CASE REPORT

Odontogenic Keratocyst with Diverse Histopathological Features

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Abstract

Introduction: WHO in 2005 included Odontogenic Keratocyst under odontogenic tumors and named it as Keratocystic Odontogenic Tumor because of its aggressive biologic behaviour. But this is not accepted by many researchers and it was removed from the WHO Odontogenic Tumor classification in 2017.

Background: The reported case was radiographically mimicking residual cyst and histopathology confirmed the diagnosis of infected odontogenic keratocyst.

Case Presentation: A 40 year old male patient reported with the chief complaint of broken restoration in relation to upper right back tooth region. Intraoral examination revealed missing mandibular first molar and a mild cortical expansion in the same area. Radiographic diagnosis was given as residual cyst.

Management and prognosis: Surgical enucleation was performed and no recurrence was reported in 3 years of follow up. Odontogenic Keratocyst is usually asymptomatic initially but there is high tendency to recur after treatment. Knowledge of pathogenesis, thorough management and periodic follow up is mandatory.

Conclusion: Histopathological examination is important to differentiate between odontogenic cysts of varying biological behaviour.

Keywords: Odontogenic, Histopathology, Infected OKC, Recurrence

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Introduction

Odontogenic Keratocyst (OKC), introduced by Philipsen in 1956 is a highly debated developmental odontogenic cyst due to its aggressive biological behaviour different from other odontogenic cysts.[1] Its aggressiveness and cardinal histopathological features led to the term "keratocystic odontogenic tumor (KCOT)" and in WHO 2005 classification this entity was included under benign odontogenic tumors of epithelial origin. But many authors stated that evidences are not sufficient enough to consider OKC as a tumor. Following such debates it was removed from 2017 odontogenic tumor classification by WHO and odontogenic keratocyst was reclassified under odontogenic cysts as in 1992 WHO classification of odontogenic cysts.[2,3] But in the new classification KCOT is used as a synonym for OKC.[3]

OKC comprises of 3 to 11% of all jaw cysts.[4] The cyst arises from the rests of dental lamina or basal cell hamartias[5] and is histopathologically characterized by a cystic lumen containing desquamated keratin, lined with a uniform parakeratinised stratified squamous epithelium of 6 to 10 cell layers, palisaded columnar cells in basal cell layer and flat epithelial connective tissue interface.[6] The connective tissue wall usually constitutes satellite cysts and odontogenic epithelial proliferations which indicate the epithelium is genetically prone to increased proliferation.[5] The increased mitotic activity of cyst epithelium and high recurrence rate denotes its aggressiveness.[6]

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Case Presentation

A 40 year old male patient reported with the chief complaint of broken restoration in relation to upper right back tooth region. On intraoral examination lower right back tooth region showed missing 46 which was extracted 20 years back.

The alveolar ridge in the 46 region showed cortical expansion and bony irregularity on palpation. Patient was asymptomatic. IOPA shows a well defined radiolucency with sclerotic border in the 46 region. Provisional diagnosis of residual cyst was given and cyst enucleation was performed. Histopathological examination of enucleated specimen revealed cystic epithelium with underlying connective tissue wall. The cystic lumen showed keratin flakes and the epithelium exhibited corrugated parakeratinization with thickness of 5-8 cell layers, areas of epithelial hyperplasia and epithelial proliferation into the connective tissue. The basal cell layer showed cuboidal and columnar cells with palisading nuclei. Few mitotic figures were appreciated in basal and parabasal layers. The underlying connective tissue exhibited parallel arrangement of collagen fibers, areas of fibrosis, capillaries and intense inflammatory cell infiltration predominantly lymphocytes. Large areas of cholesterol clefts, extravasated RBC's, odontogenic epithelial cell proliferation and satellite cyst formation with keratin in the lumen were also seen. Foci of dystrophic calcifications and rushton bodies were also appreciated in the connective tissue wall. A final diagnosis of infected odontogenic keratocyst was given.

