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Multiple keratocystic odontogenic tumors in a 9 year old female syndromic patient: Report of a case

Dr. Jagadish Chandra[1], Dr. Manav Chaturvedi[2], Dr. Veena Chandra[3], Dr. Pushparaja Shetty[4], Dr. Ganapathi Bhatt[5], Dr. Sreelatha S.V[6]

[1]Professor, Department of Oral and Maxillofacial Surgery-Yenepoya Dental College, Mangalore, Karnataka-575017
[2]Post graduate student, Department of Oral Pathology and Microbiology-A.B Shetty Institute of Dental Sciences, Mangalore, Karnataka-575017
[3]Professor, Department of Oral Medicine and Radiology-Yenepoya Dental College, Mangalore, Karnataka-575017
[4]Professor and head, Department of Oral Pathology and Microbiology-A.B Shetty Institute of Dental Sciences, Mangalore, Karnataka-575017
[5]Professor, Department of Anaesthesiology-Yenepoya Medical College, Mangalore, Karnataka-575017
[6]Professor, Department of Oral Pathology and Microbiology-A.B Shetty Institute of Dental Sciences, Mangalore, Karnataka-575017

***Corresponding author**
Dr. Sreelatha S.V
Email: sreelathakarnaker@hotmail.com

Abstract: Keratocystic odontogenic tumor (KCOT), formerly referred to as odontogenic keratocyst, is a benign neoplasm of odontogenic origin which may present an aggressive and infiltrative behavior leading to high recurrence rates. Nevoid basal cell carcinoma syndrome (NBCCS), which is also known as Gorlin syndrome, is a hereditary condition characterized by a wide range of developmental abnormalities and with a predisposition to neoplasms. These multiple KCOTs have warranted an aggressive treatment at the earliest because of the damage and possible complications. Recurrence of these lesions is a characteristic feature that has to be considered while explaining the prognosis to the patient. Here, we report a case of a 9-year-old female child with clinical features of basal cell nevus syndrome and multiple KCOTs.
Keywords: Keratocystic odontogenic tumor, neoplasm, nevoid basal cell carcinoma.

INTRODUCTION

Cystic lesions found most commonly in the maxillofacial region are odontogenic cysts which have been classified traditionally into a developmental group including keratocysts and dentigerous cysts, and inflammatory group including radicular cysts [1]. Odontogenic keratocysts (OKC) are clinically aggressive lesions which are thought to arise from the dental lamina or its remnants [2]. The OKC was first described in 1876[3], and named by Phillipsen in1956 [4] having a potential for aggressive, infiltrative behavior [5, 6]. Odontogenic keratocysts can show high rate of recurrence and the tendency of infiltrating adjacent tissues [7], and be associated many a times with nevoid basal cell carcinoma syndrome (NBCCS) [8].

Odontogenic keratocyst (OKC) is now designated by the World Health Organization (WHO) as a keratocystic odontogenic tumour (KCOT) and is defined as "a benign uni-or- multicystic, intraosseous tumour of odontogenic origin, with a characteristic lining of para keratinized stratified squamous epithelium and potential for aggressive, infiltrative behaviour" [9]. This term is recommended by WHO as it aptly represents the neoplastic behaviour [9].

Nevoid basal cell carcinoma syndrome (NBCCS) with concomitant cutaneous, skeletal, ophthalmic and neurologic abnormalities also usually has multiple keratocystic odontogenic tumors (KCOTs) as its component. Gorlin-Goltz syndrome name has been given because Goltz first described the spectrum of features associated with this syndrome in 1960 [10].Though it is very rare multiple KCOTs have been known to occur in non-syndromic cases [11].The estimated prevalence varies from 1 in 57,000 to 1 in 256,000 with a male: female ratio of 1:1[12].

