Case Report

The concept of dysplasia in the lining of odontogenic keratocyst: A case report and review of the literature

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Abstract

Odontogenic keratocyst (OKC) is an uncommon developmental cyst with a high recurrence rate. Epithelial dysplasia is a rarely recognized phenomenon in OKCs, with only a few acceptable cases reported in the literature. The exact pathogenesis of dysplastic changes in epithelial lining is difficult to explain, in the absence of molecular analyses. Here, we report a rare case of maxillary OKC with multiple cystic compartments displaying epithelial dysplasia in a 62-year-old man with immunohistochemical analyses and a comprehensive review of the literature. It may be prudent to believe that the aggressive behaviour in the epithelial lining of OKC is an inherent property of all OKCs, which is only dictated by the epithelium but is also determined by the stromal cells of the cyst wall; the dysplastic changes, however, could be resultant to chronic inflammatory reaction and inflammation-mediated carcinogenesis mechanism. It is recommended that the dysplastic features in the epithelial lining of all odontogenic cysts must be addressed in all pathology reports along with close clinical follow-up.

Keywords: COX-2, dysplasia, epithelium, inflammation, OKC

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INTRODUCTION

Odontogenic keratocyst (OKC) is a developmental odontogenic cyst that is exclusively seen in gnathic bones and sometimes on the oral soft tissues, particularly the mandibular gingiva.[1] Over the years, there have been changes in the nomenclature, but in the latest edition of the World Health Organization, the term OKC is preferred. Notably, most of the cases show no symptoms, with a growth on the expanse of medullary space in an anteroposterior direction; expansion of the cortical plates usually occurs late during the course of the disease.[2] The association of OKC with nevoid basal cell carcinoma (NBCC/Gorlin) syndrome is well established, where the lesion shows multifocality. The major concern about OKC revolves around the incidence of recurrence and the factors associated, which include the presence of satellite cysts in the wall, weak epithelial–cyst wall junction, juxtaepithelial hyalinization, basal budding, and mitoses.[3] There are reported cases in the literature demonstrating the presence of dysplasia in the epithelial lining of OKC; however, the phenomenon has not been widely explored. Here, we report a case of maxillary OKC with dysplastic epithelial lining in a 62-year-old South Indian man, with multiple cystic compartments; along with a review of the literature.

CASE REPORT

A 62-year-old man was referred from a private clinic with a

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chief complaint swelling in the upper front tooth region of six-month duration. On examination, a soft swelling was noted on the anterior palate in relation to the palatal aspect of maxillary anterior teeth. The lesion was soft, fluctuant, and cystic in consistency; measured around 2.5 × 2 cm in size. There was no associated tenderness or pus discharge. The anterior teeth showed proximal caries and tested negative for vitality. Radiologically, a large unilocular radiolucency was noted in relation to upper anterior teeth extending mesiodistally from the distal aspect of the root stump of 14, to the mesial aspect of 23. Inferiorly it extended to the mid-root level of upper anterior teeth. The upper extent could not be appreciated. The margins of the radiolucency were scalloped and corticated [Figure 1a]. Based on the clinical presentation and radiographic findings, the lesion was provisionally diagnosed as radicular cyst. The cyst was enucleated in toto from the palatal side with root canal treatment of associated teeth [Figure 1b]. On gross examination, the tissue was cystic in architecture with multiple cystic compartments [Figure 1c].

Histologically, the sections showed multiple cystic compartments separated by densely collagenous connective tissue stromal wall. The cystic compartments were lined by parakeratinized stratified squamous epithelium of 6–8 cell layer thickness with flat epithelial connective tissue interface at some areas and appeared hyperplastic with rete peg formation in other areas. There was evidence of juxtaepithelial hyalinization and focal areas of surface corrugation. The basal layer was tall columnar with palisading of nuclei. The epithelium showed features of epithelial dysplasia, such as loss of cohesion, nuclear hyperchromatism, increased nucleo-cytoplasmic ratio, dyskeratosis, and basal budding [Figure 2]. The adjacent cyst wall showed dense lymphoplasmacytic infiltrate. Immunohistochemical analysis demonstrated a high proliferation index (as evidenced by ki-67) with nuclear positivity till the surface of lining epithelium and moderate to strong nuclear p53 expression [Figure 3]. The patient is under close follow-up for the past three months with no fresh complaints.