Discussion

Terminology and classification

OKC is a developmental odontogenic cyst with characteristic clinicopathologic features and biologic behaviour. The term Odontogenic Keratocyst was coined in 1956 to designate this entity as it contains keratinized epithelial lining.[7] According to earlier literature; this entity was described by different terminologies such as dental cyst as decribed by John Hunter in 1774, dermoid cyst by Mickulicz in 1876 and primordial cyst by Robinson in 1945. The characteristic clinical and histological features of the cyst were described by Pindborg and Hansen in 1963. In 1967 Toller proposed that odontogenic keratocyst can be considered as a benign cystic neoplasm, considering its aggressive biologic behavior.[8] 2005 WHO classification of head and neck tumor included OKC under odontogenic neoplasms considering its aggressiveness and PTCH gene mutation. Many authors believed that the evidences to classify OKC as a neoplasm are insufficient which led to its reclassification under odontogenic cysts in 2017. According to them OKC regresses completely after decompression which is not so in case of neoplasms.[2] But the term KCOT is carried forward as a synonym of OKC.[3]

Orthokeratinized OKC was referred to as a type of OKC in 1981. In 2017 classification this cyst was accepted as a separate entity as it differs both clinically and histopathologically from parakeratinized OKC. They are not associated with any syndromes and do not have high recurrence rates.[3]

The case reported here is a typical infected Para keratinized OKC with diverse histopathologic features.

Pathogenesis

The cyst arises from remnants of dental lamina rests. Proliferation of basal cells of oral epithelium is also considered in pathogenesis of OKC. Multiple factors that are responsible for cyst expansion could be the following: [1]

- Increased mitotic activity of epithelial lining
- Hyper osmolality of cyst lumen
- Synthesis of Interleukin 1 and 6 by epithelial cells which induces release of parathyroid related protein resulting in bone resorption.

Clinically evident cortical expansion is a late feature of OKC because the cyst predominantly grows in anteroposterior direction along the cancellous bone. Radiographically OKC exhibit unilocular radiolucency with scalloped margins.[7] But the cyst may mimic periapical cyst or residual cyst if present near the periapical region of teeth.[8] It may also simulate ameloblastoma if present in molar-ramus region.[9] Here the radiolucency with sclerotic margin was present near the extracted mandibular first molar region which was in favour of radiographic diagnosis of residual cyst. Radiographic variants of OKC are replacemental type, collateral type, extraneous type and envelopmental type.[8] Generally OKC occur between 10-40 years of age and usually arise in the posterior body

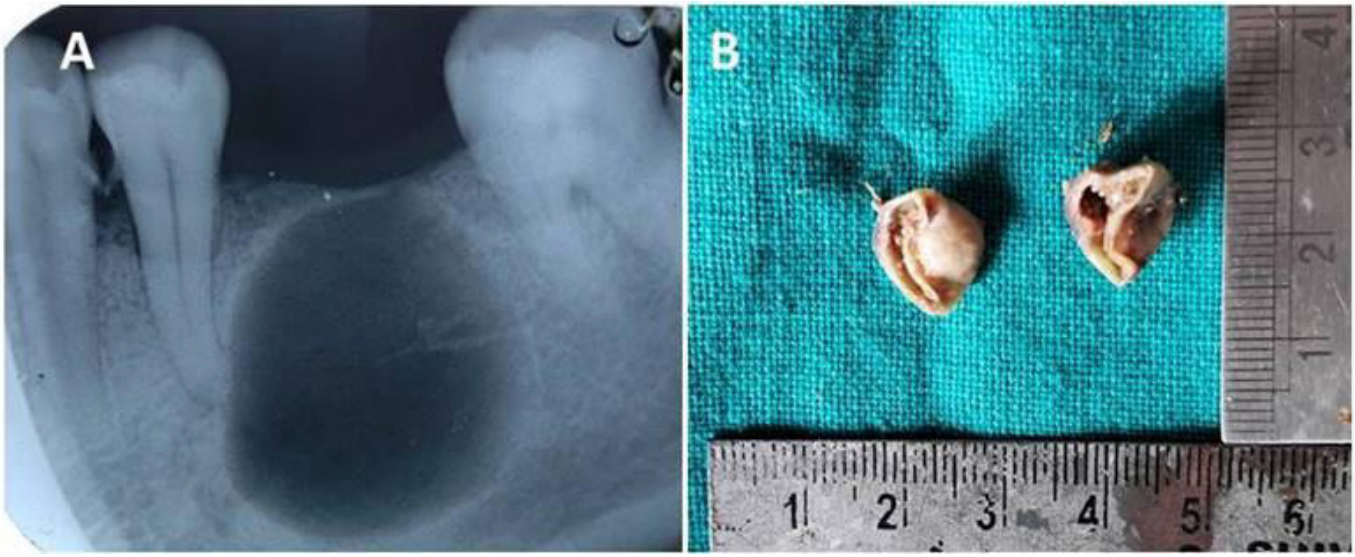

Fig. 1: Radiograph showing well defined radiolucency with sclerotic border in the 46 region **(A)**, Macroscopic cut sections of enucleated cyst specimen **(B)**.

