Case Report

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Non Syndromic Multiple Odontogenic Keratocysts In Mandible: A Case Report

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ABSTRACT

Background: In the literature, odontogenic keratocysts are very well recorded. OKCs may occur either as solitary (non-syndromic OKCs) or as multiple OKCs (syndromic OKCs) in two different types. Multiple OKCs usually occur as one of the features in Gorlin–Goltz syndrome. Multiple OKCs, though extremely rare, have been known to occur in non-syndromic situations. We report a rare case of numerous OKCs without associated with any syndromes. We address the probability of the present case being a partial expression of NBCCS and examine briefly the latest trends in the treatment of recurrent OKCs associated with this syndrome.

Keywords: Odontogenic Keratocyst, NBCC Syndrome, Enucleation.

INTRODUCTION

The cystic lesion that usually affects the oral and maxillofacial region is Odontogenic Keratocyst (OKC).[1] The lesions are arising from the dental lamina or its remains and are clinically aggressive lesions with a high risk of recurrence.[2] OKC appears to invade surrounding tissues like the bone.[3] World Health Organization(WHO) classified OKC into two types, Viz. the parakeratinized OKC and orthokeratinized OKC. These two groups were nevertheless listed as separate entities in 2005, mainly due to the differences in their ability to recur. The parakeratinized form was categorized under the branch of odontogenic epithelial tumours as a "Keratocystic odontogenic tumour" (KCOT). The orthokeratinized form has been identified as an orthokeratinized odontogenic cyst (OOC) within the odontogenic developmental cyst entity. KCOTs were reclassified as OKCs again, but are still diagnostically distinctive from OOCs according to the newest WHO classification from 2017. One of the reasons why the word OKC was reintroduced by the WHO was because PTCH1 gene mutations were observed in other developmental cysts and another explanation was that marsupialization is a successful treatment procedure for OKC and may be correlated with the return of the epithelium to normal, with lower recurrence levels which are not characteristic of neoplasms.[4-6]

Multiple OKCs are also associated with nevoid basal cell carcinoma syndrome (NBCCS). Various systems show evidence of abnormal changes in NBCCS comprising of the stomatologic system, skeletal system, ectopic calcification of the central nervous system (CNS), ocular system, genitor-urinary system, mesenteric cysts, skin, genitourinary system and cardiovascular system.[7] This study reports the case of multiple OKCs with no syndromic manifestations.

CASE REPORT

A 35-year-old male patient reported to Ray's Implant and Dental Clinic, Chrompet, Chennai, India, with a chief complaint of pus discharge from the left lower jaw region for the past 6 months. Extra-orally,

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a mild swelling was noticed in the left mandibular region of the face. An orthopantomogram (OPG) showed two radiolucencies, one is unilocular radiolucency, and another one is multilocular radiolucency in the mandible (Figure 1). A well-defined unilocular radiolucency, of about 5 cm × 3 cm, was present in the left ramus of the mandible without involving condylar and coronoid process and a multilocular radiolucency (soap bubble appearance) with an impacted tooth 48, of about 4cm x 3 cm, was present in the right angle and part of ramus region. Outside natural boundaries were clinical signs and symptoms, previous medical history, and hematologic examinations. The chest and skull radiographs were unremarkable and no cutaneous abnormality was detected. A provisional diagnosis of OKC was considered.

Under local anaesthesia, Incisional biopsy was carried out in the left ramus and right angle of the mandible. The specimens were sent for histopathological examination. The histopathological report revealed and confirmed the presence of OKC for our patient

Under general anaesthesia, extended ward's incision was placed in the right ramus region. Cyst enucleation along with the removal of 48, was performed (Figure 2). An extended ward's incision was placed in the left ramus region. Cyst enucleation was performed (Figure 3). With the protection of the inferior alveolar neurovascular bundle, Carnoy's solution was applied on the exposed bony walls of the cystic cavities for 3 minutes and the charring effect was achieved. The cystic cavities were then thoroughly irrigated with normal saline. Plasma rich fibrin (PRF) was placed in the bony defect of the mandible on both sides (Figure 4 & 5) and primary closure done with 3-0 Vicryl. The PRF preparation protocol is straightforward and easy. 10 ml of whole venous blood was obtained in four sterile Vacutainer tubes without the use of anticoagulant for the PRF preparation. The Vacutainer tubes were then centrifuged for 10 min at the speed of 3000 rpm. The resultant product consists of the following three layers: Topmost layer consisting of acellular plasma or platelet-poor plasma, PRF clot in the middle and red blood cells (RBCs) at the base. The middle layer, i.e., PRF clot, is removed and separated from RBC base and placed in the intrabony defects.

The specimens (Figure 6 & 7) were sent for histopathological examination. The patient was discharged with strict postoperative orders that, despite the reduced mandibular osseous substances that could fracture, he would not be involved in any physical sports activity. The patient has been followed up frequently for the past 24 months without any proof of recurrence. With the definitive diagnosis of OKCs in the mandible and the absence of any evidence of NBCCS in clinical evaluations, the determination of OKCs for both cystic lesions was established according to all of these features that were associated with the clinical and radiographic findings.

