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**REVIEW ARTICLE**

# ODONTOGENIC KERATOCYST (OKC) OR KERATOCYSTIC ODONTOGENIC TUMOR (KCOT) - JOURNEY OF OKC FROM CYST TO TUMOR TO CYST AGAIN : COMPREHENSIVE REVIEW WITH RECENT UPDATES ON WHO CLASSIFICATION (2017)

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**ABSTRACT**

The odontogenic keratocyst (OKC) is a dilemmatic odontogenic developmental cyst of oral and maxillofacial region which has gained very special attention since last two decades. It has characteristic histopathological and clinical features but still the cyst is very special due to its aggressive behavior and high recurrence rate. Many prior attempts have been made to classify these cysts from 1887 to finally WHO 2017. Previously classified under developmental odontogenic cyst of jaw by WHO in 1971 & 1992, OKC has been reclassified and renamed as keratocystic odontogenic tumor (KCOT) in the WHO classifications of head and neck tumors in 2005 due to its aggressive behavior, high recurrence rates and specific histological characterstics. But recently WHO classification of Head and Neck pathology (2017) re-classified KCOT back into the cystic category. Despite of many classifications and nomenclature, unfortunately, clinicians are still facing difficulties in understanding the true nature, identification and management of OKC. An attempt is hereby made to review various aspects of OKC with emphasis on recent nomenclature, recurrence, molecular aspects, and management of OKC.



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## INTRODUCTION

The term Odontogenic Keratocyst (OKC) was first coined by Philisen in 1956 (Eryilmaz *et al*., 2009) and its characterstic features was first described by Pindborg and Hansen in 1963 (Pindborg and Hansen, 1963). Over the years, many researchers have been trying to understand the nature, identification, and management of the OKC leading to classify, classify, and reclassify the disease. Previously classified under developmental odontogenic cyst of jaw by WHO in 1971 & 1992, OKC has been reclassified and renamed as keratocystic odontogenic tumor (KCOT) in the WHO classifications of head and neck tumors in 2005 due to its aggressive behavior, high recurrence rates and specific histological characterstics. According to WHO it is a benign uni or multicystic, intraosseous tumor of odontogenic origin (dental lamina and its ramnents) with characterstic lining of parakeratinised stratified squamous epithelium and potential for aggrasive and infilterative behavior. WHO proposed the terminology as keratocystic odontogenic tumor (KCOT) as it shows its neoplastic nature. However In 2017, the new WHO classification of Head and Neck pathology re-classified OKC back into the cystic category.

The Journey of classifications and nomenclature of OKC is as follows.

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|---|
| Dental cyst (John Hunter 1774), |
| Dermoid Cyst ( Mikulicz 1876) |
| Primordial cyst (Robinson 1945) |
| Keratocystoma (Shear) |
| Odontogenic keratocyst ( Philisen 1956 & Pindborg and Hansen 1963) |
| Benign neoplasm (Toller 1967) |
| Odontogenic keratocyst (WHO 1971) |
| True benign cystic epithelial neoplasm (Ahlfors 1984) |
| Odontogenic keratocyst (WHO 1992) |
| keratocystic odontogenic tumor (Benign neoplasm) (WHO 2005) |
| Odontogenic keratocyst (WHO 2017) |

