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THE ODONTOGENIC KERATOCYST ; EVOLUTION OF TREATMENT MODALITIES AND RECURRENCE RATES

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ABSTRACT

REVIEW ARTICLE

The odontogenic keratocyst (OKC) is considered one of the more aggressive cysts due to its high recurrence rate, expressed histopathologically by a delicate, friable wall containing small satellite cysts which is often difficult to enucleate from the bone in toto. First described by Philipsen in 1956, this particular entity has evoked much discussion and debate in terms of the treatment options and recurrence rates, in literature. Numerous surgical modalities have been practiced including decompression, marsupialization, enucleation with or without adjunct (such as Carnoy's solution or cryotherapy) and resection. Having been classified as a cyst of odontogenic origin for over five decades, the designation changed from a cyst to an odontogenic tumour in 2005, and reversed back to a cyst in 2017. Approximately 11 % of all cysts of the maxillofacial region are comprised of odontogenic keratocysts and it is located most commonly in the mandibular posterior region. This paper aims to review the overall recurrence rate of the OKC in relation to specific treatment methods.

INTRODUCTION:

Odontogenic cysts are relatively common lesions exhibiting varying presentations ranging from a small innocuous lesion, which may be detected incidentally or a highly aggressive and destructive lesion that could eventually transform into a malignancy. Among the latter, the most notorious are Odontogenic Keratocysts (OKC's).

The OKC usually originates from the remnants of the dental lamina of the jaws before odontogenesis is complete although it may also originate from the overlying epithelial basal cells. It was first identified and described in 1876 but was labelled by Philipsen in 1956 as the odontogenic keratocyst[1]. In 1962, Pindborg and Hansen suggested histological criteria in order to diagnose OKC[2].

In recent years, World health organization (WHO) recommended the term cystic neoplasm (referred to as keratocystic odontogenic tumor; KCOT) for this lesion, as a better indication of its combative behavior,

high mitotic rate and association with genetic and chromosomal abnormalities[3,4]. However in the latest WHO classification (2017), the nomenclature reverted back once again to the Odontogenic Keratocyst.

The choice of treatment should take into account various factors, including the age of the patient, size and location of the cyst, soft tissue involvement, history of previous treatment, and the histological variant of the lesion[5,6]. The goal is to choose the treatment modality with minimum risk of recurrence and the least morbidity, while still completely eradicating the lesion. Resection of large multinucleated lesions with cortical bone perforation and soft tissue involvement or lesions that already have recurred after conservative treatment has been advocated. On the other hand, decompression /marsupialisation of large cysts that have not perforated the cortical bone followed by peripheral ostectomy with or without chemical treatment have also been successful[7,8].

DIAGNOSIS

Radiographically, OKCs display a well-defined unilocular or multilocular radiolucency with smooth and frequently corticated margins. OKCs seldom cause bony expansion and tend to grow in an anterior to posterior direction within the medullary cavity of the bone. Root resorption is less common but displacement of teeth adjacent to the cyst occurs more frequently.

Cystic aspiration reveals a dirty white, viscoid suspension of keratin, which has an appearance of pus, but without an objectionable odour. Electrophoresis reveals low protein content (<4g/dL) of the aspirate, which is mostly albumin.

Biopsy reveals histological features of a thin epithelial lining, usually with less than six cell layers in a corrugated tissue composed of thin, irregular bundles of collagen, and often showing daughter cysts or islands of epithelium. In many cysts, there is a tendency for the epithelium to separate from the underlying cyst wall. Histopathologically, they typically show a thin, friable wall, which is often difficult to enucleate from the bone in one piece, and demonstrate small satellite cysts within fibrous wall.

Histologically, two subtypes have been demonstrated; the orthokeratinized and the parakeratinized variant. The parakeratinized variant is found to be more aggressive with a higher recurrence rate.

TREATMENT

The following treatment modalities are proposed for the management of OKC:

Enucleation (with or without adjunct) This refers to surgically shelling the cyst in toto out of the bone to remove the entire lesion without leaving behind any gross remnants. As the lining of the cyst may be friable and thin, removal of the cyst in one piece is cumbersome. Hence, a number of studies suggest that the general treatment of the primary OKC should include enucleation of the cyst, followed by chemical curettage as an adjunctive procedure.

Chemical cauterisation involves a 3-minute application of Carnoy's solution (a tissue fixative)[7,9]. This has the advantage of preserving the adjacent bone, soft tissue, and dental structures, resulting in reduced morbidity and cost of treatment. The general chemical make-up of Carnoy's solution is a ratio of absolute alcohol (6 mL) chloroform (3 mL), glacial acetic acid (1 mL), and ferric chloride (1 g)[10]. The original description on the use of Carnoy's solution was to place it into the cyst cavity before enucleation however; a more commonly employed practice is to apply it to the residual bony cavity after enucleation[11].

Cryotherapy may be used as an alternative to chemical cauterisation after removal of the lesion. A temperature of −20 °C is required to devitalize tissues and only liquid nitrogen can reliably achieve this temperature. Cell death occurs as a result of direct damage from intracellular and extracellular ice crystal formation as well as osmotic and electrolyte disturbances.

According to Schmidt and Pogrel, the initial step in management of the lesion is enucleation of the cyst. The surrounding tissues are then protected with moist gauze,

and the cavity is sprayed with liquid nitrogen twice for 1 min, with a 5-min thaw between freezes[12,13].

