

Recurrent Nonsyndromic Bilateral Keratinizing Cystic Odontogenic Tumor: A Rare Case Report

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ABSTRACT

Odontogenic keratocyst (OKC) is one of the most common cysts of the oral cavity exhibiting aggressive behavior and high rate of recurrence. In 2005, the World Health Organization (WHO) redefined the OKC as a benign tumors of odontogenic origin due to its aggressive biological behavior named it as keratinizing cystic odontogenic tumor (KCOT). Included it in the group of benign odontogenic tumors (OTs) derived from odontogenic epithelium with mature fibrous stroma without odontogenic ectomesenchyme. Keratinizing cystic odontogenic tumor has characteristic microscopic picture, kinetic growth and biological behavior. Multiple KCOTS are common in nevroid basal cell carcinoma syndrome, but sometimes multiples KCOTS are independent of syndrome. Here, we present a case report of 48 years old female patient with bilateral mandibular KCOT which has reoccurred after 10 years.

Keywords: Odontogenic tumor, KCOT, NBCC.

How to cite this article: Reddy PS, Prakash AR, Sreenath G, Kundana I. Recurrent Nonsyndromic Bilateral Keratinizing Cystic Odontogenic Tumor: A Rare Case Report. *Oral Maxillofac Pathol J* 2016;7(1):687-690.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

The odontogenic keratocyst (OKC), first described by Philipsen in 1956,^{1,2,4} which was recently designated by the World Health Organization (WHO) as a keratinizing cystic odontogenic tumor (KCOT) and was defined as 'a cyst arising in the tooth-bearing areas of the jaws or posterior to the mandibular third molar and characterized by a thin fibrous capsule with a lining of keratinized stratified squamous epithelium'.¹ The KCOT is one of the most aggressive odontogenic cysts owing to its relatively high recurrence rate (62.5%) and its tendency

to involve the adjacent tissues with prevalence up to 3 to 11% of all odontogenic cysts.⁶ The lesion can occur at any age group, but peak incidence is in 2nd and 3rd decades of life with male predilection.^{3,4,6} The histologic features of KCOTs include a thin epithelial lining, usually consisting of 4 to 6 layers of cells with surface corrugations, surrounded by fibrous capsule with irregular bundles of collagen and often contain islands of odontogenic epithelium representing daughter cyst which are responsible for recurrence of the lesion.¹

CASE REPORT

A female patient of 48 years presented with a chief complaint of swelling on left side of the jaw and pus discharge in relation to 37. Patient complains that swelling started 1 week back which was gradually increasing in size followed by pus discharge along with dull pain. Extraoral examination revealed facial asymmetry with swelling on left side of the mandible extending anteriorly 3 cm from the ala of the nose, posteriorly up to the angle of the mandible, inferiorly to the base of the mandible and superiorly up to the zygomatic arch (Figs 1 and 2). Intraorally, there was tenderness on percussion in relation to 37. Orthopantomogram (OPG) revealed multilocular radiolucencies in the left mandible; accidentally, a multilocular radiolucency was also evident on the right side (Fig. 3).

On further history, patient revealed that she had swelling, pus discharge and pain on right side of the mandible



Fig. 1: Clinical photograph showing swelling on right angle of the mandible

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10 years back for which she had undergone a surgery and got the teeth extracted. Radiographic examination on left side of the mandible revealed multilocular radiolucency with well defined borders extending from distal root of 37 to ramus and inferiorly extending 2 cm above the base of the mandible (Fig. 4). On right side, well-defined multilocular radiolucency extended from area of 48 to ramus and inferiorly involving base of the mandible (Fig. 5). Based on clinical and radiographic features, differential diagnosis was given as ameloblastoma and KCOT.

An incisional biopsy was performed initially on the left side followed by on right side of the mandible. Histopathological examination of both the lesions revealed a cystic lumen lined by parakeratinized stratified squamous epithelium surrounded by fibrous connective tissue capsule. The epithelium was 4 to 6 layered with surface corrugations and basal layer with hyperchromatic palisaded polarized nuclei. Based on the histopathological features correlating with clinical and radiographic features, final diagnosis was given as keratinizing cystic odontogenic tumor/OKC.