Odontogenic keratocyst (OKC) is so named because keratin is produced by the cystic lining. It is a Parakeratin lined cyst-like lesion within bone. OKC is the one of the rare and distinctive developmental odontogenic cyst which from the dental lamina, containing clear fluid and a cheesy material resembling keratin debris. Epidemiologically OKC accounts for approx. 7.8 % of all cyst of the jaw and incidence vary from 4-16.5% . It occurs at all ages wih peak incidence in 2nd and 4th decade of life. it predominantly occurs in white population with male :female ratio of 1.6:1. Location wise it is most commonly seen twice in mandible as compared to maxilla. In mandible it occurs usually in angle – ascending ramus region (69-83%). Mandibular cyst crosess the mid line and maxillary cyst may involve sinus and nasal floor, premaxilla and maxillary third molar region. OKC may arise from TM Joint also. OKC is mostly intraosseous lesion though peripheral counterpart also have been reported in buccal gingival in canine region of mandible. Peripheral OKCs have female predominance with male: female ratio of 2.2:1 (Chirapathomsakul *et al*., 2006). Clinically presents as swelling with or without pain, discharge, displacement of teeth, ocassionaly peresthesia of lower lip. The expansion of the cyst is very minimal in the initial stage and it is due to the classical characteristic of the cyst to grow in antero posterior direction in the medullary space of the bone. Expansion of buccal cortex in 30% of maxillary and 50% of mandibular regions (Philipsen, 2005; Hyun *et al*., 2009; Donoff *et al*., 1972). Syndromes associated with multiple OKC areNevoid Basal cell carcinoma syndrome (NBCCS), Gorlin goltz syndrome, Marfans syndrome, Ehlers danlos syndrome, Noonans syndrome, Orofacial digital syndrome, Simpson-golabi-behmel syndrome (Bakaeen *et al*., 2004; Gonzalez-Alva *et al*., 2008). Radiographically OKC presents as well defined unilocular or multilocular (25-40%) radiolucent lesion with smooth margin (corticated margin in secondarily infected cases), displacement of adjacent teeth without root resorption, lesion may contain impacted tooth (25-40% cases), Expansion of cortical plates (buccal > lingual) with or without perforation. Cyst grows in medullary spaces of bone in antero-posterior direction, so bony expansion is minimal in initial stages. (Chirapathomsakul *et al*., 2006; Philipsen, 2005; Sciubba *et al*., 1999) (Figure 1)

**Radiological Types of keratocyst**

1. Replacement type : Cyst which forms in the place of normal teeth.
2. Envelopmental type: Cyst which embraces an adjacent unerupted tooth.
3. Extraneous type: Cyst which occur in asending ramus away from the teeth.
4. Collateral type : Cyst which occurs adjacent to the root of teeth wich are indistinguishable radiologically from lateral periodontal cyst.

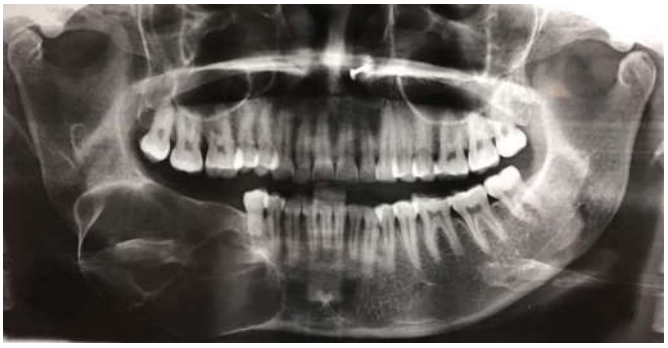

**Figure 1. OPG showing well defined multilocular radiolucent lesion with smooth margin**

Advanced Imaging like MRI finding in Keratocystic odontogenic tumours shows T1: high signal due to cholesterol and keratin contents. T2: heterogeneous signal. DWI: restricts due to presence of keratin. T1 C+: peripheral enhancement but unlike ameloblastomas no enhancing nodular component

**Differential Diagnosis**

1. Histologically : myxoma, ameloblastoma, central giant cell granuloma, odontogenic cysts.
2. Radiographically : Dentigerous cyst (40%), Residual cysts, redicular cyst, Lateral periodontal cysts (25%), Primordial cyst (25%), Globulomaxillary cyst (10%), Unicystic ameloblastoma, A-V malformation, Fibro-osseous lesion at initial stages

**Treatment modalities for KCOT:** Treatment of OKC depend on patient age, size and location of cyst, soft tissue involvement and histological variant of lesion. Treatments are usually classified as conservative like Enucleation with or without curettage and marsupialization and aggressive like peripheral ostectomy and chemical curettage with Carnoy's solution, cryotherapy, or electrocautery and resection (Zhao *et al*., 2002).

**Enucleation :** It refer ''to remove whole or clean, as a tumour from its envelope.''Although enucleation helps to provide complete specimen for histopathologic examination, but it shows recurrence rates as high as 30-60%. Minute satellite cysts within the fibrous wall, thin friable wall of OKCT and difficulty to enucleate it one go from the bone are the reasons accountable for high recurrence rate of OKCT (Giuliani *et al*., 2006).

