VARIOUS APPROACHES TO MANAGEMENT OF ODONTOGENIC KERATOCYST (A REVIEW)

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Abstract: The management of odontogenic keratocysts (OKC) remains a hotly debated topic in oral and maxillofacial surgery. Despite numerous studies and systematic reviews on treatment options, there is a lack of consensus and no accepted protocol on the management of OKC. Hence, the aim of this study was to briefly summarize all large systematic reviews in the literature on the management of OKC and formulate an evidence-based management protocol. Decompression followed by enucleation along with adjuvant methods such as application of Carnoy's solution and peripheral ostectomy can result in very low recurrence and is an acceptable first line treatment. The surgical approach should be determined by lesion size, patient age, proximity to vital structures, accessibility, soft tissue/cortical perforation, and if the lesion is recurrent.
Keywords: Odontogenic cyst, Keratocysts, Treatment, Recurrence, Clinical protocols

Introduction: Odontogenic keratocysts (OKCs), first described by Philipsen in 1956 [1], are benign intraosseous lesions of odontogenic origin that account for about 10% of jaw cysts. They are characterised by an aggressive behaviour with a relatively high recurrence rate [2]. Histologically, OKCs arise from the dental lamina and are constituted by a cystic space containing desquamated keratin, lined with a uniform parakeratinised squamous epithelium of 5 to 10 cell layers, with a distinct basal layer of palisaded columnar or cuboidal cells, whose nuclei tend to be vertically oriented. The interface with the adjacent connective tissue is normally flat with a potential for budding of the basal layer and the formation of small satellite cysts [3]. The mitotic activity is higher than other cysts of odontogenic origin [4].Because of this histologic feature, the aggressive behaviour and the fact that a large proportion of lesions are associated with a mutation or inactivation of the tumour suppressor gene, also called the protein patched homolog (PTCH) gene, in the 3rd edition of the World Health Organization (WHO) Classification of Head and Neck Tumours, this pathological entity was included in the group of odontogenic neoplasms with the name of keratocystic odontogenic tumour (KCOT) [5].In the latest (4th) edition of the WHO Classification of Head and Neck Tumours published in January 2017 [6], the consensus group concluded that, at the present time, there is insufficient evidence to support a neoplastic origin of this cystic lesion and that further research is needed [7]. Consequently, the name OKC has been reinserted, replacing the term KCOT that was removed from the classification.

Incidence, Clinical Presentation And Natural History

OKCs represent approximately 10% of odontogenic cysts and the reported age distribution is considerably wide (from 8 to 82 years), with a peak of incidence in the third decade of life [3, 8, 9]. Most series have shown a slight preponderance in males [10].The presence of multiple OKCs, also occurring in different moments during the lifetime of the patients, is typically associated with the nevoid basal cell carcinoma syndrome (NBCCS), also known as Gorlin–Goltz syndrome, an autosomal dominant multisystemic disease. In these patients, the mean age of incidence decreases to about 25 years old [11–13].Similarly to other entities having an odontogenic origin, OKCs originate in tooth-bearing regions. They occur twice as often in the mandible as in the maxilla [14]. When OKCs originate from the mandible, the most common location is the posterior sextant, the angle or the ramus [15, 16]. Conversely, the anterior sextant, mainly between canine and lateral incisor, and the third molar region are the most common sites of origin in the maxilla [17, 18]. Large size lesions are particularly common at the angle and ramus of the mandible [19]. According to the literature, OKCs may be located in a periapical position, in a pericoronal position or in a lateral root position. In about 30% of cases, they have no relationships with any dental structures [10, 17]. In spite of their aggressive behaviour, OKCs, in most cases, cause minimal bone expansion because of their propensity to spread along the intramedullary space "growing in the length of the bone" [20]. Large lesions, causing significant erosion of cortical plates and involvement of surrounding structures, may be seen in asymptomatic patients [21]. Consequently, especially in western countries, the presence of OKCs may be found at a later stage as an incidental finding during routine radiological investigations. A systematic review of the literature published in 2011 by MacDonald-Jankowski showed that patients of East Asian origin may present symptoms early, characterised by swelling and pain, while discharge and numbness of the inferior alveolar nerve are described more frequently in Latin Americans [22]. Unlike other odontogenic lesions having similar aggressive behaviour such as ameloblastomas, OKCs infrequently cause root resorption of adjacent teeth [10].The reported recurrent rate of OKCs after surgery is wide, up to 30%, with most recurrences occurring after conservative treatments of simple lesion's enucleation [2, 19, 23].Higher recurrence rates are reported in patients affected by NBCCS and in multilocular lesions [24, 25]. The recurrences might be explained by different causes: incomplete removal of highly active basal layer of the epithelial cyst lining, growth of small intramedullary satellite cysts left behind by conservative treatment and development of lesions localised in the adjacent region of the jaws [13, 19, 26]. The type of surgery may not be the only factor and some authors suggested that recurrence may be related with the biological nature of the lesion itself and the expression of proliferative markers such as Ki-67 [27, 28].

