

## A CBCT report & review emphasizing the characteristics of Orthokeratinized odontogenic cyst

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**Abstract:** Orthokeratinized odontogenic cyst (OOC) is a relatively uncommon developmental cyst of the jaw constituting about 10%. Recognition of OOC as a unique entity is of utmost importance as it bears resemblance to dentigerous cyst, and odontogenic keratocyst (OKC). In the past majority of the cases has been coded as either odontogenic keratocyst or keratocystic odontogenic tumor. In the current scenario, it is apparent that OOC is a different entity and its pathologic behavior, clinical outcome and management of OOC is distinct. Here we report a case of OOC in relation to an impacted mandibular canine with a cone beam computed tomography illustration (which showed its pseudo-dentigerous relation) and a review of this entity with an emphasis on its characteristics are highlighted.

**Key words:** Jaw cyst; orthokeratinized; keratocyst; epithelium; cytokeratin.

### I. Introduction

The Orthokeratinized Odontogenic Cyst (OOC) was first described by Schultz as dermoid cyst in 1927. In 1945, Philipsen considered this entity as a variant of odontogenic keratocyst (OKC) and in 1981 Wright separated them as a different entity and specified its clinicopathological aspects. However, till today many consider OOC as just a variant of OKC and disincline to separate them. As it has been documented and established that in addition to OKC, the majority of odontogenic cysts produce orthokeratin and with World Health Organization new classification considering odontogenic keratocyst as keratocystic odontogenic tumour (KCOT) it becomes imperative that OOC had to be separated out from KCOT as a distinct entity.<sup>1</sup> This mandates both the clinicians and pathologists to acquire a thorough knowledge of the differences between the more aggressive KCOT and the less aggressive OOC, so that patients receive the most appropriate treatment. Radiographic analysis advocating three dimensional imaging modalities are of paramount importance as it can assist in diagnosis and analyse the possible histogenesis of OOCs. This report is a case of OOC arising in the mandible and a treatise on its characteristics.

### II. Case report

A 30-year-old male patient presented with a swelling in the left side of the lower jaw of 5 months duration. History revealed that the swelling started as a peanut sized one which gradually increased to attain the present size. There was no history of any associated symptoms. Past dental history and medical history were non-contributory. Extra oral examination revealed a gross facial asymmetry seen on the left lower third of face secondary to a diffuse swelling extending anteroposteriorly from the left symphyseal region to the angle of the mandible, superiorly inferiorly it extended from the angle of mouth to the inferior border of the mandible. On palpation the swelling was firm and non tender. Intra oral examination revealed clinically missing 33 and an oval shaped swelling located over left mandibular vestibular region measuring 4x2 cm extending anteroposteriorly from the mesial aspect of 42 extending to the mesial aspect of 37, superiorly inferiorly it extended from the level of the alveolar crest towards the lower border of the mandible. On palpation, the swelling was non-tender, firm in consistency, pronounced expansion of buccal cortical plate was evident and the overlying mucosa appeared intact (Fig 1). Pulp vitality test done for the teeth in the vicinity of the swelling showed negative response.

Intraoral periapical radiograph and mandibular occlusal radiograph revealed impacted 33 with ill-defined multilocular radiolucency and expansion of the cortices (Fig 2). Orthopantomograph and cone beam computed tomography (CBCT) custom slice images also showed similar illustrations of diffuse osteolysis and contiguous expansion. Transaxial, coronal, sagittal view and three dimensional images of CBCT clearly depicted destructive bicortical expansile areas with a horizontal impacted canine present at the level of apices of premolars (Fig 3, 4 & 5). The margins of the lesion were largely corticated and did not show complete association with the impacted tooth (can be termed as pseudodentigerous relation). The radiolucency at its maximum dimension extended superiorly inferiorly at the level of the alveolar crest towards the lower border of the mandible causing thinning of the cortex at focal areas. Anteroposteriorly it extended from the distal aspect of second molars (37) on the left side to the distal aspect of 43 (Fig 6 & 7). The lesion was surgically enucleated along with the extraction of impacted canine under general anesthesia and submitted for histopathological examination.