**Enucleation with Carnoy' solution:** After enucleation carnoy's solution is applied into the cavity. It is a cauterizing agent consists of 3ml chloroform, 6 ml of absolute alcohol, 1 ml of glacial acetic acid, and 1 gm of ferric chloride. (Blanas *et al*., 2000; Stoelinga, 2003).

**Enucleation with Peripheral ostectomy:** Pheripheral ostectomy refer to reduction of peripheral bone with powered hand piece and rotary instrument after enucleation of the lesion. After enucleation of the lesion,cystic cavity walls pheripheral bone was reduced with handpieces in caudal and cranial direction, followed by filing the defect with iodofrom guage (Stoelinga, 2003).

**Enucleation with Carnoy' solution and Peripheral ostectomy:** It has combined effect of carnoy's solution and

peripheral ostectomy. The cyst is first enucleated followed by rinsing the defect with saline and then packing it with a gauge soaked with Carnoy's solution and leave it for 3 minutes. Then cystic lumen is re rinsed with saline to see cystic wall remains, which would be dark brown coloured and fixated, thus allowing complete removal of remains. After that peripheral ostectomy is performed and overlying atthched mucosa is excised. Finally dwfect is filled with vaseliene- iodofrom guage (Stoelinga, 2003).

**Enucleation + Cryotherapy:** After enulceation of KCOT should follow treatment of cavity with an agent that kill epithelial ramnants or satellite cysts. Liquid nitrogen has ability to devitalize bone in situ and leave osseous inorganic framewok untouched. It act by direct damage from intracellular and extracellular ice crystal formation leading to cell death. Also creates osmotic and electrolytes disturbance in cell. Cystic cavity is sprayed with liquid nitrogen twice for 1 minutes, with 5 min thaw between freezes. Bone grafting can be done simultaneously. (Schmidt and Pogrel, 2001; Jensen *et al*., 1988) Advantges of liquid nitrogen therapy are that Bony matrix is left in place to act as scaffold for new osteogenesis. Bone grafts can be placed immediately to promote healing and decreasing risk of pathological fracture. Act as haemostasis agent and reduce scarring.

**Marsupialization (Decompression):** It the earliest treatment used & was first described by Partsch in 1892. In this process a window of 1 cm is made into the cyst and lining is sutured to oral mucosa process to convert the cyst into pouch so that cyst is decompressed and it exposes the cystic lining into oral environment. Mandibular cyst marsupialized into oral cavityc and maxillary cyst marsupialized into maxillary sinus and nasal cavity. Cavity is then regularly packed open with iodoform guage till endeosseous healing. Partsch I procedure includes marsupialization alone and Partsch II procedure is Enucleation with primery closure (Pogrel, 2005; Seward and Seward, 1969; Partsch, 1892) Effect of marsupialization was studied by Nakamura in 2002 and developed formula to measure reduction rate (RR) on the basis pixel count of the lesion before and after marsupialization. RR (%)= X (Pixel count Before marsupialization) – Y (Pixel count after marsupialization / X x 100.

It showed greater the reduction rate, higher the success rate (Nakamura *et al*., 2002).

**Marsupialization with Cystectomy: (Waldron's method)** It is a two staged technique. Firstly marsupialization is done and cystic cavity is packed with iodoform guage and later on when cavity becomes smaller, enucleation is carried out and complete tissue is sent for histological analysis. This technique is done in cases of large cysts and vital structure are presents near by. To prevent pathological fractures, to detect any occult pathology. it fastens healing process. Disadvantage is that pt has to undergo two surgeries (Tolstunov and Treasure, 2008)

**Resection:** Resection is to either segmental resection (surgical removal of a segment of the mandible or maxilla without maintaining the continuity of the bone) or marginal resection (surgical removal of a lesion intact and a small area of uninvolved bone, maintaining the continuity of the bone). Resection have the lowest recurrence rate (0%) but the highest morbidity rate because reconstructive measures are necessary to restore jaw function and aesthetics. (Blanas *et al*., 2000)

