

Unusual Aggressive Presentation of Orthokeratinized Odontogenic Cyst - A Case Report with Systematic Review of Literature

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A B S T R A C T

Introduction: Odontogenic Keratocyst (OKC) is epithelial cyst or true cyst which is odontogenic in nature and developmental in origin. The OKC has two variants Orthokeratinized Odontogenic Cyst (OOC) and Parakeratinized Odontogenic Cyst (POC). OOC is relatively uncommon and was separated from Keratocystic Odontogenic Tumor (KCOT) by World Health Organization (WHO) in the year 2005 in its classification due to its biological behaviour. The incidence of occurrence is only 0.4% of all odontogenic cysts. It is most commonly seen in posterior mandibular region. Radiographic features of OOC are similar to the dentigerous cyst whereas histological characteristics are almost akin to odontogenic keratocyst. In literature OOC has been described as less aggressive than KCOT.

Case Report: This is a report of an unusual presentation of OOC with extensive growth resulting in the hollowing of complete mandible anteroposteriorly from the left canine involving the ascending ramus upto the condyle, with review of literature.

Conclusion: The considerable differences between OOC and KCOT variants of odontogenic cysts on the basis of clinical as well as histopathological features make them distinguished so as to be accepted as two separate entities to be treated accordingly.

Key words: Orthokeratinized odontogenic cyst (OOC), keratocystic odontogenic tumor (KCOT), Odontogenic Keratocyst (OKC)

INTRODUCTION

The orthokeratinized odontogenic cyst (OOC) is a quite uncommon cyst of developmental odontogenic cyst. It is epithelial in origin and arises from the cell rests of the dental lamina. It comprises about 10% of cases that had been previously called as odontogenic keratocysts (OKCs).¹ Orthokeratinized variant of OKC was first described by Schultz in year 1927² and Wright concluded it as an independent entity in year 1981.³

Until 1998 it was acknowledged by various terms like "orthokeratinized variant of odontogenic keratocyst" or "orthokeratinized cyst of the mandible" but in year 1998 Li et al recommended the new term "orthokeratinized odontogenic cyst," and it is the most accepted terminology so far.² The World Health Organization (WHO) classification for Head and Neck tumors (2017) has designated keratocystic odontogenic tumor (KCOT) as odontogenic keratocyst (OKC) though it has an intrinsic growth potential and propensity to recur and OOC is

designated as a separate entity. Now it is not considered as a continuum of OKC and treated as distinctive entity among jaw cysts. 5.2% to 16.2% which were previously designated as an OKC are now considered as OOC.⁴

CASE REPORT

A 45-year-old male patient presented with pain and swelling on the left cheek region and trismus since one month. Patient's history revealed that the growth was progressive and was not associated with any aggravating or relieving factors. The Past dental and medical history was non contributory. There was no habit history found related to tobacco products and alcohol consumption. Clinically the extraoral swelling was bony hard, firm and diffuses present on left side of the face extending from angle of mouth to ramus of the mandible. Submandibular lymph node were enlarged and tender on palpation. Intraorally buccal cortical plate expansion from 33 to retromolar regions was noted with the overlying mucosa

intact. The orthopantomograph shows an extensive unilocular radiolucent lesion, extending anteroposteriorly from the left canine involving the ascending ramus upto the condyle. Irregular scalloped outlines were seen. Horizontally impacted 38 distal to 37 was also noted which was within the radiolucency. The lesion produced slight mesial tilt of the second molar without any obvious root resorption (figure 1).

Based on the clinical and radiographic assessment, a provisional diagnosis of odontogenic keratocyst given and ameloblastoma was considered in the differential diagnosis. Considering the extensive involvement of the jaw, hemimandibulectomy was performed with reconstruction under general anaesthesia. The resected mandible was submitted to pathology lab for histopathological examination where fixation was done in 10% of neutral buffered formalin.

Gross examination of the hemimandibulectomy specimen with 35, 36, 37, 38 revealed intact buccal cortical plate (figure 2) where as the lingual cortical was perforated superiorly 1cm below the 37 till the lower border of mandible and anteroposteriorly from the mesial of the 37 to 1 cm behind the distal surface of the mandible (figure 3). Histopathological assessment of the Hematoxylin and Eosin (H&E) stained section showed a cystic wall of uneven thickness. Basal layer exhibited low cuboidal epithelium while upper most layer shows plenty of keratin with flecks extending into the lumen (figure 4). Granular layer beneath the keratin exhibited abundant granular cytoplasm in the superficial layers. Basement membrane was straight. Areas of follicular lining noted synchronous with the cystic lining representing associated with unerupted tooth. Connective tissue is highly reactive with plenty of plasma cells and other chronic inflammatory cells. An area of hemorrhages, adipose tissue is noted. Based on the clinical, radiographic and histopathological features, the cyst was diagnosed as orthokeratinized odontogenic cyst.