The hematoxylin and eosin (H&E) section showed 5-6 layered ribbon like stratified squamous orthokeratinized cystic lining with surface corrugations. The basal layer shows palisading low columnar cells containing hyperchromatic nuclei. Few areas show detachment of cystic lining from the capsule. The underlying connective tissue exhibited radial arrangement of collagen fibres, blood vessels, fibroblasts, blood vessels and mild inflammatory infiltrate. These features were suggestive of orthokeratinized odontogenic cyst (Fig 8).

### III. Discussion

In the past, the orthokeratinized predominated odontogenic cyst has been called with various terms in the literature such as orthokeratinized variant of OKC, jaw cyst with orthokeratinization, orthokeratinized type of odontogenic keratocyst, uncommon odontogenic keratocyst, odontogenic keratocyst - orthokeratinized variant, orthokeratinized cyst of the mandible and orthokeratinized odontogenic cyst.<sup>2</sup> Among them the term "Orthokeratinized Odontogenic cyst (OOC)" suggested by Li et al appears appropriate as it reflects its most probable histogenic origin.<sup>2</sup>

The histogenesis of this OOC is still unclear. Earlier Vuhahule et al had suggested that OOC could be a dentigerous cyst with orthokeratinization or even represent central dermoid or epidermoid cyst as both bear similar histological features. The authors believed that the reduced enamel epithelium after its tooth-forming function under various stimuli could have keratinized to produce a true dentigerous cyst with keratinization.<sup>3</sup> This possibility cannot be completely ruled out as OOC in most instances are found associated with an impacted tooth in a pseudodentigerous relation, thus clinically and radiologically giving an impression of a dentigerous cyst. Similarly, it is generally conceived that as analogous to KCOTs, OOC can have their origin from the epithelial remnants of dental lamina. This is acceptable as both have predilection for posterior mandible, the increased activity of dental lamina and the ability of dental lamina to keratinize in case of KCOTs and keratinisation of the lining epithelium in case of OOCs support this concept. Zhu et al contemplated the above concept and suggested that the OKC arise from the dental lamina with presence of the dental papilla required for its development, on the other hand OOC may arise from oral epithelium under the influence of dental papilla or only the oral epithelium.<sup>4</sup>

The exact incidence of OOC is not consistent either because of the improper identification or conflicting documentation or non-standardization of criterias in the literature. Reports on Clinicopathological studies indicate the incidence of OOC range from 3% to 16.8%.<sup>2</sup> OOC has been reported to occur among young adults, with a male predominance (male- female ratio 2.59:1).<sup>2,5</sup> Although males predominated in many reports, females were found to be predominately affected in the second decade and this may be associated with the menarche.<sup>6</sup> With relation to the jaw, mandible is more commonly affected with a predilection for the posterior region.<sup>5</sup> Incidentally, about 60-75% of OOCs are associated with impacted teeth and few with impacted supernumery tooth.<sup>7</sup> Swelling is the most frequent symptom and can be accompanied with pain. The size of the lesion can vary from less than 1 cm to more than 7 cm in diameter.<sup>2,3</sup> Paresthesia can be a rare sign secondary to irritative phenomena, such as the infection associated with the impacted tooth. Clinical presentation of OOC with regard to age, site of presentation can have resemblance to KCOT, however it is different from it with regard to its biologic behaviour.<sup>1</sup> OOCs are generally solitary asymptomatic lesions, show low local aggressiveness, and are not usually associated with the nevoid basal cell carcinoma syndrome (NBCCS). OOC has no tendency to relapse and the reported frequency is only around 2%, which is in marked contrast with OKC/KOT which has 30% or higher recurrence rate. OOC may be associated with calcifying odontogenic cyst, ameloblastoma, heterotopic cartilage or even squamous cell carcinoma.<sup>1</sup>