**Recurrence of OKC/KCOT:** It has high recurrence rate ranging from 25-60%. Recurrence rates reduced when more meticulous surgical treatment is done. Majority of cases reported recurrence within 5 years post treatment. The mean time of recurrence for males was found to be 4years and for females it came out to be 7 years. There have been few cases where recurrence was reported even after 10 years also. so long term follow up in necessary. The causes and factors responsible for KCOT recurrence are :

1. Incomplete removal of cystic lining
2. Thin and friable nature of epithelial lining,
3. Higher level of cell proliferative activity in the epithelium.
4. Budding in the basal layer of the epithelium
5. Bony perforation.
6. Adherence to adjacent soft tissue.
7. Supraepithelial and Subepithelial split of the epithelial lining.
8. Parakeratinization of the surface layer
9. Ramnants of dental lamina epitelium not associated with original OKC and development of new OKC in the adjacent area.
10. Growth of new OKC from satellite cyst /daughter cyst/remnants/cell rests.

| | |
|---|---|
| 1.enucleation | 30 % |
| 2.enucleation + carnoy' solution: | 9 % |
| 3.enucleation + peripheral ostectomy | 18 % |
| 4.enucleation + carnoy' solution + peripheral ostectomy | 8% |
| 5.enucleation + cryotherapy | 38 % |
| 6.marsupialization | 33% |
| 7.marsupialization + cystectomy | 13 |
| 8.Resection | 0% |

Table showing Recurrence rates with different treatment modalities (Madras and Lapointe, 2008)

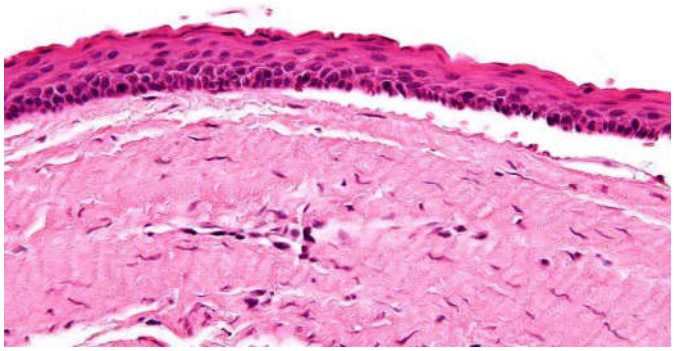

**Figure 2. Histological features of OKC**

Table showing Recurrence rates with different treatment modalities (Madras and Lapointe, 2008)

**Histological features** - Pindborg, phillipsen and Henriksen (Pindborg *et al*., 1962) suggested series of histological features for the diagnosis of OKC which includes: (Figure 2)

1. Thin Stratified squamous epithelium lining with ribbon –like appearance typically 8-10 uniform layers thick.
2. Lacks of rete ridges/pegs.
3. Well defined basal cell layer having cuboidal or columnar cells arranged in palisaded fashion described as "picket fence or tombstone appearance"

4. A thin spinous cell layerwhich often shows direct transition from basal cell layer (artefactual separation of epithelium from basement membrane) and spinous cell layer intracellular edema.
5. Surface keratinisation which is corrugated and rippled and mostly parakeratosis (keratinized cells with nuclei)
6. Cystic wall composed of fibrous connective tissue which is thin and usually uninflamed.
7. Others findings are satellite cysts, daughter cysts (7-30%), solid epithelial proliferation,odontogenic rests basal layer budding may be seen.fibrous connective tissue wall may get mineralized and may include cholesterol crystals and Rushton bodies.

**Histological variants of OKC (based on lining and types of keratin produced)**

| Parakeratinized | Orthokeratinized | Combination |
|---|---|---|
| Named askeratocystic odontogenic tumor (KCOT) or True OKC | Orthokeratinizing odontogenic cyst (OOC) | -- |
| Included in classification of Tumor by WHO | Not included | Not included |
| keratinized cells with nuclei | keratinized cells without nuclei | Both |
| Incidence – 86% | 12.2% | 1.6% |
| Recurrence rate 47.8% | 2.2% | -- |
| Aggressive surgical required | Conservative treatment | -- |