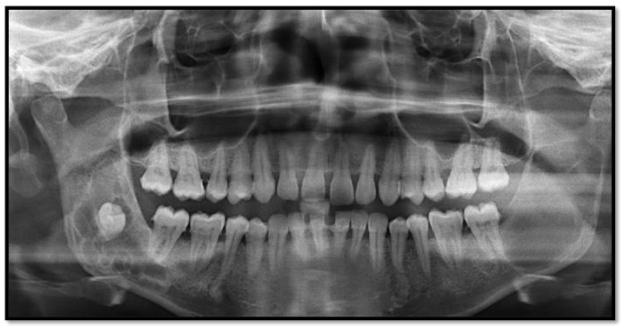

Fig 1: OPG.

Fig 2: After Cyst Enucleation in right ramus of the mandible.

Fig 3: After Cyst Enucleation in left ramus of the mandible.

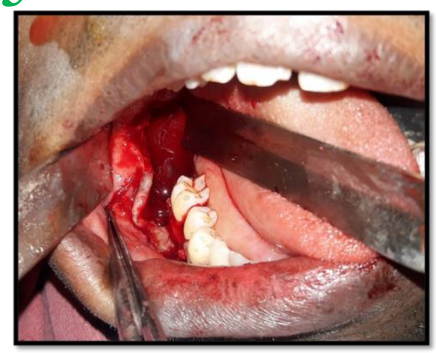

Fig 4: PRF placement – Right Side.

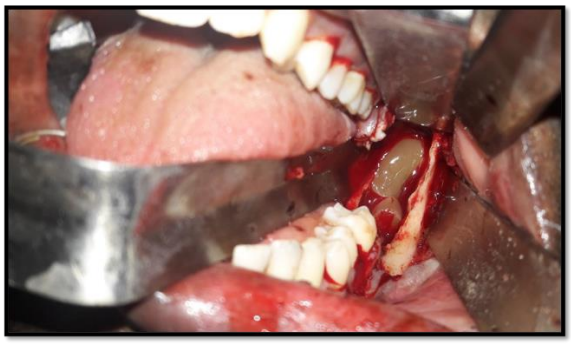

Fig 5: PRF placement – Left side.

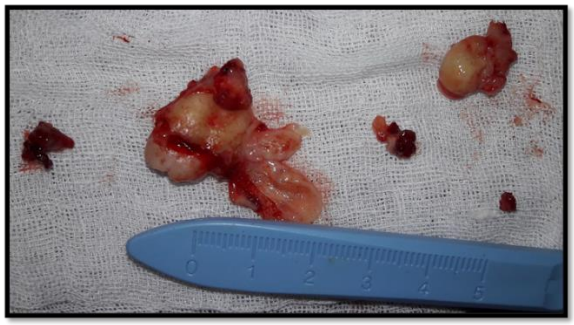

Fig 6: Specimen – Right side.

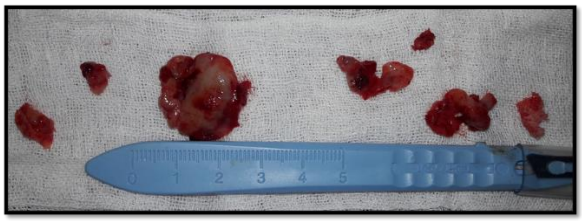

Fig 7: Specimen – Left side.

DISCUSSION

Multiple OKCs tend to occur as a component of NBCCS or Gorlin Goltz syndrome, Digital Orofacial syndrome, Noonan syndrome, Ehler–Danlos syndrome, Simpson Golabi Behmel syndrome, or other syndromes.[8] OKC is the first appearing sign of the Gorlin Goltz syndrome.[9] Without other syndromic manifestations, multiple OKCs are rarely seen. Brannon et al. recorded that of 312 cases of OKCs, 5.8% had numerous cysts without syndromic manifestations.[10,11]

The word multiple cysts do not actually mean that at a given time the patient has to have more than on cyst; instead, it refers to the development of cysts over the patient's lifetime.[12]

Our patient was generally fit and healthy without si gnificant family history and had no suggestive chara cteristics of those syndromes.

Table 1: Differences between solitary OKCs and syndromic OKCs.