Radiographically, majority of the cases appear as unilocular (87%) radiolucent lesions with well defined margins and few as multilocular (13%) as seen in the present case.<sup>5</sup> Occasionally, larger lesions can displace the inferior alveolar nerve and rarely cause root resorption. About two thirds of OOCs are associated with a unerupted or impacted tooth. In the present case left mandibular canine was impacted. Cases where OOC associated impacted tooth (as with the present one) can mimic a dentigerous cyst. In such instances, use of three dimensional imaging modalities such as CT (computed tomography), CBCT (cone beam computed tomography) can provide multiple views in various planes and can play a significant role in assessment of the lesion. In the current scenario, considering the cost and reduction in radiation dose to the patient CBCT is preferred over CT inspite of its inherent shortcomings such as low-contrast resolution and limited capability to visualize the internal soft tissue. Moreover, CBCT is also found to be of great help in localization of pathologies, association of pathology with the surrounding structures, evaluation of the extent of cortical destruction, and in assessing the soft tissue involvement, as similar with CT. The CBCT scan also provide accurate picture of spatial relationships of the impacted tooth with the lesion. In the present case, the CBCT images revealed that the impacted tooth was present closer to the lingual cortical plate at the level of the apices of premolars. The lesion extended beyond the confines of the impacted tooth suggesting a non-dentigerous association.

Histologically, OOC consistent of a fibrous cystic wall with thin, uniform epithelial lining of 4-8 cells layer thick orthokeratinized stratified squamous epithelium. They also show well developed granular cell layer with cuboidal or flattened basal cells which show little tendency to polarize or palisade. Whereas in KCOT the superficial layer is parakeratinized and the basal layer composed of palisaded columnar or cuboidal cells.<sup>1</sup> Also, the parakeratin squames are known to be very sparse in OKCs as compared to the more abundant leafy keratin flakes in OOCs as seen in the present case. Presence of remnants of odontogenic epithelium and dystrophic calcifications have also been noted.<sup>2,8</sup> Several studies have been carried out using specific markers to underline the differences in their origin and pathogenesis between dentigerous cyst, OOC and KCOT. The authors observed that the OOCs showed fully differentiated, mature keratinocytes, while KCOTs lacked them.<sup>3,9</sup> Moreover, OOCs have been found to show a pattern of normal cellular differentiation, while KCOTs showed certain alterations. With regard to the capsular tissue, OOCs seemed to be more stable than the KCOT.<sup>1</sup>

Molecular studies also indicated that KCOT and OOC expressed unique sets of keratin subtypes such as positivity for K1, K10 and Loricrin (LOR) in OOC, suggesting that keratin profile is identical to that of epidermis. On the contrary, K4, K13 and K17 expression was strongly positive in KCOT, which was similar to dental lamina. Thus the study did not

support the origin of OOC in dental lamina, in addition, positive expression of K2 and LOR in OOC indicated that the cells were in a completely differentiated state, and thus not aggressive in its behaviour.<sup>1</sup> The epithelial linings of OOC also differ from KCOT by containing significantly fewer Ki-67–positive proliferating cells confined to the basal cell layer. Studies also demonstrate that p63 expression in OOCs was significantly less intensive in comparison with KCOTs, indicating epithelial cells in OOCs may possess a lower proliferative and self-renewal potential. Others observations include negative antiapoptotic marker bcl-2 in OOC, expression of fibronectin in OKCs and negative activity of the epithelial membrane antigen (EMA) and of the carcinoembryonic antigen (CEA) in OOC. Similarly OOC has to be differentiated from dentigerous cyst as both can be found associated with an impacted tooth.<sup>3,5,10</sup> Literature suggests that CK (cytokeratin )18 and 19, the markers of nonkeratinized epithelium, were found positive in dentigerous cyst and negative in both OOC and KCOT.<sup>1</sup> However, the CK expression alone cannot be considered concrete as many weak/false/ positive expression have been noted for all three entities (DC, OOC, KOT), hence the cell of origin for OOC, still remains elusive.

