Nat. Volatiles & Essent. Oils, 2021; 8(5): 651– 655

Recurrence Of Odontogenickeratocysts In Non-Syndromicpatients- A Review

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ABSTRACT

This review article gives a brief information of the odontogenic keratocyst and its nature. It has been a topic of discussion for more than a century now and its prospective

has been changed several times in the past. From being an odontogenic cyst to being classified as a benign tumor okc has seen it all, still there are controversies about its nature. The main reason for it being a topic for discussion can be its aggressive nature which made researchers all around the world doubt its true behavior

KEYWORDS: OKC(odontogenic keratocyst), KCOT(keratocystic odontogenic tumor), Enucleation, Marsupialization, Cryotherapy, Carnoy's solution.

INTRODUCTION

In 2005, World Health Organization (WHO) changed the term "parakeratinized odontogenic keratocyst" to "keratocystic odontogenic tumor" (KCOT). However, WHO consensus group again suggested that there was no sufficient information to support the neoplastic origin of the KCOT and again KCOT was removed from the odontogenic tumor classification and odontogenic keratocyst name for this lesion in the new 4th edition (January 14, 2017) was done[(1)]. These are the benign cyst of odontogenic origin which account for 10% of all the odontogenic cyst. The Age range of odontogenic cyst is from (8 to 82 years).

DISCUSSION

Odontogenic keratocyst (OKC) is an **enigmatic developmental cyst**, which Mikulicz in 1876 described as a part of a very familiar condition affecting the jaws. However, in 1926 it was first known as a "cholesteatoma." Cholesteatoma means a cystic mass of keratin within a living "matrix". OKC was first identified in 1876, Further, the term odontogenic keratocyst was given by Philipsen in 1956. In 1962 Pindborg and Hansen described the characteristics of the cyst. They are one of the most aggressive cysts. Histologically, this cyst arises from the dental lamina and constitute of a cystic space, containing desquamated keratin and uniform rows of parakeratinized epithelium of about 5 to 10 layers. It is usually devoid of any epithelial rete ridges and has a relatively thin fibrous capsule that lacks inflammatory cell infiltrates. The distinctive feature is presence of palisaded arrangement of the basal layer (columnar or cuboidal cells) with the nuclei placed

oriented vertically. Satellite cysts generally arise from the basal layer of the cystic lining[2].

The main features that can be one of the reasons for recurrences in OKC are

- High level of cell proliferation in theepithelium
- Budding in the basal layer of theepithelium
- . Parakeratinization of the surfacelayer
- Supra-epithelial split of the epitheliallining
- Sub-epithelial split of the epitheliallining
- Presence of remnants/cell rests as well as daughtercysts

Due to this histologic feature, the aggressive behavior and the discussion that a large proportion of lesions are associated with a mutation or deactivation of the tumor suppressor gene, also known as the protein patched homolog (PTCH) gene. The PTCH gene has been mapped to the chromosome 9q22.3·q31 and it can probably function as a tumor suppressor.The PTCH1 is the important molecule in a so-called Hedgehog (Hh) signaling pathway. Usually, PTCH forms a receptor
complex with the oncogene SMO ("smoothened") for the SHH ("sonic hedgehog") ligand.

The epithelial lining of OKC/KOT express higher levels of p53 than other cystic types. This overexpression is not because of mutation of p53 gene, but due to overproduction of normal p53 protein. Other genes that can be correlated to OKC are PTCH2 and SUFU. Few authors also demonstrated loss of heterozygosity in p16, MCC, TSLC1, LTAS2, and FHIT genes. This information indeed explains the aggressive behavior of OKC at some level[3,4].

Various treatment modalities have been reported with differing recurrence rates: They are categorized in to two types.

Conservative approach

1. simple enucleation with or without curettage
2. Decompression
3. Marsupialization

Aggressive approach

1. Enucleation with peripheralostectomy
2. Enucleation with Carnoyssolution.
3. Enucleation withcryotherapy
4. Resection (en-bloc or marginal)Enucleation,
5. Enucleation with cryotherapy , marsupialization , decompression and resection .