DISCUSSION

Being similar with KCOT in age of occurrence, site predilection and histochemical profile, OOC is still a different entity in its biologic behavior which makes it significant to discuss separately and elaborately.² It has male predilection, male to female ratio is 2.59:1 which is greater than the reported cases of OKC where male to female ration is 1.42:1 to 1.76:1. OOC mainly occurs in third and fourth decades with mean age of 38.9 years.^{1,2} Site wise OOC has inclination towards mandible as compared to maxilla (90.6%:9.4%) and it is commonly seen in molar and ramus region that means it has affinity for posterior mandible. These tumours are progressive in growth and can reach a considerably larger size. The swelling grows in anteroposterior direction and can cause occasional cortical expansion. Patients



Figure-1: Radiograph showing second molar without any obvious root resorption



Figure-2: Resected hemimandibulectomy specimen about 7cm x 10cm. **Figure-3:** Specimen showing lingual cortical plate perforated and grossed specimen

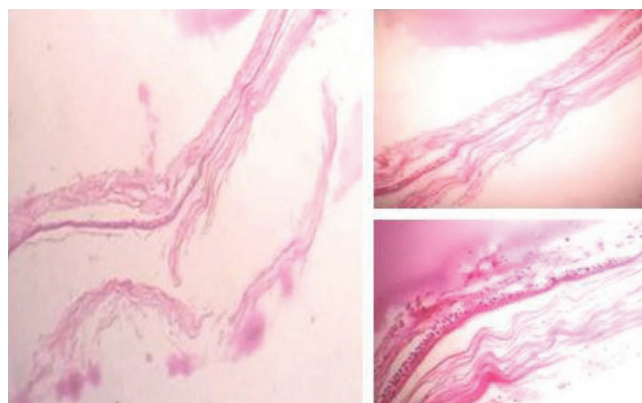


Figure-4: Stratified squamous epithelium lining, lumen shows keratin flecks

are generally asymptomatic and detected incidentally during a radiographic examination.^{2,5} On Radiographic examination the cysts are well-circumscribed, unilocular or multilocular radiolucent lesions frequently associated with an unerupted tooth and sometimes show root resorption and displacement of adjacent tooth till the inferior alveolar canal. On histopathological examination the diagnosis is confirmed as it shows a cystic cavity filled with keratin flakes, lined by thin and uniform stratified squamous epithelium. Granulosum layer showing orthokeratin granules in it and basal layer are having flat cuboidal cells.³

Multiple keratocystic odontogenic tumours are generally associated with Nevoid Basal cell carcinoma syndrome but OOC are not, which is a differentiating point between these two lesions. Surgeons finds enucleation as treatment

of choice for the OOC and recurrence rate is low for this entity.⁶ Bhasin N et al 2014 presented a unique case of OOC occurring in the anterior maxilla, which is an unusual site for OOC.⁷

Some rare forms of OOC have been also described in literature like peripheral Orthokeratinized Odontogenic Cyst, Orthokeratinized Odontogenic Cyst which is histopathologically associated with Calcifying odontogenic cyst or Ameloblastoma or Heterotropic cartilage or Squamous cell carcinoma. Bilateral Orthokeratinized Odontogenic Cysts are also reported in literatures which is relatively uncommon.^{8,9} OKC mostly shows bilateral occurrence followed by dentigerous cyst.⁸⁻¹⁰

Radiographically OOCs are more commonly presented as unilocular radiolucencies (87.0%) in comparison with OKCs which can be unilocular or multilocular (69.4% to 73.3%). The frequency of association of OOCs with an impacted tooth is 60.8% and for typical OKCs is about 7% to 47.8%.¹ The size of OOCs can vary from less than 1 cm to greater than 7 cm.¹¹ Recurrence rate has been reported from 12% to 60% for OKC where as it is less with OOC.¹²

Histopathological Features of OOC is cystic lining composed of thin and uniform stratified squamous epithelium of about 4-9-cell layer thickness. The basal layer depicts low cuboidal or flat cells, with nuclear

hyperchromatism. Suprabasal layer of epithelium shows polyhedral cells and a orthokeratin granules filled superficial layers.³ While OKC presented with a regular stratified epithelium of 5-10-cell layers. Tombstone's shaped basal cell layer with palisaded nucleus. Characteristic superficial corrugated parakeratin layer on superficial layer towards cystic cavity.¹³ Cystic cavity is filled with keratin flakes and sloughed epithelium is often seen from connective tissue (94% of the time).¹⁴ Satellite or daughter cyst is common in keratocystic odontogenic tumor is rare in OOC.¹⁵

