**ODONTOGENIC KERATOCYST-A TYPE OF BENIGN CYSTIC NEOPLASM/AGGRESSIVE CYST**

Nishtha . U. More1

morenishtha03@gmail.com

+91 8237928894

Yogita Dental College and Hospital

Narangi river side dapoli road

Khed 415709

**ABSTRACT**

Odontogenic Keratocyst (OKC) is a type of odontogenic cyst (OC) which is a distinctive form of developmental odontogenic cyst. It deserves special consideration because of its specific histopathological features and clinical behavior i.e. aggressive type. FNAC is most useful in oral cancer detection of squamous cell carcinoma. Odontogenic Keratocyst, was first identified and described in 1876. 39 cases of Odontogenic Keratocyst are reported from 1971 till date making it a rare case.

**Keywords** - Odontogenic Keratocyst (OKC), odontogenic cyst(OC), Conebeam CTScan (CBCT), Fine needle aspiration cytology (FNAC).dental lamina, resorption of bone, bone aggressive behavior, periapical cyst and dentigerous cyst.

1. **INTRODUCTION**

Odontogenic keratocysts can be described as epithelial-lined pathologic cavities surrounded by fibrous tissue that originate from odontogenic tissues that occur in tooth-bearing regions of the maxilla and mandible. Cystic conditions of the jaw cause bony destruction and may cause resorption or displacement of adjacent teeth. More cases are found in the adult age group than pediatric population. Periapical cysts and dentigerous cysts are reported regularly in dental practice... Odontogenic cysts are diagnosed using Fine needle aspiration biopsy (FNAB)/Fine needle aspiration cytology (FNAC).FNAC is most useful in oral cancer detection of squamous cell carcinoma. Early recognition and referral to an Oral Surgeon minimize the extent of jaw bone destructure and can be treated by enucleation. Odontogenic Keratocyst was first identified and described in 1876. From 1971 to date, only 39 cases of Odontogenic Keratocyst have been found. This Odontogenic cyst is a relatively common lesion and accounts for a major part of total biopsies received by any pathology service. The cyst arises from the cell rests of the dental lamina. This cyst shows different growth mechanisms and biological behavior from the more common dentigerous cyst and radicular cyst. These two cysts enlarge as a result of increased osmotic pressure within the lumen of the cyst. This mechanism does not appear to hold for Odontogenic Keratocyst as its growth may be related to unknown factors inherent in epithelium itself or enzymatic activity in the fibrous wall but, what makes this cyst special is its aggressive behavior and high recurrent rate. In 1962, Pindborg and Hansen suggested that histological criteria are necessary to diagnose Odontogenic Keratocyst. In recent years, the World Health Organisation (WHO) recommended the term Cystic neoplasm (now known as KOCT) for this lesion. Histologically high mitotic rate and association with genetic and chromosomal abnormalities. Odontogenic Keratocyst is found in patients who range in age from infancy to old age, but about 60% of all cases are diagnosed in people between 10-40 years of age. There is slight male predilection. Mandibule is involved in 60% to 80% of cases, with a marked tendency to involve the posterior body and ascending ramus.

Small Odontogenic keratocysts are usually asymptomatic and discovered only during radiographic examination. Later Odontogenic Keratocyst may be associated with pain, swelling, or drainage. Some extremely large cysts, however, may cause no symptoms. Odontogenic Keratocyst shows a thin, friable wall that is often difficult to enucleate from bone in one piece. The cystic lumen may contain a clear liquid similar to the transudate of serum or may be filled with cheesy material consisting of keratinaceous debris. Microscopically, the thin fibrous wall is devoid of any inflammatory infiltrate. The epithelial lining is composed of a uniform layer of stratified squamous epithelium, usually 6-8 cells in thickness. The epithelium and rete ridge formation is inconspicuous. Detachment of portions of cyst lining epithelium from the fibrous wall is commonly observed. Luminal cells are para-keratinized.