and ascending ramus of mandible. Smaller cysts are usually asymptomatic but larger cysts may be associated with pain and swelling.[4]

Histopathologically OKC is characterized by cystic lumen lined with 6-8 layers of corrugated parakeratinized stratified squamous epithelium of uniform thickness. Lining epithelium is characterized by basal layer of tall columnar cells with palisading arrangement of nuclei and reversal of polarity. The epithelial connective tissue interphase is flat and connective tissue wall may contain odontogenic epithelial islands or satellite cysts.[7] Apart from these classic features there were areas of dystrophic calcification, keratin within the cystic lumen as well as in satellite cysts, basal cell proliferations with mitotic figures and changes induced by inflammation such as epithelial hyperplasia, cholesterol clefts and inflammatory cells in the connective tissue in this reported case.

Focal areas of basal cell proliferations into connective tissue and mitotic figures are indicative of active epithelial proliferation in Odontogenic Keratocyst which are also described as causative factors for their recurrence after treatment. Features like presence of satellite cysts and odontogenic epithelial islands in connective tissue are also responsible for recurrence of OKC.[5]

Inflammation in the connective tissue wall is a feature of 75% of reported cases of OKC. The epithelium turns into hyperplastic type and develop rete ridges which is also appreciated in this case in focal areas. Presence of chronic inflammatory cells, rushton bodies and cholesterol clefts in the connective tissue are also suggestive of histopathological diagnosis of infected OKC. Rushton or hyaline bodies are eosinophilic, straight, curved, rounded or irregular homogenous structures seen in odontogenic cysts which could be of either odontogenic or hematogenous origin.[10] The probable source of infection be the extracted mandibular right first molar in this case. According to literature other sources of inflammation could be probably the communication of cystic lesion with oral mucosa through perforations of cortical plate or via periodontal ligament.[11]

The dystrophic calcification is a rare finding in OKC. Its occurrence may be due to metaplastic transformation or due to calcification of rushton bodies. Biochemically cystic fluid