Wysocki and Sapp showed that there are distinct ultrastructural differences between the OKC and OOC. The surface morphology of the OCC is more uniform and is entirely covered with a layer of keratin squames. There is an increase in tonofilaments as the cell mature, and the granular cell consist of compact layer of degenerated cells having keratohyaline granules in large amount. The luminal face consists of shreds of orthokeratin.¹³ This reflects that the maturation and proliferation OKC and OOC lining are different and OOC reveals a lower cellular activity than OKC.¹

Etiopathogenesis of OOC is odontogenic cyst epithelial in origin and arises from cell rests of the dental lamina or may arise from oral epithelium. According to Zhu KCOT arise from the dental lamina with dental papilla. Further

Cyst	Incidence (among jaw cyst %)	Bilateral occurrence
Radicular cyst	52.2	*Rare
Dentigerous Cyst	17.1	0.6% (21 cases reported)
Odontogenic Keratocyst	11.6	7%
Orthokeratinized odontogenic cyst	10 of OKC	Rare (4 cases reported)
Nasopalatine Duct cyst	11.2	Rare (2 cases reported)
Paradental cyst	2.7	4%
Solitary bone cyst	1	1/5 th
Calcifying odontogenic cyst/ Calcifying cystic odontogenic tumor.	0.8	Rare (2 cases reported)
Nasolabial cyst	0.6	10%
Glandular odontogenic cyst	0.012-1.3	Rare (1 case reported)

* Excluding radicular cyst of maxillary left and right central incisor post trauma

OOC	OKC
Clinical features Male:Female = 2.59:1 ³ Mandible:Maxilla = 9.17:1 ³	Male:Female = 1.42:1 ¹³ Mandible:Maxilla = 2.08:1 to 4.4:1 ¹³
Radiographic features Unilocular or multilocular radiolucencies: 87% Association with impacted tooth: 60.8% ¹³	Unilocular or multilocular radiolucencies: 69.4% Association with impacted tooth; 7-48% ¹³
Histopathological features Thin uniform orthokeratinized stratified squamous epithelium ³ Prominent granular cell layer Basal cells are flat or cuboidal with less tendency for hyperchromatism Basal cells lack palisading ¹⁶	Superficial corrugated layer of parakeratinized epithelium ³ Lacks a prominent granular layer Basal cells are columnar and hyperchromatic Basal cells exhibit polarization and palisading ¹⁶
Recurrence rate 2.2% ¹³	42.6% ¹³

Comparison between OOC AND OKC

Markers	OKC	OOC	Significance
Cell surface carbohydrates ¹⁷ EMA CEA	Present in the surface parakeratin layer	Absent	Increased aggressiveness of OKC
Cell surface glycoprotein gp38	Present in basal and parabasal layers	Negative	Depicts neoplastic potential of KCOT
Cytokeratin CK 1, 2, 10 CK 4, 13, 17, and 19 ³ CK 10: Early marker of keratin differentiation CK 13: Expressed in dental lamina, enamel organ, non-keratinized stratified squamous epithelium ¹⁸	- Positive In upper and surface parakeratin layers	Positive - All the layers of the epithelium except basal layer.	Suggest a normal differentiation of the epidermis Related to epithelial cell maturation and proliferation. OOC presents a well formed cystic
Proliferative marker Ki-67 ¹⁹ p53 ³ p63 ¹ IPO-38 (monoclonal antibody of IPO (Institute of Problems of Oncology, Kiev) directed against the nuclear antigen of proliferative cells)	Intense expression	Low expression	Higher proliferative potential of OKC
Cell migration and tumor invasion Podoplanin	Intense expression	Low expression	Depict neoplastic potential of OKC ¹⁷
Antiapoptotic marker bcl-2	Present in the basal layer	absent in the basal layer	
Fibronectin	Increased expression	scantily scattered	
Immunohistochemisry			

studies should be carried out as this will explain their common interest for posterior mandible.^{2,12} Management for OOC Surgical enucleation is the treatment of choice. Recurrence rate is low that is 0 and 2% of cases contrast with OKC having 40% rate.³

CONCLUSION

The noteworthy clinicopathologic differences between orthokeratinized and parakeratinized odontogenic cysts make it imperative that the orthokeratinized cyst be recognized as a distinct entity and accordingly treated so.

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