1. **CASE REPORT**

A 31-year-old male reported to the clinic with a history of epigastric pain, stromal discomfort, burning, nausea, and vomiting. Treatment was done by diet counseling and antacid/acid-blocking mediators. It was thought that it was a case of Gastritis but later when the patient revisited with a complaint of pain and pus discharge in the lower left back region of the jaw; after diagnosis, it was recognized as a case of OKC. Investigations showed CBCT of the lower jaw (fig.2) and multiloculated scalloped radiolucent panoramic body and ramus region of the left mandible. The patient was advised for FNAC treatment by surgical intervention under GA. After some years, the patient again reported with growth of lesions over time. OKC recurrence rate is 2.5% to 62%(14). So it can be considered rare Intervention - As usual treatment protocol; marsupialization was 1st attempted 1st immunohistochemical analysis revealed reduced expression of ki-67 and B-cell lymphoma 2 (bcl-2) markers after marsupialization. However, due to the incomplete resolution lower left posterior region, an aggressive approach was taken by cutting it out surgically. Later more recurrence has been seen. The diagnosis concluded that OKC originated from Odontogenic epithelium i.e. dental lamina in the alveolus left from tooth development stages. Mainly thought to arise from the rest of Serres. Regzi and others(13) have attempted to explain the pathogenic mechanism of OKC. They mention the mechanism that favors the growth and expansion of OKCs are high proliferation rate, overexpression of antiapoptotic proteins (bcl-2), and expression of matrix metalloproteinase (MMPs2 and9). Mutation in the PTCH1(patched) gene has also been considered responsible for the pathogenesis of this cyst(12,13,14).



**Figure 1: Odontogenic Keratocyst (OKC) noted in the basal epithelial layer**



**Figure 2: shows the Conebeam CT Scan (CBCT) of the lower jaw and multiloculated scalloped radiolucent panoramic body and rahmus region of the left mandible.**



**Figure 3: This Image shows (Black region) that the cyst has caused resorption of bone with the pus formation(white part 50 -54).**

**III.GENETICS**

The PCTH gene has been mapped to chromosome 9q22.3-q31 and it probably functions as a tumor suppressor(3). The Protein Patched Homolog1 (PCTH1) is an important molecule in the so-called Hedgehog (Hh) signaling pathway(14). Normally, PTCH forms a receptor complex with the oncogene SMO ("smoothened") for the SHH ( "sonic hedgehog") ligand(18). Studies on NBCCS and Sporadic KCOT have provided molecular evidence of a two-hit mechanism in the pathogenesis of these tumors demonstrating allelic loss, at two or more loci, of 9q22 (19,20) leading to the over-expression of bcl-1 and TP53 in the Neviod Basal carcinoma syndrome (NBCCS). This supports the concept that KCOT represents a neoplasm(20). There is also accumulating evidence that the PTCH gene might be a significant factor in the development of sporadic KCOT. Furthermore, preliminary results have shown over-expression and amplification of genes located in 12q(21). The epithelial lining of OKC/KOT is PTCH2 and SUFU. Few authors also have demonstrated loss of LTAS2, and FHIT genes(14). These findings help explain the aggressive behavior of OKC.