DISCUSSION

A comprehensive review of the literature was done to analyse the dysplastic changes in the epithelial lining of OKCs. The details of the cases retrieved are shown in Table 1.[1,4-8] Including the present case, eight cases were retrieved with a wide age range from 18 years to 62 years. There was a clear predilection for the mandible, only the present case was noted in the maxilla. All but one case showed unilocular radiolucency. Ki-67 was performed in two cases with a high proliferation index. Additionally, many studies showed basal and suprabasal nuclear positivity for p53, immunohistochemically. Interestingly, in one study, when the included two cases of OKC with dysplasia were amplified by polymerized chain reaction, no variation was detected in the mutated exons of p53. All the cases were managed by excision or resection; two cases were recurrent.

There was a slight ambiguity in the histopathological diagnosis, in particular, regarding the grade of epithelial dysplasia ranging from mild to moderate epithelial dysplasia. It must be noted that the grading of epithelial dysplasia for odontogenic cysts may not be done akin to the grading of oral epithelial dysplasia, where the grading relies on a set of various architectural and cytological features. The grading based on 'thirds' or 'risk stratification into binary system'

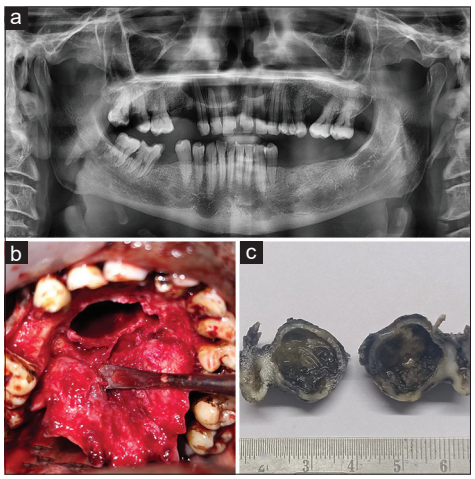

Figure 1: (a) Orthopantomogram showing a large radiolucency in relation to the periapical area of maxillary anterior teeth, with scalloped borders; (b) Intraoperative photograph demonstrating cystic lesion centred towards the palate; and (c) gross image of the specimen showing multiple cystic compartments

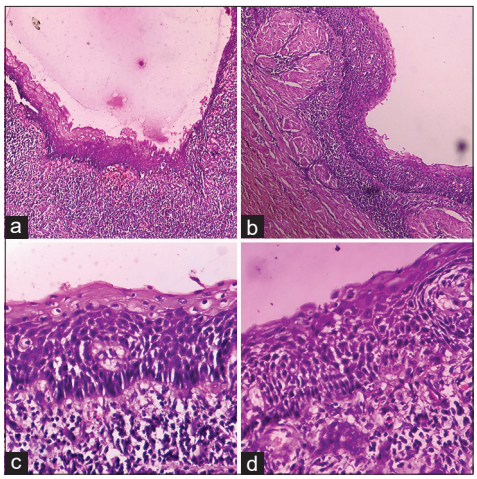

Figure 2: Photomicrographs of the H&E-stained sections showing (a and b) odontogenic cystic lining with dense chronic inflammatory reaction in the adjacent wall (40X), and (c and d) feature of epithelial dysplasia, like nuclear hyperchromatism, basilar hyperplasia, loss of cohesion, and dyskeratosis (400X)

used for dysplasia of oral epithelium cannot be applied to the odontogenic cysts, which in fact show variable thickness and variegated keratinization which tend to alter secondary to the inflammation in the cyst wall.[9] This important feature of chronic inflammation in odontogenic cyst wall deserves special consideration, as unlike oral dysplasia which is either habit-related or secondary to biological factors, the role of biological carcinogenesis is ambiguous in odontogenic lesions. Inflammation-induced damage of DNA and proteins and resultant altered gene expression leads to genetic mutations, which further is linked to malignization in various human cancers. It has been opined that in the absence of chronic inflammation, the malignant transformation of the odontogenic epithelial lining is very low.[10]

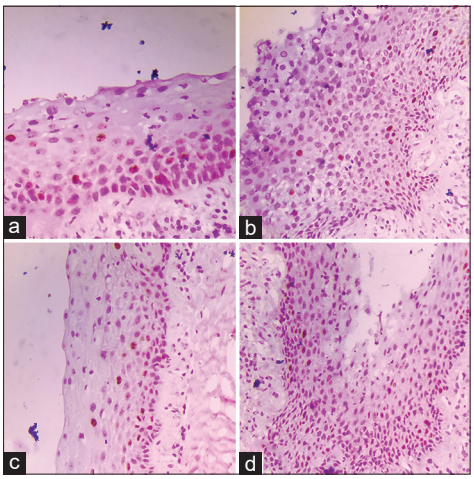

Figure 3: Photomicrographs showing immune expression of ki-67 (a and b) and p53 (c and d)