OOC as an intraosseous counterpart of epidermoid cyst within the jawbone was also considered by many as both the entities bear resemblance clinically and radiographically.<sup>11</sup> This was supported by the fact that since OOC expresses cytokeratins, which are primarily expressed in epidermis, sequestration of the stomodial ectoderm into the developing jaw during embryogenesis is possible. The histopathological features of OOC also overlap with epidermoid cyst and the only differentiation would be absence of skin appendages.<sup>12</sup>

Conservative surgical enucleation is the treatment of choice for OOC as it is less aggressive and has a low recurrence rate.<sup>2, 5, 6, 13</sup> In case of OOC associated with an impacted tooth removal of the entire cystic lining along with the extraction of impacted tooth is the principal treatment modality unless the tooth has a chance of eruption. However, prior to treatment a thorough vigilant sampling of the specimen should be done to rule out presence of areas of parakeratinization and polarization as this can lead the lesion being diagnosed as a KCOT which requires more aggressive treatment approach such as peripheral ostectomy, chemical curettage or block resection.

#### IV. Conclusion

Orthokeratinized odontogenic cyst is an uncommon developmental cyst of the jaw. In the past reports have recognized them as either odontogenic keratocyst/ KCOT and were included in differential diagnosis of the radiolucent lesions of the jaws. With the advent of advanced imaging modalities and molecular studies now it is recognized that OOCs are a distinctive clinicopathological entity. Thus it becomes essential for both the diagnosticians and treating surgeons to have a thorough knowledge of this entity.

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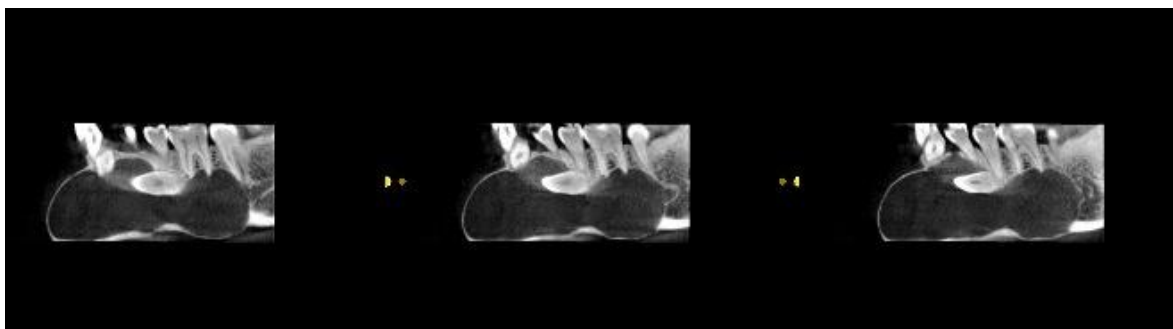
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**Fig 1:** Intraoral photograph showing diffuse swelling obliterating the lower anterior and left vestibular spaces



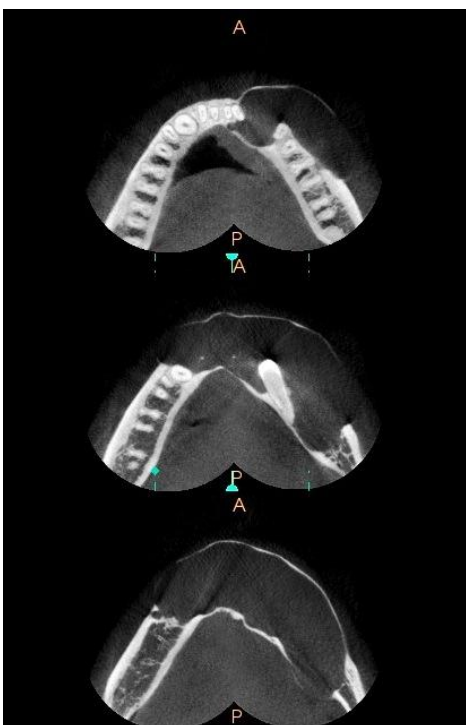
**Fig 2:** Intraoral periapical radiograph showing impacted canine associated with multilocular radiolucencies