**IV.TREATMENT**

OKC is well known for its strong tendency to recur(11). Much debate has been done and various studies performed, on a certain ideal treatment modality for OKC/KOT. Mostly these arguments revolve around whether to treat OKC as a cyst or as a benign neoplasm. Whatever modality has been implied, none of these have been shown to completely prevent the recurrence of the lesion, the problem is still compounded in the case of NBCCS and multiple lesions. Eyre and Zakrezewska in 1985, have stated the following treatment modalities for OKC / KOT- like enucleation with primary closure / with packing / with chemical/fixation with cryosurgery; Marsupialization only followed by enucleation; Resection (22). The choice of treatment has always been difficult, since the patient's well-being is of prime concern, although not compromising the chances of recurrences. Morgan and his colleagues(23) have categorized surgical treatment methods for KOT as conservative/aggressive. The conservative treatment is 'cyst oriented ' and this includes enucleation, with or without curettage or marsupialization. The advantage is the presentation of anatomical structures and reduced morbidity to the patient. The aggressive treatment is done considering the 'neoplastic nature' of KOT and includes peripheral osteotomy, chemical curettage, or en bloc resection. It is mostly recommended for large lesions, recurrent cases, and syndromic patients. Decompression has also been used to treat KOTs, which have aggressive behavior and tend to recur(14). Few authors recommended a "site and size based" approach for the treatment of KOT. Dammer et al have suggested a conservative approach for small KOTs ( maximum 1cm in diameter) near the alveolar process, and radical excision for larger lesions near the base of the skull that have invaded soft tissue(24). On the contrary, Forsell and coworkers have reported that the size of the lesion does not affect the recurrence rate (25).

**V. CONCLUSION**

Odontogenic Keratocyst is still considered a diagnostic challenge and should be considered especially in patient with predominance with it. Prognosis is very much favorable in patients when diagnosed earlier as prevents resorption of bone. Suspected cases should be subjected to histological investigation and should consider the possibility of Odontogenic Keratocyst after 5-10 years. So the whole process of classifying and renaming the odontogenic cyst and tumors continues as the understanding of these lesions takes a giant leap in its stride. There is as yet no international consensus, either on the question of the cyst's neoplasmic nature or on a name change. A famous oral surgeon "Gordon Hardman" was quoted saying "We always knew some cysts recurred so the patient came to have them curetted out every 5-10 years. So what, we never had to give them separate names"(6) This attitude of the surgeons overlooking the multiple recurrences has always been suppressing the concept of reclassifying these lesions (favorite work of the pathologists). The controversies over the nature of OKC are a reflection of our limited knowledge of this fascinating entity. (14) "A rose is a rose is not a rose," when it implies to OKC/KOT. The term "odontogenic keratocyst" is so engraved in the literature that only time can tell us whether the term "Keratocystic odontogenic tumor" can substitute this term successfully or not. Recent advances in genetic and molecular understanding have led to eventually eliminating the need for aggressive treatment modalities. This article is in the hope of suggesting that the naming of KOC as a benign tumor allows the surgeon to tailor their treatment aptly.