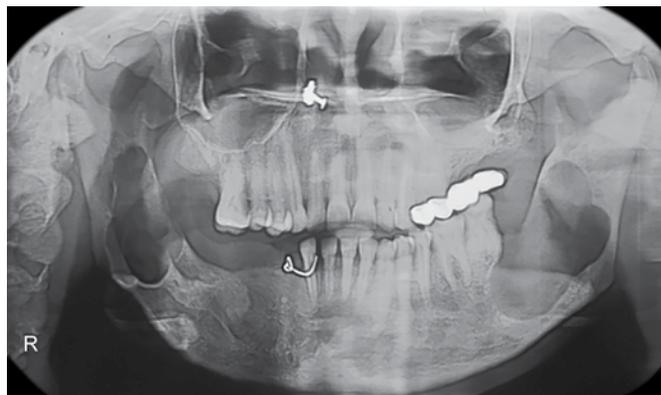


Fig. 2: Orthopantomograph showing multilocular radiolucency on both left and right body, angle of the mandible

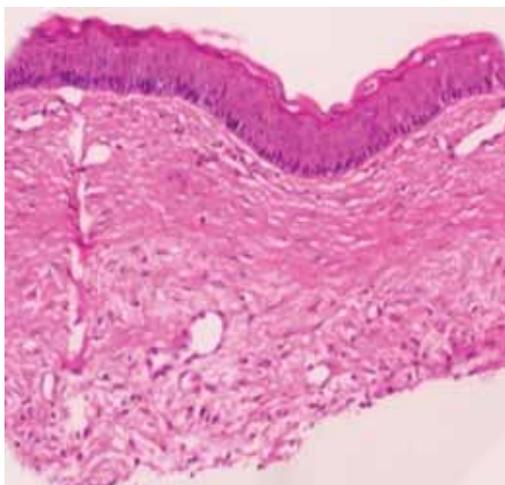


Fig. 3: Hematoxylin and eosin-stained section showing orthokeratinized epithelium with palisaded and polarized arrangement of the basal cell nuclei from the lesion on the right side of the mandible

DISCUSSION

The KCOT has a multicentric and infiltrative growth pattern in anteroposterior direction along with cortical bone penetration and rarely extending into adjacent soft tissues.⁷ Keratinizing cystic odontogenic tumors are aggressive lesions which arise from remnants of dental lamina, cell rests of malassez, basal layer of oral epithelium and hamartomatous odontogenic epithelium.^{4,8} Usually, KCOT occurs as solitary lesions, but multiple KCOTs can be seen in syndromes like nevoid basal cell carcinoma syndrome (NBCCS), orofacial digital syndrome, Marfan's syndrome, Gorlin-Goltz syndrome, Ehlar-Danlous syndrome, Noonan syndrome and Golabi-Behmel syndrome.^{9,10}

Nevoid basal cell carcinoma syndrome is characterized by, multiple odontogenic cysts, nevoid basal cell carcinoma of skin, bifid rob, calcification of flax cerebri, palmar and plantar pits, frontal bossing. Keratinizing cystic odontogenic tumor when associated with NBCCS present along with skeletal, cutaneous, neurologic, ophthalmic abnormalities and sexual abnormalities.^{3,4,5,9} These features of any syndromes are not seen clinically and radiographically in present case.

Nevoid basal cell carcinoma syndrome is associated with the protein patched homolog (PTCH) gene [9q (22.3-q31)]. Mutation with PTCH occurs with sporadic KCOT as well as with those associated with the syndrome. It is suggested that a 'two hit' mechanism may underly the variable expression of syndromic and sporadic OKCs. In this syndrome, the basal cell carcinomas and keratocysts arise as a consequence of a 'first hit' of allelic loss of PTCH within the precursor cell. The development of basal cell carcinoma and keratocysts in the absence of syndrome reflects two somatic hits in which there are mutations

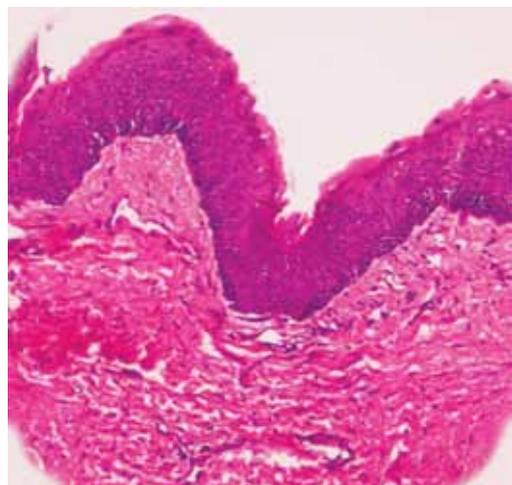


Fig. 4: Hematoxylin and eosin-stained section showing orthokeratinized epithelium with palisaded and polarized arrangement of the basal cell nuclei from the lesion on the left side of the mandible

of PTCH within locally susceptible cells that ultimately result in allelic loss. The absence of all the manifestations of the syndrome may be due to variability of the PTCH gene expression as mentioned by Auluck et al.⁶

