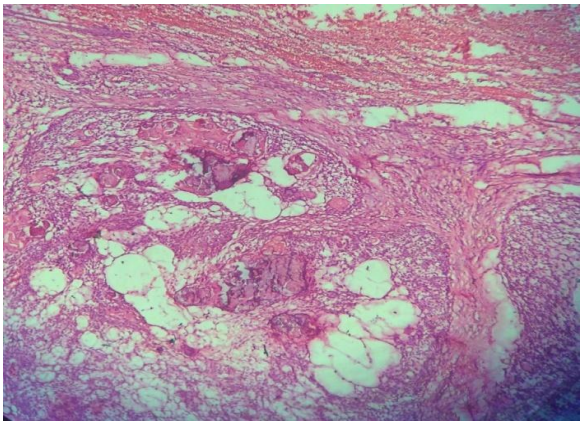

Figure 5: Islands with a cellular morphology similar to that of the lining epithelium within the connective tissue stroma (H and E Stained ×100).

DISCUSSION

The term odontogenic ghost cell lesions embraces a heterogeneous group of odontogenic lesions that share cytological and histomorphological features in terms of epithelium with that of ameloblastoma, but in contrast to ameloblastomas they exhibit a conspicuous presence of ghost cells with a tendency for calcification and shows formation of dentinoid in the juxtaepithelial connective tissue. [4]

It was initially described by Gorlin et al. in 1962 as calcifying odontogenic cyst and has been published with various terminologies over the period since it was first reported. After the initial recognition of the lesion as a distinct entity, numerous single and series case reports have appeared in the literature and it became apparent that the lesion was not always a cyst; sometimes it was a solid lesion, and in other cases it was found in association with other odontogenic lesions. Thus, arose the controversy and confusion regarding it being a cyst or a tumor. [2,5] The authors have divergent opinion on its classification and nomenclature with some following the monistic, whereas the others the dualistic concept. WHO has adhered with the monistic concept and considered the lesion to be a cyst in 1971, reclassifying it to tumors with the term Calcifying odontogenic cyst (COC) in 1992, changed the terminology to CCOT to remove ambiguity in 2005. But in 2017, they have reclassified it back to the cysts, supporting it

with the evidence that over 85% of ghost cell lesions are simple cysts or cysts in association with other developmental lesions and rarely recurs and runs a completely benign course and a completely solid lesion considered a true neoplasm should be termed as Dentinogenic ghost cell odontogenic tumour (DGCT). [6-9] The other authors that followed the dualistic concept considered it essentially to be of two subtypes i.e. cyst or neoplasm. All the authors have tried to further subtype it but controversy over the terminologies and classification still prevails. The present authors are of opinion that Toida (1998) [10] has been able to cover the whole spectrum of lesions comprehensively i.e. cyst, neoplasm further categorized into cystic and solid variant, and combined lesion i.e. associated with the other odontogenic lesions. As the present lesion shows both solid and cystic areas, it could be a solid neoplasm with cystic areas.

The odontogenic origin of the lesion is widely accepted. The lesion has been reported both extraosseously and intraosseously. The extraosseous cysts in gingiva are believed to arise from remnants of dental lamina, and less likely from the basal cells of the surface epithelium. The intraosseous variant is believed to originate from reduced enamel epithelium of unerupted teeth or remnants of dental lamina in terms of proliferating epithelium on the top of dental follicle of an unerupted tooth. [4] COC is not a common lesion and DGCT is even less common and should be considered rare. There is an almost even gender predilection. It is usually seen with more frequency in second and third decade. There seems to be an even distribution among the jaws. The most common site of occurrence is the anterior part of the jaws. In maxilla 77% of the cases are located in the incisor-canine region whereas in mandible it is reported to be 55%. Buchner reported that in Asians there is a predilection for the maxilla, whereas in whites, a 62% disposition is in the mandible. [11]

