Case Report

Odontogenic keratocyst- Mimicking residual cyst in maxilla

Nalini Tomar^{1,*}, Kuldeep Singh Bhadauria²

¹YMT Dental College & Research Institute, Navi Mumbai, Maharashtra, India

²Thyrocare Technologies Limited, Navi Mumbai, Maharashtra, India

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ABSTRACT

OKC was classified as cystic lesion by WHO in 1971 & 1991, based on aggressive nature, growth pattern, clinical, histological and immunohistochemical nature in 2005 they again classified it as benign lesion, however in 2017 WHO head and neck pathology reclassified it as cystic lesion. It more commonly occurs in posterior mandible and rarely occurs in maxilla, in this case occurrence of OKC in maxillary posterior region is very rare with distinctive expansion and lifting of maxillary sinus floor without perforating in edentulous area makes it more difficult to detect and justify from residual cyst. Here a 65 years old patient came with chief complaint of pus discharge from upper left posterior region since 7 months, having a small opening in edentulous ridge, which provisional diagnosis was given as residual cyst later after excision of lesion and histopathological analysis it was given as OKC.

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1. Introduction

Philipsen in 1956, first described the term 'odontogenic keratocyst' (OKC), as developmental cyst of jaw.¹ Histologic criteria to detect OKC was given by Pindborg and Hansen.² Initially it was given as odontogenic keratocyst, but later on WHO classified it as Keratocystic odontogenic tumour because of its aggressive nature and growth pattern and mutational changes,³ it is non inflammatory and arises from cell rest of dental lamina. Now in 2017 again WHO reclassified it as OKC.⁴ They are usually seen in mandibular posterior regions and rarely in maxilla, about 70-80% occur in the lower jaw, about 90% occur posterior to the canines and 50% in the ascending ramus of the mandible, very rarely in the maxilla.⁵

WHO gave new classification in which they changed the designation to OKC from keratocystic odontogenic tumour (KCOT) and described it as a benign uni or multilocular, intraosseous tumour of odontogenic origin, with aggressive and invading behaviour".³ Usually there are no significant clinical symptoms, although mild swelling

and pain can be seen likely due to secondary infections.⁵

As they are often confused with other cysts and tumours because of vague appearances and similar features it is important to diagnosis. Similar in our case OKC occurred in edentulous area with history of long term presence but it cannot be proved clinically or radiological as OKC but on histopathology it was proved. So complete diagnosis and proper treatment is necessary to reduce recurrences.

2. Case Report

A 65 years old female patient reported to the department with chief complaint of pus discharge from upper left posterior region of jaw since 7 months. Initially patient was asymptomatic, later on sudden onset of swelling with pus discharge in that area. Swelling was smaller in size and gradually increased to present size. Patient gives history of extraction 2 years back after which she had experienced mild pain during chewing for which she has taken medication from local dentist, patient is diabetic and hypertensive since 2 years and under medication.

* Corresponding author.

E-mail address: mrskuldeep26@gmail.com (N. Tomar).

2.1. On examination

(Figure 1 a and b) Mild facial fullness and tenderness over left side of cheek. Intraoral (Figure 2) single diffuse swelling present in maxillary left posterior region which is of 3 x 3cms in size obliterating buccal vestibule, Anteroposteriorly from 24 to 28 region, Supero-Inferior from alveolar ridge to depth of vestibule, expanding the ridge overlying surface appears normal and surrounding too. Intraoral examination showed a tiny draining sinus is seen in crest of edentulous ridge in 27 region.

Fig. 1: (a),(b) front and lateral profile showing mild facial fullness left cheek

Fig. 2: Showing diffuse swelling in left buccal vestibule

Fig. 3: Aspiration showing cheesy fluid with blood.

On palpation swelling is firm in consistency, mildly tender, compressible, egg shell crackling and expansion felt. Clinically present 13, root pieces-14,15 and mesioproximal caries with 17. Single left submandibular lymph node is

Fig. 4: Showing after excision of lesion, opening in alveolar ridge

Fig. 5: Iopa showing interrupted floor of maxillary sinus

Fig. 6: a and b reveals large lesion involving left maxillary sinus with anteroposterior and buccopalatal expansion

palpable which is soft, mobile, mildly tender. So provisional diagnosis is given as residual cyst of left maxillary region.