CASE REPORT

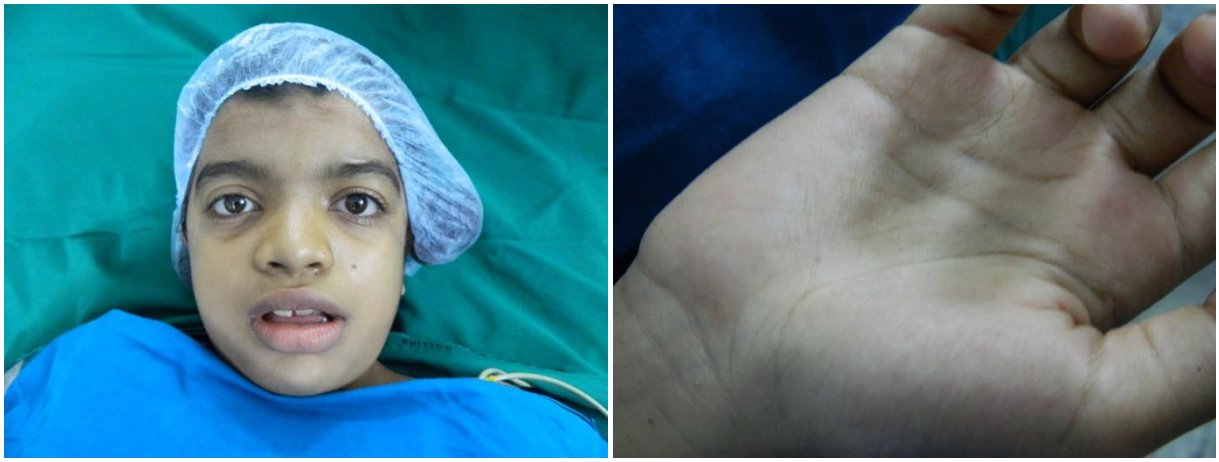
A 9 year old girl reported to the clinic with the chief complaint of swelling on the right side of her face since 3 months. Patient had associated mobility of the teeth in the upper jaw.

Patient's mother also had similar lesion which was removed 5 years back with no reported recurrences till now.

On examination patient had swelling in the upper right vestibule obliterating the buccal vestibule. Swelling on to the buccal vestibule was also present on the lower right posterior region. Egg shell crackling was palpated on the buccal cortex. Associated teeth were mobile. No other associated symptoms were reported. On general examination it was found that the patient has low IQ, frontal bossing, mild hypertelorism, widened nasal bridge, palmar and plantar pits. OPG was taken which showed multiple radiolucent lesions on the maxillary right canine region and bilaterally on the mandible angle region.

Incisional biopsy was done and sent for histopathological examination which was reported as keratocystic odontogenic tumour (KCOT). Considering the extent of the lesion it was decided to enucleate the lesion under GA. Patient was prepared under standard aseptic technique and nasal intubation was done.

Vestibular incision was placed on the on the maxillary buccal vestibule and mucoperiosteal flap elevated. Involved teeth were extracted first following which the cystic lining identified through the buccal perforation. Carnoy's solution was injected into the cyst taking care not to drip the solution anywhere but the cyst. After 2 minutes the cystic lining became more firm and less friable which facilitated easy removal of the cyst contents along with the lining. Cristal incision was placed posterior to the first molar extending to the anterior aspect of the ramus. Mucoperiosteal flap was elevated and the cystic lining identified. Carnoy's solution was injected into the cyst as before and waited for 2 minutes for the otherwise friable cystic lining to become more firm and slightly elastic also.



(a) (b)

Fig.1a: Patient with hypertelorism and strabismus along with an extra oral swelling on the right side of the face. b. Patient exhibiting palmar pitting

The cystic lining along with the contents was removed. Likewise an incision was placed on the opposite side also exposing the cystic lesion. Carnoy's solution was injected and the cyst was removed in a single piece. Carnoy's solution was applied to the body cavities after removal of the cyst for 2 minutes to devitalize any cystic lining which may have been left behind. Wound closure done with 3-0 vicryl. Patient was kept under regular follow up to check for any recurrences.

The histopathologic report revealed that the cystic lining of all 3 lesions was para keratinized stratified squamous epithelium with superficial corrugation. The lining epithelium mostly uniform 5-6 cell thickness except in areas of inflammation consisted of well-defined columnar basal cells in a palisade arrangement with polarized nuclei and absence of rate ridges(Figure 2a and 2b).The connective tissue capsule showed variable amount of inflammation, satellite cysts, and odontogenic cell rests/islands. Histopathological diagnosis of keratocystic odontogenic tumour (KCOT) was established in all the three lesions.