Imaging Procedures: The radiological imaging techniques most commonly used in the study of OKCs are conventional radiography (mainly panoramic radiography), computed tomography (CT) and magnetic resonance imaging (MRI). These imaging modalities differ significantly in their technical characteristics, acquisition modalities, indications and information provided. Radiographically, OKCs appear as a well-defined unilocular or multilocular radiolucency bounded by corticated margins . Unilocular lesions are predominant, whereas the multilocular variant is observed in approximately 30% of cases, most commonly in the mandible (Fig. (Fig.1b)1b) [9, 29]. On panoramic radiography, mandibular unilocular OKCs may show few and incomplete septa within the lesions; this finding is more common in larger than in smaller OKCs. Approximately 30% of OKCs are associated with at least one unerupted tooth, most commonly the third molars (Fig. (Fig.1a)1a) [9, 29]. This association occurs particularly in younger patients [15].The radiographic features of OKCs are not pathognomonic, particularly in smaller unilocular lesions [15]. When a small unilocular OKC occurs in the anterior sextant of the maxilla, it may simulate other odontogenic and non-odontogenic cysts, such as radicular cyst , lateral periodontal cyst or nasopalatine cyst [17, 30].

Management Approaches :Based on extensive research, recommended treatment modalities for OKC that are known to reduce/prevent recurrence include enucleation, excision of overlying mucosa followed by application of Carnoy's solution, marsupialization/decompression followed by cystectomy, and mandibular resection. However, in our case enucleation had the possibility of pathologic jaw fracture, whereas cystectomy and resection had their own share of morbidity including functional, psychologic, cosmetic, and financial implications. Marsupialization as a potential treatment modality for parakeratinized OKC has received a great deal of attention after the research work of Pogrel [31]

Enucleation has been the most used treatment modality for decades; however, applying this technique without adjuvants contributes to high recurrence rates [36,37]. In a study by Zecha *et al.* on 58 OKC treated by enucleation, 20.7% of cases relapsed after a mean of 46 months of follow-up. Previously, another similar study by Jensen *et al.* [37] showed that 33% of OKC treated by simple enucleation recurred in a period between 17 and 58 months. One of the main reasons that would explain these high recurrence rates could be the incomplete removal of the cyst, due to the well-known difficulties for enucleating and perform the complete removal of the cyst, due to the thinness and friability of its capsule [37]. Other reasons that would explain the recurrences could be the presence of daughter cystic into the adjacent bone or mucosa, or the presence of epithelial islands within the lining mucosa. Although the resective therapeutic modality obtains the lowest recurrence rates , this approach constitutes a severe mutilation . Faced with these two opposite therapeutic approaches, in this clinical case we tried to identify an intermediate treatment that would allow for an acceptable long-term success rate and a relatively low morbidity throughout the implementation of a close clinical control as well as careful radiographic evaluation.

Decompression and enucleation alone were performed as the first-choice treatment, and the use of screw-retained plate to avoid pathological fracture in the residual bone. In the contemporary literature, it was recommended and established that more aggressive treatment have many disadvantages when compared with the clinical results of the conservative approach [38], because the former produced significant morbidity such as facial deformities , loss of bone continuity (maxillary/mandible)

Marsupialization was considered as an appropriate treatment plan, as the lesion was quite extensive. So, bone windows were made by excising mucoperiosteum along with the bone in the left mandibular buccal vestibule and anterior mandibular labial vestibule. Since the extraction socket of mandibular right first molar provided a potential means of irrigation of the cystic cavity, it was enlarged by removal of interradicular bone by means of bone rongeur and rotary instruments with copious saline irrigation. The cystic contents were evacuated, and the cystic cavity was packed with tape gauze soaked (and squeezed) in 2% povidoneiodine for 3 days. This was followed by periodic irrigation and suction of the cystic cavity with 2% povidone-iodine and normal saline (1:1 proportion). The irrigation of the cystic cavity was initially done every alternate day for 15 days, then twice weekly for about 4 months followed by weekly irrigation. Acrylic plugs were prepared to prevent premature closure of the bony defects. Orthopantomograms were taken at regular intervals to monitor the progress. Histopathological examination was carried out from the base of the resolved lesion in the anterior mandibular area.

The pretreatment biopsy specimen and the lesional tissue from the base of the resolved lesions were subjected to immunohistochemical analysis to assess the expression of Ki-67, a proliferative marker, and bcl-2, an antiapoptotic marker (BioGenex reagent and Super Sensitive polymer horseradish peroxidase kit Sigma Aldrich, Germany).

Summary: Odontogenic keratocysts (OKCs) are benign lesions of odontogenic origin accounting for about 10% of all odontogenic cysts and characterised by an aggressive behaviour.

Radiological imaging, mainly computed tomography (CT) and, in selected cases, magnetic resonance imaging (MRI), plays an important role in the diagnosis and management of OKCs. Although radiological imaging does not always provide a specific diagnosis, the knowledge about typical and atypical radiological features of OKCs is essential for their diagnosis and treatment planning. In particular, the combination of clinical and radiological findings is useful in evaluating the extent of the lesions and the relationships with adjacent structures.

The relatively high recurrence rate, especially after conservative surgery, make it necessary to perform a periodic radiographic monitoring of patients with surgically treated OKCs, at least for the first 5 years.

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