The intraosseous lesion clinically presents as a painless, bony hard expansile swelling which may be fairly extensive. Occasionally the lesion can perforate the cortical plate and extend into the soft tissue. The extraosseous lesion usually presents as a firm or soft circumscribed, smooth surfaced mass usually of size ranging from 0.5-4 cm in diameter located in the gingival or alveolar mucosa. Radiologically, the lesions are essentially radiolucent with well-circumscribed borders and variable amounts of radiopaque material ranging from tiny flecks to conspicuous masses, being present in about 50% of them. Resorption of the roots of adjacent teeth is a frequent finding. Extraosseous lesions may show superficial bony erosion. [1,12] On histopathological examination the lesion is characterized by fibrous capsule with a lining of odontogenic epithelium. The basal layer is made up of well-defined reversely polarized columnar cells, overlined by loosely arranged stellate shaped epithelial cells. Generally, the epithelial-connective tissue interface is flat. Mitosis is rare. Melanin is sometimes present in the epithelial linings. And the most striking feature of this entity is the presence of ghost cells, which can be seen individually or as clusters within the epithelium. They present as large, pale eosinophilic cells devoid of nuclei, retaining their basic cell outline and considerably larger than the epithelial cells from which they are thought to arise. They show a tendency towards calcification. [4] Ghosts cells can be easily accentuated by means of trichrome or Ayoub Shklar histochemical stains or with rhodamine B stain visualized under fluorescent light. [2,4] The presence of ghost cells within a proliferative epithelial lining is the essential characteristic for diagnosis, but their presence alone is not sufficient for diagnosis, as they may be observed in odontomas, ameloblastomas, ameloblastic fibro-odontomas, craniopharyngioma to name a few. [2]

The lesions lying in the ghost cell spectrum have been subjected to immunological studies. CK8, 4, 19,

AE1/AE3 and 34βE12 were expressed in suprabasal cells, whereas CK14 and AE1/AE3 were expressed in the basal cells. Ghost cells expressed only cytokeratins AE1/AE3 and 34βE12. Proto-oncogene bcl-2 expression was evident in the basal and suprabasal cells, whereas it was missing from the ghost cells. [13] Presence of enamel proteins amelogenin, [14] enamelin, [15] sheathlin, [16] and enamelysin [17] showed immunoreactivity for ghost cells with varying intensity, but was in general absent from the epithelial cells. Ki-67 was higher in the proliferative than in the non-proliferative lining. [13] Molecular studies suggests the involvement of Wnt signaling pathway in the pathogenesis of ghost cell lesions as β-catenin, a downstream transcriptional activator of Wnt showed somatic mutation. [18]

Certain deviations from the conventional cases have been reported in the recurrent cases of the calcifying cystic odontogenic tumour, such as they are more common in males and have a site predilection for maxilla, owing to the fact that obtaining an adequate surgical margin in maxilla is difficult, thereby leading to increased recurrence rate. Malignant transformation of CCOT, although rare, mostly takes place in recurrent and long standing cases. Bassel Tarakaji et al. in a recent literature review from 2003-13 came across 29 cases of GCOC, out of which 8 cases had probably developed from CCOT. Out of 29 cases, 5 death were reported because of local recurrence and metastasis to brain and lung. [19] Li and Gao reported a case of CCOT in the maxilla, which transformed to GCOC after 5 recurrences during a 21-year period. The lesion was first found to be malignant on the third recurrence i.e. after 17 years. After each recurrence, mitotic rate was higher and pleomorphism was more evident. [20] The present lesion however is still benign, after the third recurrence; a period of 13 years, but shows more solid areas than before. Hence, long term follow up of these lesions is required. Motosugi et al. reported a case of malignant transformation in recurrent CCOT and observed elevated Ki-67 and p53 expression in the recurrent lesions. [21]

CCOT is essentially a benign lesion and in most cases enucleation and curettage of 1-2 mm of the surrounding bone to remove any tumor remnant is done unless it is associated with the other odontogenic tumours, where the treatment is governed by the associated lesion. However, recurrences are frequently seen in some cases. Therefore, in cases where lesions are clinically aggressive, exhibits solid proliferations within stroma and their proliferative labeling index is higher, a more radical surgery is warranted. Prognosis is good for cystic lesion and in solid lesions it is based on the associated odontogenic tumours. [1]

CONCLUSION

The present case of 52 year old male was diagnosed as Calcifying ghost cell odontogenic tumour, cystic variant, so as to take in account the solid areas present within the stromal tissue which were similar in histomorphological appearance to the cystic lining, characterized by presence of ameloblastomatous epithelial lining and presence of ghost cells. Our case showed multiple recurrences, first after a year, followed by another recurrence after 12 years. We strongly recommended that these patients be followed up for many years for two reasons; first as the possibility of malignant transformation increases with the recurrences, and the second in order to determine the long term recurrence rate, as the already available literature is sparse due to the rarity of the lesion.