Approximately half of all keratocysts occur at the angle of the mandible and extend to varying distances in the ascending ramus and move ahead into the body. In many cases, patients are free of symptoms until the cyst reaches a large size and involves the maxillary sinus and the most of the ascending ramus,

including the condylar and coronoid processes. There have been reports of recurrences ranging from 0% to 100%. These differences are identified with the distinctive duration of postoperative follow-up periods, surgical procedures used and if cases are associated with nevoid basal cell carcinoma disorder(NBCCS).

Blanas et al [(1)]have found a recurrence rate of around 17% to 56% when treated by simple enucleation in their systematic review of 14 investigations. They have also suggested that addition of Carnoy's solution to the cystic cavity for 3minutes after enucleation. This reduced the recurrence to 1.6% which is comparable to resection, without associated morbidity.

Stoelinga [(2)] has also proposed a treatment strategy based on the pattern of behavior of OKC. He has suggested careful cystic enucleation with excision of overlying mucosa and recommended electrocoagulation/Carnoy's solution application in selective areas where the cyst was attached to the soft tissues

On the other hand, marsupialization alone as the sole treatment modality for OKC was suggested by Pogrel [(3)] with an average of 2.9 years follow-up. He even found uprighting and eruption of teeth in the cyst. His explanation to this was Immunohistochemistry evidence of higher interleukin-1 alpha levels in OKC that significantly reduced after marsupialization.[(4)] In all his cases, histologic material taken after marsupialization showed normal epithelium with no daughter cysts or

remnants or budding of basal epithelial layer. He found preoperative bcl-2 protein expression strictly limited to basal layer and postoperative bcl-2 negative normal oral mucosa specimen. To the best of authors' knowledge, this rare extensive nature of lesion has been reported only once in the literature by Gupta et al. [(5)] The line of management in our case was influenced by the classic work of Pogrel [(6)] who had demonstrated that marsupialization can be considered as a definitive treatment modality for OKCs.

GENETICAL INVOLVEMENT

The reduced expression of Ki-67 after marsupialization indicates the reduced proliferative activity and potential for recurrence and that of bcl-2 indicates the conversion of the classic OKC epithelium to the stratified squamous epithelium[(9)].

The bcl-2 gene, which is located at chromosome 18q21, is characterized by its ability to abort apoptosis (programmed cell death) without even promoting cell proliferation.[(7,8)] Bcl-2 aborts apoptosis helping in cellular proliferation on the basal and supra-basal layers, whereas apoptosis maintains the homeostasis of the thickness of the lining epithelium and also allows the synthesis of large amounts of keratin in the surface layer of OKCs. Thus, there is a regulatory balance between cell proliferation, cell differentiation, and cell death in such kinds of lesion. This can answer the question as to why OKCs do not transform into tumor masses, instead of having neoplastic behavior with an increased potential to proliferate [(10)].

CONCLUSION

Based on many researches done in the past, recommended treatment modalities to reduce/prevent recurrence of OKC include enucleation, excision of overlying mucosa followed by application of Carnoy's solution, marsupialization /decompression followed by cystectomy, and mandibular resection.

Decompression is similar to marsupialization just there is use of drain to reduce the pressure in cystic cavity. Whereas, resection is a procedure mainly done in patients with multiple instances of recurring cysts

Marsupialization as a potential treatment modality for parakeratinized OKC has received a great deal of attention after the research work of Pogrel.

Therefore, in case of okc a proper histopathology profile, recurrence rates influencing factors being more clear in the present times some principles have to be followed to achieve the best result possible are as follows :

1. Accurate diagnosis
2. Repeating the surgery ifrequired
3. Doing the treatment as conservatively aspossible
4. Using Cryosurgery ifavailable
5. Follow-up of about 5years
6. Use of agents like Carnoy's solution and also at the same time maintaining its exposure to vitalstructures.

OKC being one of the most aggressive cyst requires additional attention when compared to other cysts. The recurrent potential of this cyst is far greater than the rest, which requires precise treatment. Several factors effect this and there should be further more research and randomized clinical trials to improve patients quality of life .

Ethical clearance – Not required since it is a review article
Source of funding – nil
Conflict of interest – nil

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