FEATURES	SOLITARY OKCs	SYNDROMIC OKCs
AGE	Middle Or Older Aged Individuals	Younger Individuals
CYSTS	Single	Multiple In Number
SITE	Mandibular Posterior Region	Maxillary Posterior Region
RECURRENCE RATE	Lower (61%)	Higher (82%)
ODONTOGENIC ISLANDS	Less	More Frequent
EPITHELIUM	More Thickness	Less Thickness

The biological activity of NBCCS-associated OKCs is more aggressive, and these cysts have higher recurrence levels (82%) relative to single keratocysts (61%)[13]. The higher recurrence rates are due to epithelial remnants of the cystic lining or satellite cysts left behind after the procedure.[14]

The radiographic findings that are more effective in making a provisional OKC diagnosis are[15]

1. A well-defined unilocular osteolytic lesion in the posterior region of jaws
2. A large osteolytic mandibular lesion with few septa and minimal bucco-lingual expansion

OKCs appear, radiographically, as a well-defined unilocular or multilocular radiolucency bounded by a corticated margin. Unilocular lesions predominate and while in about 30% of cases, the multilocular

form is found, most often in the mandible. Mandibular unilocular OKCs can show few and incomplete septa within the lesions on panoramic radiography; this finding is more common in larger than in smaller OKCs.[16,17]

Our patient's OPG showed two radiolucencies, one is unilocular radiolucency, and another one is multilocular radiolucency in the mandible.

Histologically, parakeratinisation, intramural epithelial remnants and satellite cysts are more common in NBCCS-associated OKCs than in solitary keratocysts.[8]

The histopathological study showed that the mucous membrane of both cystic lesions was parakeratinized stratified squamous epithelium, of uniform 6 8 cell thickness. The lining epithelium consisted of well-defined columnar basal cells in a palisade arrangement and with polarized nuclei. The epithelial cells were decreased in height and the number of nuclei they contained. Satellite cysts and epithelial remnants were observed in the connective tissue capsule. It should be noted that the satellite cysts were only contained inside the OKCs capsule. A widespread misconception that the satellite cysts, or so- "daughter cysts," occur within the osseous regions surrounding an OKC persists. No histological studies have proved this. [19] In the epithelial lining, Ki-67 levels were found to be double in syndrome-related OKCs compared to sporadic cysts, suggesting a higher level of the proliferative activity in the former.

The reduced expression of Ki-67 after marsupialization indicates reduced proliferative activity and recurrence potential, and that of BCL-2 indicates the conversion of the classic OKC epithelium to stratified squamous epithelium.[20]

The major differences between OKCs associated with Gorlin–Goltz syndrome and solitary OKCs are listed in Table 1.[13,18] Clinically; the diagnosis is made using criteria suggested by Kimons et al. Our patient did not fulfil any of those NBCCS diagnostic criteria. But given the clinical history and histopathological correlations, we suggest that this case could be a partial expression of NBCCS.

Enucleation, curettage and marsupialization are commonly considered to be the conservative aspects of surgical management in the treatment of OKCs, while resection with or without a continuity defect and disarticulation represent the radical spectrum of surgical treatment. In addition, the term "peripheral ostectomy" was used to describe an adjunctive surgical procedure after enucleation or curettage by abrading the osseous walls of the defect with surgical or acrylic burs to ensure the removal of any residual peripheral neoplastic tissue.

Stoelinga et al. have also suggested an OKC behaviour pattern based treatment plan. He suggested careful cystic enucleation with excision of the overlying mucosa and recommended the application of electrocoagulation / Carnoy's solution in specific areas where the cyst was attached to the soft tissues.[14]

In their systematic analysis of 14 inquiries, Blanas et al. found a recurrence rate of about 17% to 56% when treated with simple enucleation. They also proposed that Carnoy's solution be added to the cystic cavity for 3minutes after enucleation. This reduced the recurrence to 1.6%, which is equivalent to resection, without morbidity.[21]

The use of mechanical and chemical curettage is based on the assumption that recurrence occurs from satellite cysts, cyst wall budding and remnants of cyst epithelium that remain after enucleation.

In our case, we performed cyst enclucation with application of Carnoy's solution and placed plasma rich fibrin (PRF) in defect region on both sides. PRF makes cell migration and proliferation much like a network of fibrins. It is obtained from the processing of blood without anticoagulants. PRF releases other growth factors, such as the growth factor produced from platelets and the transforming growth factor.[22] The use of autologous PRF as surgical adjuvant opens new possibilities for accelerated healing and rapid functional recovery. This is inexpensive and more effective than any other traditional regenerative materials. To authenticate its stimulating effect in bone healing, further clinical trials and histological studies are needed. The use of autologous PRF as an operational adjuvant is a creative, economical method of bone healing.[23]

CONCLUSION

Any patient revealing with the numerous OKCs ought to be assessed completely for the chance of

NBCCS as OKCs might be the sole indication of this syndrome. Likewise, for the way that OKCs related with this disorder have a higher pace of recurrence than the solitary OKCs, an extremely exacting follows up must be followed for an extensive stretch of time. The chance of different highlights of NBCCS must be disclosed to the patient just as his family members, in order to permit proper hereditary advising and sequential screening for the improvement of malignancies and different confusions other than OKCs.

CONFLICTS OF INTEREST

The authors declare they have no potential conflict of interests regarding this article.

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