## DISCUSSION

A Odontogenic keratocyst (OKC) or keratocystic odontogenic tumor (KCOT) is a rare and benign but locally aggressive developmental cystic neoplasm. The cystic nature of odontogenic keratocyst (OKC) has been a matter of discussion since a long time. Some investigators classify the OKC as a benign tumor butthe aggresive behavior of OKC has put the dilemma that it is cyst or neoplasm. In 1967 TOLLER suggested that OKC is to be named as benign neoplasm inspite of conventional cyst due to its aggressive clinical behavior. In 1984 Ahlfors proposed that if OKC were to be recognized and seen as a true, benign cystic epithelial neoplasm, then the question pertaining toits treatment scheduled and modality would be raised and questioned. WHO reclassify the lesion as a tumor (WHO Histological classification of tumours of the oral cavity and oropharynx 2005) under category benign tumours of odontogenic epithelium with mature, fibrous stroma without odontogenic ectomesenchyme (Figure 3).

Redesignation of the OKC as the KCOT by the World Health Organization (WHO 2005) is based on the well-known aggressive behaviour of this lesion, its histology and new information regarding its genetics. The decision is based on following factors.

**1.Behavior:** KCOT is locally destructive, highly recurrent and have Aggressive behavior. It recurrence rates is 3-60%. Recurrence rates reduced when more meticulous surgical treatment is done. Its penetration into cancellous bone can be very extensive. It is part of NBCCS.

**Growth and Growth measurement is like a benign tumor:** KCOT grows not by osmotic expansion like other odontogenic cysts, it growth is by epithelial proliferation of wall with infolding of epithelial lining. It has unremitting growth. Mean mitotic count = 8.0 similar to ameloblastoma. (other cysts = 2.3 and radicular cyst = 4.5). Tritiated thymidine studies hows OKC = 13%; 1.7% for non OKC, buccal mucosa 7%.

**Markers in cyst fluid of KCOT:** Soluable protein content of cyst fluid in OKC < other cysts. AgNORs not diagnostic of OKC or other odontogenic cyst or unicystic ameloblastoma. Trypsin activity higher in RC and DC than OKC. Ratio of 83 kDa MMP9 to 92kDa in OKC fluids >> than other cysts.

**2.Histopathology** : Basal layer of KCOT budding into the connective tissue and mitotic figures are frequently found in suprabasal layers. (Ahlfors *et al*., 1984; Barnes *et al*., 2005)

**Genetics/Immunohistochemistry**: Expression of P53, proliferating cell nuclear antigen (PCNA) and Ki-67 markers is strongly associated with OKCs than other types of dontogenic cysts. Expression of P53 gene protein is strongly associated with aggrasive behavior and high recurrence of KCOT (Kichi *et al*., 2005). gp38, an epithelial specific 38-kD cell surface glycoprotein was consistently found positive with all basal and suprabasal cell layers in a study of 30 cases of odontogenic keratocyst (OKC) and satellite cysts were present in all parakeratinized OKCs. The neoplastic potential of odontogenic keratocyst (OKC) was further substantiated by these findings which suggests an alteration in gene expression. (Shear, 2002) Study reveals 91.9% cases shows strong positive for p53 in suprabasal layers of cystic epithelium. PTCH ("patched" ) gene plays important role in pathogenesis of KCOT. PTCH is a tumor suppressor gene,occurs on chromosome locus 9q22.3-q31.

Cytokeratin -10 expression in suprebasilar layers of KCOT with loss of keratinisation following cyst decompression and irrigation has been shown in studies. There strong relationship among intracystic pressure, expression of IL-1a and bone resorption. Positive pressure plays role in KCOT growth via stimulation the expression of IL-1 in epithelial cells (Lombardi *et al*., 1995; Philipsen *et al*., 2005; Sun *et al*., 2008). Molecular analysis of the expression of PTCH, SMO, GlI-1 and bcl-2 in KCOT shows a profile similar to ameloblastoma rather than other odontogenic cysts (Vered *et al*., 2009).