Patient is advised for IOPA, OPG, CBCT, routine investigation, aspiration and biopsy. Aspiration- (Figure 3) Milky white cheesy liquid with RBCs aspirate on investigation revealed keratocyst. IOPA (Figure 5) and OPG reveals unilocular radiolucency surrounded by corticated border which is interrupted at base and opening in soft tissue which is hazy and appears like involving maxillary sinus.

Fig. 7: CBCT sections showing unilocular hyperdense area in maxillary sinus encroaching and obliterating it except superior aspect.

CBCT (Figures 6 and 7) reveals well defined, corticated, unilocular hyperdense areas in left maxillary sinus measuring around 26.7mm in vertical height and 33.3mm in mediolateral dimensions. Antero-posterior extensions are approximately 31.4mm in length. Missing 17, 16, 12, 11, 21, 22, 23, 24, 25, 26 and 27 is observed. Hyperdense area obliterating left maxillary sinus from all aspects except the superior aspect of left maxillary sinus. Floor of left maxillary sinus is displaced superiorly due to the extension of the lesion. Coronal Sections depicts the well defined border of lesion involving and encroaching the lower part of left maxillary sinus. Buccal and palatal bone in left posterior region in relation with edentulous area of 26, 27 and 28 is lost. The alveolar crest in the edentulous region is destroyed in relation with 26 and 27, given as residual cyst in relation to left maxilla.

Curettage & enucleation of the lesion followed by application of Carnoy's solution used for reducing the recurrence rate under general anaesthesia (Figure 4). Excised tissue specimen was submitted for the histopathological examination. On histopathological examination it was confirmed as OKC. Patient was kept on follow up for 6 months and no recurrent lesion seen.

3. Discussion

In the earlier literature, the OKC was described as a cholesteatoma (Hauer, 1926; Kostecka, 1929). Forssell (1980) concluded that the first account of this lesion was given by Mikulicz in 1876, described it as a dermoid cyst.¹

The epithelium of the keratocyst is strongly believed to arise from either the dental lamina or the residue of the dental lamina (cell rests of Serre).⁴

OKC are relatively common developmental odontogenic cysts and account for 10–12% of all jaw cysts.⁶ The term Odontogenic Keratocyst (OKC) was first coined by Philipsen in 1956 (Eryilmaz et al., 2009) and its characteristic features was first described by Pindborg and Hansen in 1963.¹ 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.⁷

Its journey of nomenclature is as follows:

1. Dental cyst (John Hunter 1774),
2. Dermoid Cyst (Mikulicz 1876)
3. Primordial cyst (Robinson 1945)
4. Keratocystoma (Shear) Odontogenic keratocyst (Philipsen 1956 & Pindborg and Hansen 1963)
5. Benign neoplasm (Toller 1967)
6. Odontogenic keratocyst (WHO 1971)
7. True benign cystic epithelial neoplasm (Ahlfors 1984)
8. Odontogenic keratocyst (WHO 1992)
9. Keratocystic odontogenic tumor (Benign neoplasm) (WHO 2005)
10. Odontogenic keratocyst (WHO 2017)^{1,8}

The keratocystic odontogenic tumor is more common in males than females with ratio of 1.6:1 and occurs over a wide age range. White more common, it is typically diagnosed during the second to fourth decade. In our case, the patient was in his sixth decade.⁹ Peripheral OKCs have female predominance with male: female ratio of 2.2:1.⁷

KCOTs (Figures 8 and 9) mostly occur in the body of the mandible, most commonly in the molar region and vertical ramus.⁹ However in present case, there was involvement of maxillary posterior region which is edentulous and lifting of the maxillary sinus seen. In our case shows a rare site of occurrence in a female. Literature suggests that less than 1% of the KCOT cases occur in the maxilla with maxillary antrum involvement. In the maxilla, the canine region is the most common location for KCOTs.¹⁰

The clinical features include pain or without pain, soft-tissue swelling, displacement of teeth, expansion of bone in anteroposterior in medullary space of bone, drainage, and various neurological manifestations, such as, paresthesia of the lip or teeth in case of lower jaw involvement. The maxillary KCOT tends to be secondarily infected with greater frequency than the mandibular ones, due to its vicinity to the maxillary sinus.¹⁰ In this case too, the lesion was secondarily infected, with the presence of mild pain, a sinus opening and pus discharge. Expansion of buccal cortex in 30% of maxillary and 50% of mandibular regions.³ Syndromes associated with multiple OKC are Nevroid Basal cell carcinoma syndrome (NBCCS), Gorlin goltz syndrome, Marfans syndrome, Ehlers danlos syndrome,

