Controversies in Oral and Maxillofacial Pathology

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KEYWORDS

• Keratocystic odontogenic tumor • Giant cell lesion • Ameloblastoma • Unicystic ameloblastoma • Odontogenic keratocyst • Giant cell granuloma • Benign jaw tumor

KEY POINTS

- Benign aggressive neoplasms of the maxillofacial region, such as the keratocystic odontogenic tumor, giant cell lesion, and ameloblastoma, remain controversial in etiology and treatment.
- Inconsistency in terminology, classification, and treatment protocols contributes to the lack of consensus in ideal treatment.
- The identification of the genetic profile of these neoplasms is making directed medical treatment possible.

INTRODUCTION

Several benign pathologic entities that are commonly encountered by the oral and maxillofacial surgeon remain controversial. From etiology to treatment, little consensus exists in the literature regarding benign lesions such as the keratocystic odontogenic tumor, giant cell lesion, and ameloblastoma.

Despite being seen in everyday practice, benign maxillofacial tumors are underrepresented in the literature. The lesions are rare in the general population and do not represent "public health problems," like cancer or diabetes. The gold standard in the management of these lesions remains a resection with negative margins given the tendency for recurrence. Other less-invasive treatments have been reported, but success rates do not approach marginal or segmental resections. As we enter the genomic era, it is hoped that many of the controversies outlined herein will be solved with directed medical therapy.

Controversies in the diagnosis and management of the benign aggressive lesions are reviewed here with an update on future directions in management.

KERATOCYSTIC ODONTOGENIC TUMOR

Despite being reclassified and named by the World Health Organization (WHO) as a tumor (keratocystic odontogenic tumor [KCOT]) from a cyst (odontogenic keratocyst), this entity remains a mystery.[1] The etiology is thought to be from the residual dental lamina, similar to a primordial cyst,[2] but has also reported to originate from overlying gingiva/mucosa growing into the jaw.[3] The reclassification did not provide much clarity in etiology of the KCOT,[4] but putative molecular markers have been reported.[5,6] Adding to the confusion, clinicians and researchers alike still commonly refer to the lesion as its longstanding moniker "odontogenic keratocyst." despite being over a decade after the WHO report.[7]

Many aspects of the lesion's behavior and molecular makeup supported the concept of the KCOT as a true neoplasm. The lesion has a high recurrence rate after enucleation and can behave aggressively.[8–13] Although most occur within 5 years of treatment, reports exist of recurrences after more than 10 years.[3,14] Mitotic figures are often identified in the cyst wall above the basal layer and the lesion has been associated with

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mutations in the Sonic hedgehog pathway (in isolated lesions in addition to those associated with nevoid basal cell carcinoma syndrome).[14–17]

Management

Management of the KCOT varies immensely, resulting in significant heterogeneity of outcomes studies in the literature. Resection with negative margins has been reported to have recurrence rates approaching 0%.[18–21] Given the benign nature of the disease and morbidity of en bloc resection, less-invasive treatment options have been extensively reported. Resection is still used for cases of extensive disease, aggressive behavior, or exceptional circumstances.[22,23]

Enucleation alone has been problematic. On a macro level, the thin, friable lining, multilocularity, and tendency to be intimately associated with tooth roots makes access difficult and often results in piecemeal removal.[24] The lesion also has the tendency to form "daughter cysts" beyond the main osseous wound not visible to the surgeon after enucleation. On a microscopic level, any remaining neoplastic cells within a daughter cyst or in the overlying mucosa can lead to recurrence.[3]

For the preceding reasons, it is generally agreed on that if treatment is less than en bloc resection, adjunctive measures to enucleation are necessary to avoid recurrence. The type of adjunctive treatment varies immensely in the literature between and even within institutions. The options for adjunctive treatment to enucleation include but are not limited to physical destruction via peripheral ostectomy, cryotherapy, or chemical treatment with Carnoy solution.[25] Another technique used for large lesions is decompression by maintaining an opening from the lesion to the oral cavity. This technique can be carried out via marsupialization or stenting with a drain,[22,26,27] which results in a smaller lesion amenable to enucleation/adjunctive treatment or as definitive treatment.[26,28]

Performing a peripheral ostectomy after enucleation is thought to eliminate remaining neoplastic cells or daughter cysts beyond the lesion's osseous cavity. This technique uses mechanical removal of additional bone (1–2 mm in depth) from the osseous cavity after visible lesion removal. It is typically performed with a carbide bur (round or pineapple shaped). To ensure consistent and complete bone removal, methylene blue can be applied to the cavity. Bone is then removed until the dye is gone.[29] It remains unclear what actually happens to daughter cysts or residual tumor cells in bone when a bur is used. Are cells driven farther into the bone, seeded into soft tissue, or mechanically destroyed? Regardless, this technique has been shown to decrease recurrence.[30]

Enucleation with adjunctive cryotherapy has recurrence rates comparable to other adjunctive treatments.[31] Liquid nitrogen has been used to freeze the residual osseous cavity, resulting in cell death to a depth of 1.5 mm.[32] The disadvantages are the need to carefully protect the surrounding soft tissue and teeth to avoid tissue necrosis. The liquid nitrogen must be dispensed through a metal cannula, so accessing all areas of the lesion while protecting soft tissue can be challenging (**Fig. 1**). In addition, the mandible is significantly weakened and fractures have been reported particularly with thin residual bone.[33] For this reason, it may be prudent to place autogenous bone graft for defects at risk of fracture, limit the patient's diet, or even place into maxillomandibular fixation. Exposure of the inferior alveolar nerve in a osseous cavity after removal is more amenable to cryotherapy. Use of a surgical drill in an around the nerve for ostectomy is challenging. Cryotherapy applied to exposed nerve has been shown to result in paresthesia, but with reasonable recovery of sensation.[34]

Chemical treatment of the osseous cavity after enucleation has been popular, but current use is contentious. Carnoy solution (absolute alcohol, chloroform, ferric chloride, glacial acetic acid) has been extensively reported to reduce recurrence rate over enucleation alone.[35,36] Chloroform has been classified as a carcinogen and banned as a therapeutic agent. Despite this, chloroform has remained in common use among oral and

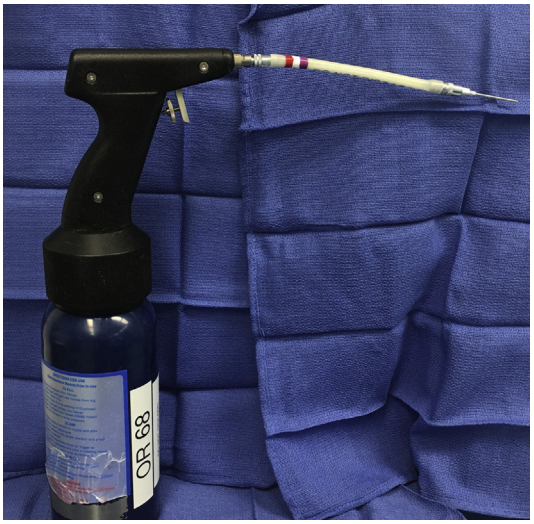

Fig. 1. Liquid nitrogen canister with metal cannula extension.