Histochemical and molecular studies shows that there ishigher expression of oxidative enzymes (NADH2-, NADPH2-, G6PD and acid phosphatase) in OKC when compared to. radicular, residual and dentigerous cysts. Leucine aminopeptidase is greater in OKC attributed to invasiveness of lesion. Parathyroid hormone related protein PTHrP higher levels in OKC as compared to residual and dentigerous cysts which is related to bone resorption

**Immunohistochemistry**

There is staining of p53 in supra basal layers of kcot which plays role in blocking apoptosis inducing and growth inhibitory actions which may precipitate the proloferative potential of epithelial cells, thus enhancing biologic aggressiveness of cyst (Gurgel *et al*., 2008). Matrix metalloproteins (MMP) are the enzymes which play important function in regulating the integrity and composition of extracellular matrix and thus degradation, proliferation,differatiation and cell death.MMP1 is one of the major proteases which can degrade type 1 collegen,which maintainstrength and rigidity of connective tissue. MMP1 is associated with kcot bone matrix and causing dissemination of this cyst through trabecular spaces.MMP2 also resides in basement membrane of KCOT and involved in degradation of etracellular matrix around the cyst.

**MALIGNANT TUMOURS:**

**Odontogenic carcinomas**
Metastasizing (malignant) ameloblastoma
Ameloblastic carcinoma - primary type
Ameloblastic carcinoma - secondary type (dedifferentiated)

***Intraosseous***
Ameloblastic carcinoma - secondary type (dedifferentiated),
***Peripheral***
Primary intraosseous squamous cell carcinoma – solid type
Primary intraosseous squamous cell carcinoma derived from keratocystic odontogenic tumour
Primary intraosseous squamous cell carcinoma derived from odontogenic cysts
Clear cell odontogenic carcinoma
Ghost cell odontogenic carcinoma

**Odontogenic sarcomas**
Ameloblastoma fibrosarcoma
Ameloblastic fibrodentino-and fibro-odontosarcoma

**BENIGN TUMOURS**
**Odontogenic epithelium with mature, fibrous stroma without odontogenic ectomesenchyme**

Ameloblastoma, solid/multicystic type
Ameloblastoma, extraosseous/peripheral type
Ameloblastoma, desmoplastic type
Ameloblastoma, unicystic type
Squamous odontogenic tumour
Calcifying epithelial odontogenic tumour
Adenomatoid odontogenic tumour
**Keratocystic odontogenic tumour**

**Odontogenic epithelium with odontogenic ectomesenchyme, with or without hard tissue formation**

Ameloblastic fibroma
Ameloblastic fibrodentinoma
Ameloblastic fibro-odontoma
Odontoma
- Odontoma, complex type
- Odontoma, compound type

Odontoameloblastoma
Calcifying cystic odontogenic tumour
Dentinogenic ghost cell tumour

**Mesenchyme and/or odontogenic ectomesenchyme with or without odontogenic epithelium**

Odontogenic fibroma
Odontogenic myxoma/myxofibroma
Cementoblastoma

**Bone-related lesions**

Ossifying fibroma
Fibrous dysplasia
Osseous dysplasia
Central giant cell lesion (granuloma)
Cherubism
Aneurysmal bone cyst
Simple bone cyst

**OTHER TUMOURS**

Melanotic neuroectodermal tumour of infancy

**Figure 3. WHO Histological classification of tumours of the oral cavity and oropharynx 2005**

**Odontogenic carcinomas**
Ameloblastic carcinoma
Primary intraosseous carcinoma
Sclerosing odontogenic carcinoma
Clear cell odontogenic carcinoma
Ghost cell odontogenic carcinoma

**Odontogenic carcinosarcoma**

**Odontogenic sarcomas**
**Benign epithelial odontogenic tumours**
Ameloblastoma
Ameloblastoma, unicystic type
Ameloblastoma, extraosseous/peripheral type
Metastasizing ameloblastoma
Squamous odontogenic tumour
Calcifying epithelial odontogenic tumour
Adenomatoid odontogenic tumour

**Benign mixed epithelial & mesenchymal odontogenic tumours**

Ameloblastic fibroma
Primordial odontogenic tumour
Odontoma
Dentinogenic ghost cell tumour

**Benign mesenchymal odontogenic tumours**
Odontogenic fibroma
Odontogenic myxoma/myxofi broma
Cementoblastoma
Cemento-ossifying fibroma