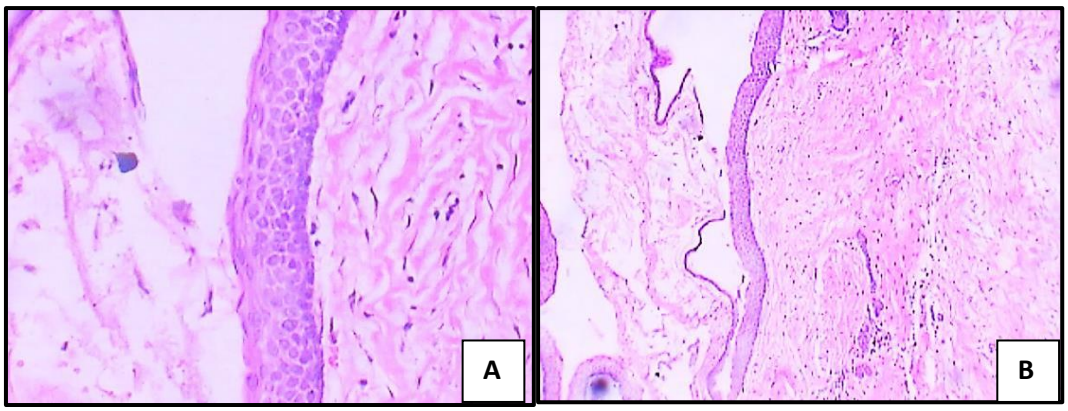


Fig.2a. Lining of Kerato cystic odontogenic tumor is para keratinized stratified squamous epithelium of uniform 5-6 cell thickness and palisaded basal cell layer without rete pegs (40X)
b. Presence of odontogenic islands/rests within the connective tissue capsule. (10X)

DISCUSSION

Multiple KCOTs commonly occur in nevoid basal cell carcinoma syndrome or Gorlin-Goltz syndrome, orofacial digital syndrome, Noonan syndrome, Ehler-Danlos syndrome, and Simpson-Golabi-Behmel syndrome [13].

These jaw cysts usually develop during the first decade of life and reach its peak during the 2nd or 3rd decade. However, in our case the patient is a young girl of 9 years which is almost a decade earlier than much more common isolated Keratocystic odontogenic tumor not associated with syndrome. They are often very large before they affect expansion of jaw.

In this case location of the multiple KCOT was bilaterally on the angle region and on the maxillary right canine region which demonstrated unilocular radiolucency on OPG. KCOTs are found more commonly in the mandible and may be relatively small, single or multiple, but more often are large, bilateral, unilocular or multilocular, and asymmetric, involving both jaws. Canine to premolar area, in the mandibular retro molar –ramus area, and in the region of maxillary second molar are the areas where KCOTs occur commonly [14].

On general clinical examination it was found that the patient had low IQ, frontal bossing, mild hypertelorism, widened nasal bridge, palmar and plantar pits. And since patient's mother also had similar lesion which was removed 5 years back with no reported recurrences till now this case met 2 major and 1 minor criteria as per Evans Diagnostic criteria for NBCCS [18]. **(See table 1)**

Table 1: Diagnostic criteria for nevoid basal cell carcinoma syndrome according to Evans *et al.;* [18] (2 major or 1 major and 2 minor criteria should be satisfied for positive diagnosis).

Major Criteria	Minor Criteria
More than 2 basal cell carcinomas (BCCs), 1 BCC before 30 years of age; or more than 10 basal cell nevi	Congenital skeletal anomaly (e.g., bifid rib, fused, splayed or missing rib, wedged or fused vertebrae)
Any odontogenic keratocyst (proven on histology) or polyostotic bone cyst	Occipital–frontal circumference higher than the 97th percentile, with frontal bossing
3 or more palmar or plantar pits	Cardiac or ovarian fibroma
Ectopic calcification; lamellar or early (< 20 years of age) falx calcification	Medulloblastoma and Lympho mesenteric cysts
Family history of nevoid basal cell carcinoma syndrome	Congenital malformations, such as cleft lip or palate, polydactylism or eye anomaly (cataract, coloboma, microphthalmos)

Histopathology features typical for such cases are the para keratinized surface corrugation. Uniform thickness of the epithelium which was seen in most of the areas except where heavily infected.