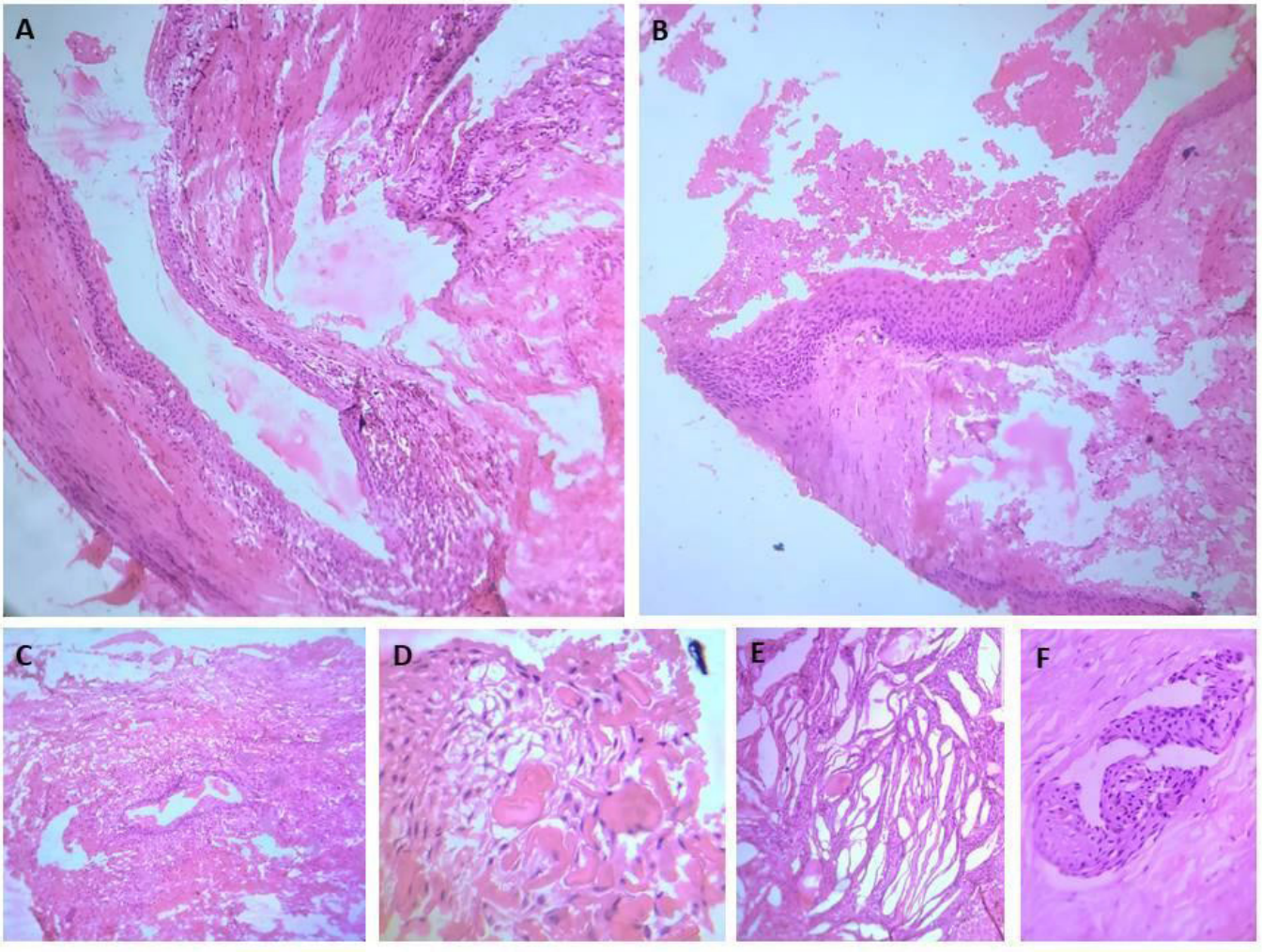

Fig. 2: Photomicrograph showing cystic lumen lined by corrugated parakeratinized stratified squamous epithelium of uniform thickness and underlying connective tissue wall **(A)**, Areas of basal cell layer hyperplasia **(B)**, satellite cyst in the connective tissue wall **(C)**, Rushton bodies **(D)**, cholesterol clefts and dystrophic calcification **(E)**, odontogenic epithelial islands **(F)**.

in OKC usually contain high amount of crystalline calcium phosphates, inorganic phosphates and whitlockite which may also be responsible for calcium deposits in the cystic wall. According to the study by Gardner and Sapp these calcifications can represent dentinoid material. But a true inductive effect in OKC is debated and exact mechanism of calcifications is still unclear.[12]

OKC is usually treated by enucleation of cyst along with removal of overlying mucosa and curettage of underlying bone to prevent recurrence.[5] Treatment with antibiotics prior to surgical enucleation is advised generally in developmetal odontogenic cyst with secondary infection.[13] In this case enucleation was done followed by application of Carnoy's solution. Application of Carnoy's solution, cryotherapy and peripheral ostectomy are usually done to prevent recurrence. 10 years follow up period is recommended to determine any recurrence.[14] The present case is on regular follow up and there is no recurrence reported over a period of 3 years. The following factors are responsible for recurrence.[5]

- Presence of satellite cysts which may remain even after surgical removal of cyst.
- Epithelial lining which is very friable and easily separates from connective tissue wall as there are no rete ridges and there is metalloproteinase mediated degradation of collagen in the juxtaepithelial connective tissue.
- Extension of cyst through cancellous bone as it causes difficulty in determination of surgical margins and removal of cystic lining.
- High mitotic index of cyst epithelium

Conclusion

OKC is a developmental odontogenic cyst and radiographically there exists a diagnostic dilemma, due to its varied radiographic appearance and different sites of occurrence. The infected OKC shows a transition from the characteristic corrugated parakeratinized epithelium to a nonkeratinized epithelium with rete ridges which makes the histopathological diagnosis dubious. Since OKC have high chances of recurrence, it should be diagnosed accurately and treated accordingly.

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