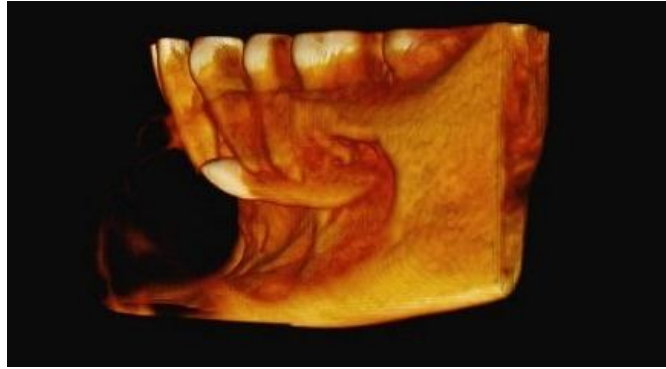
**Fig 3:** Oblique CBCT image showing radiolucency associated with impacted canine at different levels



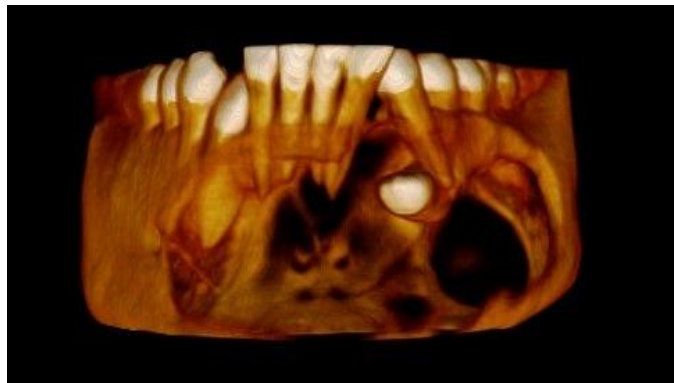
**Fig 4:** Sagittal CBCT image showing radiolucency associated with impacted canine at different levels



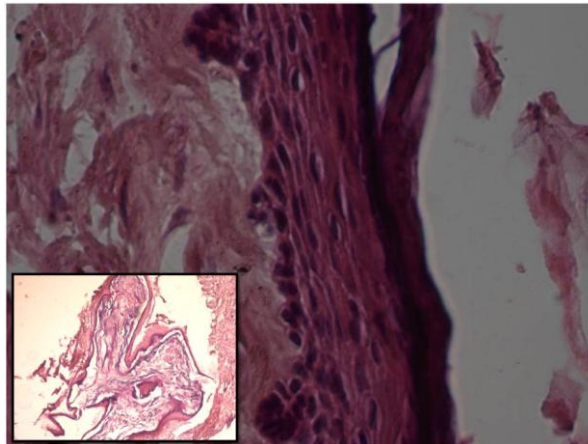
**Fig 5:** Axial CBCT image showing radiolucency associated with impacted canine at different levels



**Fig 6:** CBCT 3D reformatted lateral view showing diffuse osteolysis with impacted canine lying at the apices of premolars



**Fig 7:** CBCT 3D reformatted anterior view showing diffuse osteolysis with displacement of premolars and crown of the impacted canine seen visible at the apices of premolars



**Fig 8:** Photomicrograph (40x) showing epithelial surface corrugations consisting of orthokeratinized layers, prominent granular cell layer and basal columnar cells. Insert showing clumps of keratin filling the entire cystic cavity