REFERENCES

1. Shear M, Speight P. Calcifying odontogenic cyst (Calcifying cystic odontogenic tumour): Cyst of the Oral and Maxillofacial Regions. 4th ed. New York: Blackwell Munksgaard; 2008. p. 100-7.
2. Tomich CE. Calcifying odontogenic cyst and dentinogenic ghost cell tumor. Oral Maxillofac Surg Clin N Am. 2004; 16(3):391-7.

3. Erasmus JH, Thompson IOC, Van Rensburg LJ et al. Central calcifying odontogenic cyst. A review of the literature and the role of advanced imaging techniques. Dentomaxillofac Radiol. 1998; 27(1):30-5.
4. Prœtorius F. Odontogenic tumours. In: Leon Barnes, editor. Surgical Pathology of the Head and Neck. 3rd ed. New York: Informa healthcare; 2008.p.1201-1337.
5. Philpsen HP, Reichart PA. Odontogenic Tumors and Allied Lesions. Hanover Park (Illinois): Quientessence Publishing; 2004.
6. Pindborg J, Kramer I (1971) WHO International Histological Classification of Tumours. Histological typing of odontogenic tumours, jaw cysts and allied lesions. WHO, Geneva.
7. Kramer I, Pindborg J, Shear M (1992) WHO International Histological Classification of Tumours. Histological typing of odontogenic tumours, 2nd edn. Springer-Verlag, Berlin.
8. Barnes L, Eveson JW, Reichart P, Sidransky D (2005) Odontogenic Tumours. Ch 6, WHO classification of tumors: pathology and genetics of head and neck tumours. IARC, Lyon.
9. Speight PM, Takata T. New tumor entities in the 4th edition of the World Health Organization classification of Head and Neck tumors: odontogenic and maxillofacial bone tumors. Virchows Arch (2017). https://doi.org/10.1007/s00428-017-2182-3.
10. Toida M. So-called calcifying odontogenic cyst: Review and discussion on the terminology and classification. J Oral Pathol Med.1998; 27:49-52.
11. Buchner A. The central (intraosseous) calcifying odontogenic cyst: an analysis of 215 cases. J Oral Maxillofac Surg. 1991; 49(4):330-9.
12. Buchner A, Merell PW, Hansen LS et al. Peripheral (extraosseous) calcifying odontogenic cyst. A review of forty-five cases. Oral Surg Oral Med Oral Pathol. 1991; 72(1):65-70.
13. Fregnani ER, Pires FR, Quezada RD et al. Calcifying odontogenic cyst: clinicopathological features and immunohistochemical profile of 10 cases. J Oral Pathol Med. 2003; 32(3):163-70.
14. Mori M, Yamada K, Kasai T et al. Immunohistochemical expressions of amelogenin in odontogenic epithelial tumours and cysts. Virchows Arch [Pathol Anat].1991; 418(4):319-25.
15. Saku T, Okabe H, Shimokawa H. Immunohistochemical demonstration of enamel proteins in odontogenic tumours. J Oral Pathol Med. 1992; 21(3):113-9.
16. Takata T, Zhao M, Uchida T et al. Immunohistochemical demonstration of an enamel sheath protein, sheathlin in odontogenic tumours. Virchows Arch. 2000; 436(4):324-9.
17. Takata T, Zhao M, Uchida T et al. Immunohistochemical detection and distribution of enamelysin (MMP-20) in human odontogenic tumours. J Dental Res. 2000; 79(8):1608-13.
18. S. Sekin, S. Sato, T. Takata et al. Beta-catenin mutations are frequent in calcifying odontogenic cysts but rare in ameloblastomas. Am J Pathol. 2003; 163 (5):1707-12.
19. Bassel T, Nipun A. Ibrahim A et al. Malignant transformation of calcifying cystic odontogenic tumor-a review of literature. Contemp Oncol (Pozn) 2015; 19(3):184-186.
20. Li BB, Gao Y. Ghost cell odontogenic carcinoma transformed from a dentinogenic ghost cell tumor of maxilla after multiple recurrences. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2009; 107(5): 69-5.
21. Motosugi U, Ogawa I, Yoda T et al. Ghost cell odontogenic carcinoma arising in calcifying odontogenic cyst. Ann of Diagno Pathol. 2009; 13(6):394-7.

How to cite this article: Beena VT, Shalu, Paul S et al. Calcifying cystic odontogenic tumor conundrum continues: A case report of multiple recurrences in maxilla. Int J Health Sci Res. 2018; 8(5):415-420.

****