**VI. REFERENCES**

1. Philipsen HP, Reichart PA. Classification of odontogenic tumors. A historical review. J Oral Patho Med.2006;35:525-9.
2. Hauer A. Ein Cholesteatom I'm linken Unterkiefer unter eninem retinierten Weisheitszahn. Zeitsschrift fir Stomatologie. 1926;24:40-59.
3. Barnes L, Eveson JW, Reichart P, Sidranksy D, editors. Lyon:IARC Press;2005. Pathology and genetics of head and neck tumors.
4. Toller P. Origin and growth of cysts of the jaws. Ann R Coll Surg Engl. 1967;40:306-36.
5. Robinson HB. Primordial cysts versus keratocysts. Oral Surg Oral Path Oral Med.1975;40:326- 4.
6. Pogrel MA, Schmidt BL. The odontogenic keratocyst. Oral Maxillofac Surf Clin North Am.2003;15:321-6
7. Soskolne WA, Shear M. Observations on the pathogenesis of primordial cysts. Br Dent J. 1967;123:321–6.
8. Forssell K, Sainio P. Clinicopathological study of keratinized cysts of the jaws. Proc Fin Dent Soc. 1979;75:36–45.
9. Philipsen HP. Om keratocyster (kolesteatom) i kaeberne. Tandlaege bladet. 1956;60:963–81.
10. Pindborg JJ, Hansen J. Studies on odontogenic cyst epithelium. 2. Clinical and roentgenologic aspects of odontogenic keratocysts. Acta Pathol Microbiol Scand. 1963;58:283–94.
11. Ahlfors E, Larsson A, Sjögren S. The odontogenic keratocyst: A benign cystic tumor? J Oral Maxillofac Surg. 1984;42:10–9.
12. Shear M. The aggressive nature of the odontogenic keratocyst: Is it benign cystic neoplasm? Part 1 Oral Oncol. 2002;38:219–26.
13. Regezi, Sciubba, Jordan . 4th ed. St. Louis, Missouri: Saunders Company; 2003. Oral Pathology Clinicopathological correlations; pp. 250–2.
14. TJ. The odontogenic keratocyst: A cyst, or a cystic neoplasm? J Dent Res. 2011;90:133–42.
15. Brannon RB. The odontogenic keratocyst A clinicopathologic study of 312 cases. Part I. Clinical features. Oral Surg Oral Med Oral Pathol. 1976;42:54–72.
16. Reichart PA, Philipsen HP. London: Quintessence Publishing; 2004. Odontogenic tumors and allied lesions.
17. Neville BW. Update on Current Trends in Oral and Maxillofacial Pathology. Head Neck Pathol. 2007;1:7580.
18. Madras J, Lapointe H. Keratocystic odontogenic tumor: Reclassification of the odontogenic keratocyst from cyst to the tumor. J Can Dent Assoc. 2008;74:165–65h.
19. Levanat S, Gorlin RJ, Fallet S, Johnson DR, Fantasia JE, Bale AE. A two-hit model for developmental defects in Gorlin syndrome. Nat Genet. 1996;12:85–7.
20. Lo Muzio L, Staibano S, Pannone G, Bucci P, Nocini PF, Bucci 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. J Dent Res. 1999;78:1345–53.
21. Heikinheimo K, Jee KJ, Morgan PR, Nagy B, Happonen RP, Knuutila S, et al. Gene expression profiling of odontogenic keratocyst. J Oral Pathol Med. 2004;33:462.
22. Eyre J, Zakrezewska JM. The conservative management of large odontogenic keratocysts. Br J Oral Maxillofac Surg. 1985;23:195–203.
23. Morgan TA, Burton CC, Qian F. A retrospective review of the treatment of odontogenic keratocyst. J Oral Maxillofac Surg. 2005;63:635–9.
24. Dammer R, Niederdellmann H, Dammer P, Nuebler-Moritz M. Conservative or radical treatment of keratocysts: A retrospective review. Br J Oral Maxillofac Surg. 1997;35:46–8.
25. Forssell K, Forssell H, Kahnberg KE. Recurrence of keratocysts. A long-term follow-up study. Int J Oral Maxillofac Surg. 1988;17:25–8.
26. di Magliano Pasca M, Hebrok M. Hedgehog signaling in cancer formation and maintenance. Nat Rev Cancer. 2003;3:903–11.
27. Taipale J, Chen JK, Cooper MK, Wang B, Mann RK, Milenkovic L, et al. Effects of oncogenic mutation in Smoothened and Patched can be reversed by cyclopamine. Nature. 2000;406:1005–9.

Zhang L, Sun ZJ, Zhao YF, Bian Z, Fan MW, Chen Z. Inhibition of SHH signaling pathway: Molecular treatment strategy of odontogenic keratocyst. Med Hypotheses. 2006;67:1242–4.

References

The incidence of recurrence of OKC has varied from 2.5% to 62%. (14) The great degree of variation in these reports is mainly because some series included cysts from patients with Nevoid Basal cell carcinoma syndrome (NBCCS), while other reasons for this variation can be due to the duration of the follow-up period and method of treatment used. (14)

In 1976, Brannol (15) proposed three mechanisms for OKC recurrence: Incomplete removal of the cyst lining, growth of a new OKC from satellite cysts( or Odontogenic rests left behind after surgery), and development of a new OKC in an adjacent area.

Histopathological features that can be considered to predict recurrence in OKC are

Higher level of cell proliferative activity in the epithelium

Budding in the basal layer of the epithelium

Parakeratinization of the surface layer

Subepithelial spilt of the epithelial lining

Subepithelial split of the epithelial lining

Presence of remnants/cell rests as well as daughter cysts.