Genetic defect or mutation in the human "patched" gene can be responsible for the relatively early occurrence of multiple KCOTs [15]. NBCCS is caused by the gene whose mutations has been mapped to the long arm of chromosome 9q22.1-3.1 and has no apparent heterogeneity. Allelic losses at this site are associated with approximately 50% of cases of NBCCS [16]. As this gene controls growth and development of normal tissues its products may act as a tumour suppressor [16]. Reports suggest genetic influences stimulating the formation of KCOTs in NBCCS [17].

Significant differences were found between KCOT from patients with the basal cell naevus syndrome and single KCOT without syndrome matched for age and site in the numbers of satellite cysts, solid islands of epithelial proliferation and odontogenic rests within the capsule, and in the numbers of mitotic figures in the epithelium lining the main cavity. Syndrome KCOTs have greater growth potential as suggested by the index of activity derived from these parameters [19].

Nevoid basal cell carcinoma syndrome apleiotropic, autosomal disorder presents a spectrum of developmental abnormalities and has a predisposition for the development of different neoplasms is associated with the Keratocysts Odontogenic tumor occasionally (4-5%).

KCOTs shows clinically aggressive behaviour associated with nevoid basal cell carcinoma. In a study by L.lomuziol *et al.;* comparision for expression of proliferating cell nuclear antigen (PCNA) and p53, bcl-2, and bcl-l (cyclin D1) oncoprotein in KCOTs associated with syndrome and sporadic KCOTs was done and found that the differences in cellular proliferation rate and/or in the expression of oncoproteins and tumor suppressor genes when with most of the epithelial lining of Keratocystic odontogenic tumor associated with the nevoid basal cell carcinoma syndrome showed nuclearimmuno positivity for p53 protein and over expression of cyclin Dl with various degrees of staining intensity and all sporadic keratocystic odontogenic tumor were negative for p53 and cyclin Dl. Cyclin Dl and p53 proteins, involved in a check-point control of cellular proliferation if dysregulated could be considered a hallmark of a mutated cellular phenotype. Thus finding of cyclin Dl and p53 over expression in Keratocystic odontogenic tumor associated with the nevoid basal cell carcinoma syndrome leads to the hypothesis that their aggressive clinical behaviour could be due to a dysregulation of the expression of these two markers [19]. New cyst which originates from epithelial residue or a micro cyst left behind in the overlying mucosa can be a recurring KCOT. KCOTs can occur in bone grafts if the overlying mucosa is not excised reinforces this fact [21, 22]. Histologically, para keratinization, intramural epithelial remnants, and satellite cysts are more frequent among KCOTs associated with NBCCS than in solitary KCOTs [19].

The treatment of the KCOT remains controversial. Treatments are generally classified as conservative or aggressive. Conservative treatment generally includes simple enucleation, with or without curettage, or marsupialization. Aggressive treatment generally includes peripheral ostectomy, chemical curettage with Carnoy's solution, cryotherapy, or electrocautery and resection [23-27].

CONCLUSION

In conclusion, there could be still a possibility of NBCCS in a patient reporting with the multiple KCOTs and therefore it should not be ignored as the presentation could be show only single criteria which could be the first manifestation of this syndrome. KCOTs associated with this syndrome have higher rate of recurrence than the isolated KCOTs therefore a very strict follow up has to be followed for a long period of time. Patient and relatives should be encouraged for appropriate genetic counselling and serial screening for the development of malignancies and other complications besides KCOTs and the possibility of other features of NBCCS should be explained to them as well.