Keratinizing cystic odontogenic tumor grows mostly in the anteroposterior dimension and the lesions may attain remarkable size without significantly deforming the jaw skeleton.¹¹ Tendency for rapid growth of KCOT is due to higher activity of the epithelial cells in the cyst lining stimulating osteolytic activity of prostaglandin substances in the cell population of the cyst lining and higher accumulation of hyperkeratotic scales in the lumen of the cyst with resulting greater difference in hydrostatic pressure.^{4,11}

Most common radiographic presentation of KCOT is a unilocular radiolucency with well-defined sclerotic borders. It may also present as a multilocular radiolucent lesion.¹² Histologically, KCOT show the presence of a thin band-like parakeratinized or orthokeratinized stratified squamous epithelium, with a prominent basal layer of columnar or cuboidal cells, and an inflammation-free connective tissue wall.⁴ Histopathological examination in our case revealed parakeratinized stratified squamous epithelium with absence of rete pegs and palisaded basal cell layer, giving an appearance of tombstone or picket fence. The connective tissue revealed dense fibrovascular tissue giving a picture of OKC.

It is conservatively treated by simple enucleation, with or without curettage or marsupialization. Aggressive treatment of keratinizing cystic odontogenic tumor includes curettage with peripheral ostectomy, curettage plus liquid nitrogen cryotherapy curettage plus application of Carnoy's solution, localized *en bloc* resection and occasionally, mandibular segmental resection. Simple enucleation was associated to a higher recurrence rate, while resection and enucleation with bone curettage presented lower recurrence rates.

Keratinizing cystic odontogenic tumor are well known for recurrence. Recurrence rate was found to vary from 0 to 62%, depending on the kind of treatment management and follow-up period. According to literature, cause of high recurrence includes, incomplete removal of the original lesion, remnants of the dental lamina within the jaws, and the presence of 'daughter' or 'satellite' cysts within the epithelial cyst wall. By using Carnoy's solution or cryotherapy can eliminate possible satellite cells.

In the past decade, some conservative surgical approaches (lateral cystectomy, enucleation, cryosurgery, decompression and marsupialization) have been proposed in order to reduce the negative effects of an aggressive surgery and, thus, respecting the delicate anatomical structure of the jaws, giving the patient a better quality of life.

Genetic and molecular research regarding odontogenic tumors and KCOTs, in particular, has led to an

increasing amount of knowledge and understanding of their physiopathological pathways. A review of the biological behavior of this recognized aggressive pathological entity of the jaws and a contemporary outline of the molecular [(growth factors, p53, proliferating cell nuclear antigen (PCNA) and Ki-67, bcl-2)] and genetic [PTCH, Sonic hedgehog (SHH)] alterations associated with this odontogenic neoplasm provides a better understanding of the mechanisms involved in its development and strengthen the current concept that the KCOT should, indeed, be regarded as a neoplasm.¹⁴

Ninomiya et al results show that strong expression of IL-1 α mRNA and protein, mainly detected in the epithelial cells of KCOTs, significantly decreases after marsupialization. The grade of IL-1 α mRNA expression, after the marsupialization, suggesting that marsupialization may reduce the size of KCOT by inhibiting IL-1 α expression and the epithelial cell proliferation. The COX-2 metabolite PGE2 is a potent inducer of IL-10 and IL-1 α , they hypothesize that COX-2 inhibitors lead to antitumor responses by downregulating production of this potent immunosuppressive cytokines.¹⁴

In our present case, we followed a treatment technique of marsupialization bilaterally and patient is under regular follow-up without recurrence from past 12 months.

CONCLUSION

Multiple OKCs may occur without the notable features indicating syndrome and need not be because of gene defect and probably as a result of the multifocal nature of KCOT. Overall, it seems that there are many factors associated with the high recurrence rate, including clinical and radiological appearances together with surgical management. It is the responsibility of the dentist or surgeon to rule out the presence of any associated syndrome and start the adequate treatment as soon as the diagnosis is made. Because of the high rate of recurrences associated with such cases, careful follow-up is mandatory.^{9,10} Marsupialization is usually preferred for conditions like preserving vital structures, very large extending lesions where resection is not indicated and in medically compromised patient.

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