Noonans syndrome, Orofacial digital syndrome, Simpson golabi-behmel syndrome.^{10,11}

Radiographically most KCOTs are unilocular or multilocular, presenting a well-defined peripheral rim (corticated), with scalloped borders, root resorption, displacement of teeth with involvement of impacted tooth. Buccal bone expansion more compared to lingual with or without perforation. Small lesion have minimal expansion due to its growth pattern in antero posterior direction when it increases it involved buccal and lingual bones too.^{3,7,10} In the present case, the radiographic evaluation revealed unilocular radiolucency in left maxillary posterior region which is aggressive osteolytic lesion, involving edentulous area causing perforations in the buccal and palatal cortical plates in the 24, 25, 26, 27 region, lesion encroaching and lifting maxillary sinus floor without perforating it and maintaining its border.

Radiological Types of keratocyst

1. Replacement type: Cyst which forms in the place of normal teeth.
2. Envelopmental type: Cyst which envelopes adjacent impacted tooth.
3. Extraneous type: Cyst which occur in ascending ramus away from the teeth.
4. Collateral type: Cyst which occurs adjacent to the root of teeth which are indistinguishable radiologically from lateral periodontal cyst.⁸

KCOT: In 1967, Toller suggested that the OKC should be considered as benign tumour because of its clinical nature.^{1,4} In 1984, Ahlfors et. al¹² suggested that “if we consider OKC as benign neoplasm, the question of modified treatment would be raised.” Since, many published reports in these years have influenced WHO to again classify the lesion as a tumour.

1. Behaviour: KCOT is localised catastrophic and high chances of recurrence.
2. Histopathology: Studies such as that by Ahlfors and others¹⁰ show the basal layer of the KCOT budding into connective tissue. In addition, WHO notes that mitotic figures are frequently found in the suprabasal layers.²
3. Genetics: PTCH (“patched”), a tumour suppressor gene involved in both NBCCS and sporadic KCOTs, occurs on chromosome 9q22.3-q31.^{13–16} Normally, PTCH forms a receptor complex with the oncogene SMO (“smoothened”) for the SHH (“sonic hedgehog”) ligand. PTCH binding to SMO inhibits growth-signal transduction. SHH binding to PTCH releases this inhibition.¹⁴ If normal functioning of PTCH is lost, the proliferation-stimulating effects of SMO are permitted to predominate.
4. Recent studies revealed that the etiology of NBCCS and KCOTs has a “2-hit mechanism,” with allelic

<u>MALIGNANT TUMOURS</u>	
Odontogenic carcinomas	Odontogenic epithelium with odontogenic ectomesenchyme, with or without hard tissue formation
Metastasizing (malignant) ameloblastoma	Ameloblastic fibroma
Ameloblastic carcinoma - primary tumour	Ameloblastic fibro-dentinoma
Ameloblastic carcinoma - secondary tumour (dedifferentiated)	Ameloblastic fibro-odontoma
	Odontoma
	- odontoma, complex type
	- odontoma, composite type
Intraosseous	Odontoameloblastoma
Ameloblastic carcinoma - secondary type (dedifferentiated)	Calcifying cystic odontogenic tumour
	Dentinogenic ghost cell tumour
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	Mesenchyme and/ odontogenic ectomesenchyme with or without odontogenic epithelium
Clear cell odontogenic carcinoma	Odontogenic fibroma
Dhost cell odontogenic carcinoma	Odontogenic myxoma/ myxofibroma
	Cementoblastoma
Odontogenic sarcomas	
Ameloblastoma fibrosarcoma	
Ameloblastoma fibro-dentino - fibro-odontosarcoma	Bone-related lesions
	Ossifying fibroma
	Fibrous dysplasia
	osseous dysplasia
<u>BENIGN TUMOURS</u>	
Odontogenic epithelium with mature fibrous stroma without odontogenic ectomesenchyme	Central giant cell granuloma
Ameloblastoma	Cherubism
Ameloblastoma, unicystic type	Aneurysmal bone cyst
Ameloblastoma, extraneous/ peripheral type	Simple bone cyst
Metastatisizing ameloblastoma	
Squamous odontogenic tumour	
Calcifying epithelial odontogenic tumour	Other tumours-
Adenomatoid odontogenic tumour	Melanotic neuroectodermal tumour of infancy
Odontogenic keratocyst	

Fig. 8: Showing WHO 2005 classification in which OKC is included in benign lesion as KCOT and 2017 reclassified as cystic lesion as OKC.