The role of inflammatory cytokines, chemokines, prostaglandins, and free radicals is established in inflammation-mediated carcinogenesis. Amongst these, COX-2 is widely studied in oral cancer and oral dysplasia.[11,12] Previous studies have found increased expression of COX-2 in the dysplastic epithelium of oral squamous cell carcinoma patients, in contrast to no expression in normal oral mucosa.[12] Additionally, COX-2 inhibitors have been displayed to play a significant role in the regression of oral dysplasia in another study.[13] COX-2 expression has been demonstrated more in OKC and is correlated with increased cell survival and proliferative activity.[14,15] In a recent study, Li *et al.*[16]

Table 1: Clinico-demographic profile of reported cases of odontogenic keratocysts showing dysplastic changes in epithelial lining

Author and year	No of case	Age	Sex	Site	R/G	Diagnosis and features	IHC	Treatment and follow-up
Cox DP, 2012[4]	2	NA	NA	NA	NA	OKC with mild dysplasia	p53: strong basal and suprabasal staining	
Kalele KP, 2015[5]	1	32	F	Left body of the mandible	NA	KCOT with dysplasia; hyperchromatism basilar hyperplasia (satellite cyst noted)	ND	Segmental mandibulectomy (recurrence, six months)
Pandiar *et al.*, 2021[1]	1	51	M	Mandible (37 to 45 region)	U/L R/L with scalloped margins	OKC with moderate dysplasia; nuclear hyperchromatism, basilar hyperplasia, loss of cellular adhesion, loss of stratification, nuclear and cellular pleomorphism	CK14 + p53 strong basal and parabasal ki-67 12–15%	Excision, no recurrence, three months
Thomas *et al.*, 2021[6]	1	45	M	Left body and ramus of the mandible	U/L R/L	OKC with dysplastic features; basilar hyperplasia, loss of polarity, and drop-shaped rete-ridges (satellite cyst noted)	ND	Excision
Likhithaswamy *et al.*, 2023[7]	1	18	M	Symphysis, para-symphysis region		Epithelial dysplasia in OKC; loss of polarity, cellular and nuclear pleomorphism, hyperchromatism, altered N/C ratio, dyskeratosis, and mitotic figures in suprabasal layer (satellite cyst noted)	ND	Excision, no recurrence, three years
Vivekbalamithran *et al.*, 2024[8]	1	47	M	Right ramus of the mandible	M/L R/L	OKC with moderate epithelial dysplasia; hyperchromatism, increased N/C ratio, abnormal superficial mitosis, basilar hyperplasia, and loss of cohesion (satellite cyst noted)	ND	Resection
Present case	1	62	M	Maxilla	U/L R/L	OKC with dysplasia; loss of cohesion, nuclear hyperchromatism, increased nucleo-cytoplasmic ratio, dyskeratosis, and basal budding (multiple cystic compartments)	p53 strong basal and parabasal ki-67 high	Excision, no recurrence, three months

OKC—odontogenic keratocyst, KCOT—keratocystic odontogenic tumour, U/L—unilocular, M/L—multilocular, R/L—radiolucency, M—male, F—female, ND—not done, NA—not available, CK—cytokeratin, IHC—immunohistochemistry

found that dysplastic changes and malignant conversion of epithelial lining of OKCs are positively correlated with chronic inflammation. Another important point worth mentioning here is 'inflammation-metaplasia-dysplasia-carcinoma' sequence.[17] As aforementioned and described in the literature, chronic inflammation could lead to metaplastic changes in the epithelial lining. Kaplan and Hirshberg[18] in their study found metaplasia in 90% of the cases of OKC with inflammation in the cyst wall. Inflammation is known to produce reactive oxygen species (ROS).[19] Pertaining to OKC, inflammation is also seen secondary to incisional biopsy as a part of the healing mechanism. A higher level of proliferative markers in OKC depicts higher cellular activity, comparable to ameloblastoma.[20,21] Irrespective of all, further steps include expansion of the metaplastic clones which progress to dysplasia through increased cell cycle and DNA aneuploidy. The dysplastic epithelium bears a high chance of malignant transformation.

These lesions should be closely followed up as odontogenic cysts with dysplasia bear a higher tendency for frank invasion, resulting in broader bone destruction, demanding wider surgical excision.

CONCLUSION

Thus, we believe that after incisional biopsy for primary diagnosis, the cysts should be immediately enucleated, as the healing process with inflammatory reaction after incision with secondary exposure to oral flora could be the driving mechanism for inflammation-induced dysplastic changes, during the gap period between the incisional biopsy and final enucleation.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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