**Giant cell lesions and simple bone cyst**
Central giant cell granuloma
Peripheral giant cell granuloma
Cherubism
Aneurysmal bone cyst
Simple bone cyst
**Haematolymphoid tumours**
Solitary plasmacytoma of bone

**Odontogenic cysts of inflammatory origin**
Radicular cyst
Inflammatory collateral cysts

**Odontogenic and non-odontogenic developmental cysts**
Dentigerous cyst
**Odontogenic keratocyst**
Lateral periodontal cyst and botryoid odontogenic cyst
Gingival cysts
Glandular odontogenic cyst
Calcifying odontogenic cyst
Orthokeratinized odontogenic cyst
Nasopalatine duct cyst

**Malignant maxillofacial bone and cartilage tumours**

Chondrosarcoma
Mesenchymal chondrosarcoma
Osteosarcoma
**Benign maxillofacial bone and cartilage tumours**
Chondroma
Osteoma
Melanotic neuroectodermal tumour of infancy
Chondroblastoma
Chondromyxoid fibroma
Osteoid osteoma
Osteoblastoma
Desmoplastic fibroma

**Fibro-osseous and osteochondromatous lesions**
Ossifying fi broma
Familial gigantiform cementoma
Fibrous dysplasia
Cemento-osseous dysplasia
Osteochondroma

**Figure 4. WHO 2017 classification odontogenic and maxillofacial bone tumours**

(Cavalcante *et al*., 2008) Vascular endothelial growth factors (VEGFs) are multifunctional proteins acts as angiogenic potentials of a lesion. VEGFs have been involved in pathogenesis of cysts and tumors. They have beenintensly espressed in OKCs (Philipsen *et al*., 2005; Mitrou *et al*., 2009). Although traditionally known as Odontogenic Keratocyst this lesion was reclassified as Keratocystic Odontogenic Tumor (KCOT) by the World Health organization in 2005, to better reflect its nature as a neoplasm based both on its clinical behavior and its molecular biology but recently Odontogenic keratocysts which were eliminated from the 3rd 2005 edition were again included in odontogenic cyst category in the 4th edition of WHO 2017 classification odontogenic and maxillofacial bone tumours. (Figure 4) It was concluded that most cases of KCOT and CCOT behave clinically as non-neoplastic lesions and are treated as cysts. Therefore, there was consensus that they should be reclassified as OKC and COC, respectively until there is more definite evidence for classifying them as KCOT and CCOT, thus reintroducing the time-honoured names in use before their labelling as tumour in the former WHO classification" (WHO Blue Book 2017) (Raja R. Seethala, 2017)

**Advanced and Future Treatment modalities**

Due to the recent advances and thus determination of molecular basis of this entity, a new novel methodology concentrating on molecular aspects has been devised. The Hh pathway can be blocked at different levels, and Hh inhibitors could serve as attractive antitumor agents. (di Magliano Pasca and Hebrok, 2003) According to some studies, cyclopamine, a plant-based steroidal alkaloid, blocks activation of SHh pathway caused by oncogenic mutation. (Taipale *et al*., 2000) Other studies also show antagonists of SHh signaling factors could effectively treat KOT. (Zhang *et al*., 2006)

**Conclusion**

The nature of Odontogenic Keratocyst (OKC) either cystic or tumor, has been a matter of discussion since decades and few researchers classified the OKC as a benign tumor. In last decade in 2005 the WHO has given the term "keratocystic odontogenic tumor" (KCOT) to r the place the term "odontogenic keratocyst" (OKC), as it closely reflects the neoplastic property of the pathology. The aggressive behavior of the cyst, high histological mitotic activity, and evidence of associated genetic and chromosomal abnormalities (eg, mutation of the PTCH gene) often seen in neoplasia are some major reasons which serve as the basis for this new classification. But again WHO has categorized OKC into Odontogenic and non-odontogenic developmental cysts (2017). This new WHO classification of Head and Neck pathology re-classified OKC back into the cystic category. It is no longer considered a neoplasm as the evidence supporting that hypothesis like clonality is considered insufficient. There is as yet no international consensus, either on the question of the cyst's neoplastic nature, or on a name change. However, this is an area of debate within the head and neck pathologists, maxillofacial surgeons and clinicians community, and some still regard OKC as a neoplasm despite the re-classification.

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