REFERENCES

1. High AS, Robinson PA, Klein CE; Discrimination of para keratinized odontogenic keratocysts from other odontogenic and non-odontogenic cyst types by expression of a 38kd cell-surface glycoprotein. J Oral Pathol Med. 1993; 22:363–7.
2. Kramer IR, Pindborg JJ, Shear M; Histological typing of odontogenic tumors. 2nd ed. Berlin: Springer Verlag; 1992.
3. Dolphine oda, valiente Rivera; The Journal of Contemporary Dental Practice, Winter Issue, 20004; 1(2).
4. Philipsen HP; Om keratocyster (kolesteatom) I kaekberne. Tandlaegegebladet 1956; 60:963-81.
5. González-Alva P, Tanaka A, Oku Y, Yoshizawa D, Itoh S, Sakashita H, *et al.;* Keratocystic odontogenic tumor: A retrospective study of 183 cases. J Oral Sci. 2008; 50:205–12.
6. Maurette PE, Jorge J, de Moraes M; Conservative treatment protocol of odontogenic keratocyst: A preliminary study. J Oral Maxillofac Surg. 2006; 64:379–83.
7. Brannon RB; The odontogenic keratocyst. A clinicopathological study of 312 cases (Part I). Clinical features. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1976; 42(1):54-72.
8. Crowley TE, Kaugars GE, Gunsolley JC; Odontogenic keratocysts a clinical and histologic comparison of the parakeratin and orthokeratin variants. J Oral Maxillofac Surg 1992; 50:22-6.
9. Barnes L, Eveson JW, Reichart P, Sidransky D; editors. Pathology and genetics of head and neck tumours. Lyon: IARC Press; 2005. WHO classification of tumours series.
10. McGrath CJ, Myall RW; Conservative management of recurrent keratocystsin basal-cell naevus syndrome. Aust Dent J 1997; 42(6):399–40.
11. Auluck A, Suhas S, Pai KM; Multiple odontogenic keratocysts: report of a case. J Can Dent Assoc. 2006; 72(7):651–6.

12. Lo Muzio L; Nevoid Basal Cell Carcinoma Syndrome (Gorlin Syndrome) Orphanet J Rare Dis 2008:3; 32.
13. Koseoglu BG, Atalay B, Erdem MA. Odontogenic cysts: A clinical study of 90 cases. J Oral Sci 2004; 46:253-7.
14. Gorlin R.J; Nevoid Basal-Cell Carcinoma Syndrome. 1987; 66(2).
15. Lench NJ, Telford EA, High AS, Markham AF, Wicking C, Wainwright BJ; Characterisation of human patched germ line mutations in nevoid basal cell carcinoma syndrome. Hum Genet 1997; 100(5-6):497–502
16. Lo Muzio L, Nocini P, Bucci P, Pannone G, Consolo U, Procaccini M; Early diagnosis of nevoid basal cell carcinoma syndrome. J Am Dent Assoc 1999; 130(5):669–74.
17. Shear M; Odontogenic keratocyst: natural history and immunohistochemistry. Oral Maxillofac Surg Clin N Am 2003; 15:377–82.
18. Evan DG, Farndon PA; Nevoid basal cell carcinoma syndrome. Gene Reviews Seattle(WA): University of Washington, Seattle,1993-2015.2002 Jun 20 [Updated 2013 Mar 7]
19. Chiang ML, Huang WH; Odontogenic keratocyst clinically mimicking an eruption cyst: report of a case. J Oral Pathol Med 2004; 33(6):373–5.
20. Woolgar JA, Rippin JW, Browne RM; A comparative histological study of odontogenic keratocysts in basal cell naevus syndrome and control patients J Oral Pathol. 1987; 16(2):75-80.
21. LoMuziol L, Staibano S, Pannone G, Buccil P, Nocini P.R, Buccil E, *et al.;* Expression of Cell Cycle and Apoptosis-related Proteins in Sporadic Odontogenic Keratocysts and Odontogenic Keratocysts Associated with the Nevoid Basal Cell Carcinoma Syndrome
22. Stoelinga PJ; Excision of the overlying, attached mucosa, in conjunction with cyst enucleation and treatment of the bony defect with carnoy solution. Oral Maxillofac Surg Clin North Am 2003; 15:407-14.
23. Yeo JF, Loh FC; Multiple odontogenic keratocysts of the jaws. Case report. Aust Dent J 1989; 34:503- 6.
24. Morgan T.A, Burton C.C, Qian F.A; retrospective review of treatment of the odontogenic keratocyst. J. Oral Maxillofac. Surg. 2005; 63:635–639.
25. Meiselman F; Surgical management of the odontogenic keratocyst: conservative approach. J. Oral Maxillofac. Surg. 1994; 52:960.
26. Williams T.P, Connor F.A; Surgical management of the odontogenic keratocyst: Aggressive approach. J. Oral Maxillofac. Surg. 1994; 52:964.
27. Bataineh A.B, Al Qudah M; Treatment of mandibular odontogenic keratocysts. Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod. 1998; 86:42.