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, extraneous/ peripheral type	
Metastasizing ameloblastoma	
Squamous odontogenic tumour	
Calcifying epithelial odontogenic tumour	
Adenomatoid odontogenic tumour	
Benign mixed epithelial & mesenchyme odontogenic tumours	
Ameloblastic fibroma	
Primordial odontogenic tumour	
Odontoma	
Dentinogenic ghost cell tumour	
Benign mesenchymal odontogenic tumour	
Odontogenic fibroma	
Odontogenic myxoma/ myxofibroma	
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	
Hematolymphoid tumour	
Solitary plasmacytoma of bone	
Odontogenic cysts of inflammatory origins	
Radicular cysts	
Inflammatory collateral cysts	
Odontogenic and non odontogenic developmental cysts	
Dentigerous cyst	
Odontogenic keratocyst	
Lateral periodontal cyst and botryoid odontogenic cysts	
Gingival cyst	
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 fibroma	
Familial Gigantiform cementoma	
Fibrous dysplasia	
Cementosseous dysplasia	
Osteochondroma	

Fig. 9: Showing WHO 2005 classification in which OKC is included in benign lesion as KCOT and 2017 reclassified as cystic lesion as OKC.

loss at 9q22.42,43.¹³ Tumour suppressor gene is inactivated in “2 hit mechanism”. The first hit is a mutation in one allele, which, although it can be dominantly inherited, has no phenotypic effect. The second hit refers to loss of the other allele and is known as “loss of heterozygosity” (LOH). In KCOTs, this leads to the dysregulation of the oncoproteins cyclin D1 and p53. Lench and others¹⁵ indicate that LOH in the 9q22.3-q31 region has been reported for many epithelial tumours, including basal cell carcinomas, squamous cell carcinomas and transitional cell carcinomas; they note that LOH is, “by definition a feature of tumorigenic tissue”.¹⁷

Numerous surgical modalities have been suggested for the treatment of KCOTs, including, enucleation with primary closure, enucleation with open packing, marsupialization, enucleation with use of Carnoy’s solution or cryotherapy, with a marginal or radical section. Although KCOTs are stated to be the most aggressive and recurrent form of tumors, there are cases where KCOTs have been treated by enucleation. In the present case also it has been noted that there has been complete healing following the enucleation with carnoys’s solution procedure. Nevertheless, a long-term follow-up is required to check recurrence.

1. Enucleation - 30%.
2. Enucleation + carnoy’s solution - 9%..
3. Enucleation + peripheral osteotomy - 18%
4. Enucleation + carnoy’ solution + peripheral osteotomy - 8%.
5. Enucleation + cryotherapy - 38%.
6. Marsupialization - 33%.
7. Marsupialization + cystectomy - 13%.
8. Resection - 0%.

Recurrence rates with different treatment modalities (Madras and Lapointe, 2008).^{4,11}

Histological features - Pindborg, phillipsen and Henriksen (Pindborg et al., 1962)¹⁸ suggested series of histological features for the diagnosis of OKC which includes:

1. Stratified squamous epithelium lining which is thin and having wavy appearance – 8-10 layers thick.
2. Lacks of rete ridges/pegs / epithelial extensions.
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 layer which often shows direct transition from basal cell layer (artifactual separation of epithelium from basement membrane) and spinous cell layer intracellular oedema.
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 uninfamed.

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 mineralised and may include cholesterol crystals and Rushton bodies.

The mutiple factors could be responsible for reoccurrence of okc are :

1. After incomplete removal of cystic lining
2. Very 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. Supra-epithelial and Sub-epithelial split of the epithelial lining
8. Parakeratinization of the surface layer
9. Remnants of dental lamina epithelium 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 rest.^{4,8}

Recurrence of OKC/KCOT: Recurrence rate was found to vary from 0% to about 62%, depending on the kind of treatment management and follow-up period.⁸

4. Conclusion

Although we have many diagnostic tools to research articles still OKCs are routinely seen but their diagnosis is as difficult as previously, because of its appearances in both multi and unilocular fashion with occurrence in wide age group to any site and due to varying pattern its difficult to precise it. Its difficult to give exact diagnosis and treat it, as high chances of occurrences is there. So it should be considerate in differential diagnosis of cystic lesion and tumours.

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None.

6. Conflict of Interest

There is no conflict of interest.

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Author biography

Nalini Tomar Senior Lecturer

Kuldeep Singh Bhadauria Consultant Pathologist

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