Radical enucleation involves removal of the entire cyst lining together along with overlying mucosa, and removal of any residual cystic epithelium through excision of surrounding bone and thorough curettage of the cavity. The procedure can be undertaken using both hand and rotary instruments. This is also known as enucleation with peripheral ostectomy. This treatment option is along the lines of conventional enucleation without the use of adjunctive measures[7,11].

Marsupialization (also known as decompression) is the process of exposing the internal cyst cavity to the oral environment by excising part of the cyst wall to create an opening and suturing the cut edges of the remaining wall to adjacent mucosa[14]. Marsupialization is proposed as a non-destructive and a more physiologically acceptable treatment method with minimal surgical morbidity. The marsupialization technique was described by Pogrel as a window at least 1 cm in diameter in the cyst wall[15]. An attempt is made to suture the cyst lining to the oral mucosa. In the maxilla, the cyst is usually packed open with the packing protruding through the opening. The packing consists of iodoform gauze impregnated with bacitracin ointment. When the pack is removed in the maxilla, the patient needs to irrigate twice a day to prevent food accumulation or closure of the deliberate fistula created. In the mandible, there is a greater tendency for spontaneous closure of the fistula and reformation of the cyst, particularly in the posterior mandible.

Studies have shown that when the OKC is open to the oral cavity by marsupialization, a number of changes occur in the cyst lining[8,15]. Histologically, the lining of OKC is only 5 or 6 cells thick and tears easily on attempted enucleation; which is one of the causes of the high recurrence rate. With decompression or marsupialization, the lining appears to become thicker and easier to enucleate at a later stage (Partsch II procedure).

Resection refers to either segmental resection or marginal resection—mainly undertaken in the mandible[16].The difference between the 2 techniques is that segmental resection results in loss of bone continuity through removal of an entire section of bone, whereas marginal resection maintains the continuity of the mandible, at its posterior or inferior borders.

Researchers have suggested that resection may be the only appropriate therapy in the face of a recurrent lesion. When feasible, a marginal type is the resection of choice. A segmental resection, which creates a substantial gap in the bone, is perhaps the most radical treatment described. Absolute indications for this radical treatment comprise recurrent/extensive lesions, involvement of the condyle, a pathologic fracture, or ameloblastomatous or carcinomatous degeneration within an OKC.

Future modalities Due to the recent advances aiding in the perception of the molecular basis of this entity, a new contemporary method concentrating on its molecular aspects has been devised. SHh (Sonic Hedhehog) inhibitors could serve as attractive antitumor agents as the SHh pathway may be blocked at different levels. It is the abnormal activation of this pathway during tooth formation that leads to defects and tumours. According to literature, cyclopamine, a plant-based steroidal alkaloid, blocks activation of SHh pathway caused by oncogenic mutation. Other studies also show antagonists of SHh signaling factors possibly may effectively treat OKC[17].

RECURRENCE

The incidence of recurrence of OKC reported in literature varies from 2.5% to 62%[2,6].

Brannon in 1976 proposed three possible processes leading to recurrence of the cyst: Incomplete removal of the lining, growth of a new entity in a different region or development of a new lesion from satellite cysts (or remnants after surgery)[4].

Two possible causes for recurrences are hypothesized:

First, epithelial rests from the cyst wall may be left behind. This is particularly the case with larger cysts, which are located in areas with difficult anatomical access. Carnoy's solution supposedly eliminates these cells.

Secondly, clusters of epithelial islands and microcysts are consistently found in the overlying mucosa, attached to the cyst through a bony perforation. It increases the chances of cysts subsequently developing in those regions when these cell islands are not entirely eliminated. This hypothesis is supported by case reports demonstrating recurrent OKCs which arose in bone grafts[14,16,18].

Histopathological features that predict recurrences are :

- Higher level of cell proliferative activity in the epithelium
- Budding in the basal layer of the epithelium
- Parakeratinization of the surface layer
- Supraepithelial split of the epithelial lining
- Subepithelial split of the epithelial lining
- Presence of remnants/cell rests as well as daughter cysts.

Recurrence rates are highest with enucleation alone and range from 9% to 62.5%. Enucleation with Carnoy's solution provides the least recurrence (4.8%) from any of the conservative techniques. According to Blanas et al, enucleation has a recurrence rate of 17% to 56% whereas enucleation with adjuncts has recurrence rates of 1% to 8.7%[19]. In a systematic review of the literature from 1999 to 2010 by enucleation with Carnoy's solution presented a recurrence rate of 7.9% while resection had a recurrence rate of 6.3%[20]. In a systematic review, the authors reported that resection was found to have the lowest recurrence rate (0%) but the highest morbidity rate[19].This was in accordance with Johnson et al who reported a recurrence rate of 1.85% although with maximum suffering for the patient[20].

Pogrel drew a conclusion that decompression and/or marsupialisation has a comparable success rate to other aggressive modalilities, and boasts lower morbidity with preservation of vital structures. The recurrence rate following enucleation and liquid nitrogen cryotherapy has been reported at 3-9%[12,13].

CONCLUSION:

Simple enucleation of the OKC is not advised because of the high recurrence rate. A small OKC where the margins can be accessed may be enucleated with adjunctive measures.

A large, expansive OKC is best treated with a 2-stage approach. Marsupialization first, followed by enucleation and adjunctive measures to decrease the surgical injury to the patient. Marginal or segmental resection offers the lowest recurrence rate. It is not advocated as a primary treatment modality because of its morbidity and the benign nature of the disease. However, it may be considered in certain clinical scenarios, such as multiple recurrences.

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