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Management of Ameloblastoma – An Insight

Dr. Premalatha Shetty[1], Dr. Pritika Srivastava[2*], Dr. Nancy Agarwal[3]
[1]Professor and Associate Dean, Department of Oral and Maxillofacial Surgery, Manipal College of Dental Sciences, Manipal Academy of Higher Education, Mangalore, India
[2,3]Postgraduate, Department of Oral and Maxillofacial Surgery, Manipal College of Dental Sciences, Manipal Academy of Higher Education, Mangalore, India

Review Article

***Corresponding author**
Dr. Pritika Srivastava

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Abstract: Ameloblastoma is the most frequent odontogenic tumor ascending from dental epithelium, and is branded by its histological resemblance to the enamel organ of the developing tooth germ. Although defined as a benign neoplasm, ameloblastomas are locally disparaging and a high recurrence rate is observed if the lesions are not entirely expurgated. Management should be built on precise clinical details, radiographs, special imaging and a illustrative biopsy, followed and reviewed by an oral pathologist and a maxillofacial surgeon. Each case is distinctive and has to be considered in the clinical context and the relationship of the lesion to its surrounding tissues, histological type, and recurrence rate. The present article is a review of the existing literature concerning management of ameloblastoma.
Keywords: Ameloblastoma, odontogenic tumor, unilocular, multilocular, curettage, resection.

INTRODUCTION

Ameloblastoma is a neoplasm of the enamel organ, which recapitulates the cells necessary for tooth crown development. It is often accompanied by the presence of an unerupted tooth. These lesions can occur in both the mandible and maxilla, but 75% of them occur in the ascending ramus of the mandible. When ameloblastomas are present in the maxilla, they have a tendency to spread into the sinus cavities and the floor of the nose, resulting in pain and deformities [1].

Preoperative diagnostic evaluation includes imaging and biopsy. Radiographically, the margins of the lesion in the mandible are usually well-defined, corticated and occasionally scalloped whereas margins in the maxilla are severely ill-defined as the lesion tends to grow along the bone rather than expanding it.

In the multilocular type the bone is replaced by a number of small, well-defined radiolucent areas, giving the whole lesion a honeycomb or soap-bubble appearance as compared to unilocular type where there is a well-defined area of radiolucency that forms a single compartment. If this type is associated with an unerupted tooth, the appearance closely resembles that of a dentigerous cyst or an odontogenic keratocyst[2].

Ueno *et al*. found that among 97 cases of solid/multicystic ameloblastomas, 47% were unilocular and 37% were multilocular; 16% had a soap-bubble or a combination of soap-bubble and multilocular appearance [3].

Treatment

The treatment of ameloblastomas is controversial and management differs among various surgical centers. In general, there are two different approaches – conservative and radical.

For managing an ameloblastoma, the following factors should be considered ¯ age, systemic condition, clinical type of ameloblastoma, anatomic site, size of the lesion, availability of patient for follow up[4].

Compact bone is eroded rather than invaded by tumor. Kramer *et al*. demonstrated that the Haversian system of compact bone at the inferior border of the mandible was not invaded beyond clinical and radiographic margins. Hence, the inferior border should not be resected unless significantly involved to maintain the continuity and since the lateral and medial cortical plates of the mandible are also compact bone, they need to be removed only for surgical access.

Medullary bone is invaded by tumor. Invasion however may not be evident radiographically unless the cortical plate is eroded. Therefore, retrospective studies reporting recurrence following even wide resection could be explained by failure to recognize the true extent of medullary bone invasion between uninvolved

cortical plates. Large fungating lesions involving both soft tissue and bone may, however, require more radical treatment.

Conservative approach

Conservative approach involves enucleation or curettage of the bony cavity. Excisional biopsies are performed for small lesions and once the diagnosis is confirmed the lesion is enucleated and curetted including the surrounding healthy bone[5].

Unilocular or multilocular cystic lesions are usually marsupalized before surgery. Lesions of solid – type tumor with clear margin viewed by means of radiographical examination are usually curetted extensively, and lesions with unclear margins, such as those with a soap – bubble appearance, or those with ineffective marsupialization are subjected to marginal or segmental resection depending on their size and location. When the nerve is exposed in the surgical field, it is lifted out from the bony canal when curetting the bone to avoid damage to the nerve. After the surgical treatment, the patients should be observed clinically and radiographically every year for atleast 5 years[6].

In posterior maxilla, curettage should never be done as it lacks dense cortical plate which acts as a barrier to the tumor's spread in mandible. Ameloblastomas in this site should be treated by marginal or segmental resection whereas in ascending ramus, curettage is advisable as it is in close proximity to the vital structures.

The ameloblastoma grows slowly and curettage would be justified for a small tumor in the body of the mandible in an elderly patient or in a patient whose medical condition precludes more extensive surgery. Advantages of enucleation include the fact that it is an outpatient procedure able to be performed by many different service providers (Oral and Maxillofacial Surgeons and ENT), requiring no reconstruction.

Radical Treatment

It is the current standard of care for ameloblastoma. Treatment options available for mandible are- Marginal mandibulectomy and Segmental resection

Marginal mandibulectomy

It is an excellent alternative to segmental resection for non-oncologic processes such as osteonecrosis, osteomyelitis, or benign tumors that leave at least 10 mm of basilar bone[7]. Also useful for malignant lesions that affect the soft tissues of the alveolus, buccal vestibule or floor of mouth but do not invade into the marrow space of the mandible. However, edentulous patients with an affected atrophic mandible should not undergo marginal mandibulectomy as there could be insufficient remaining basilar bone to withstand the forces of mastication and potentially lead to pathologic fractures [8].

Panoramic radiograph is used for assessing the superior – inferior height of the mandible. When there is extensive bone invasion or a thin atrophic mandible, segmental resection is preferred. Irradiated bone is more susceptible to osteoradionecrosis with an increased likelihood of bony invasion of the disease process and fracture of the residual mandible. So patients with history of radiation therapy should not be selected for marginal resection.

Reciprocating saw with 90- degree angulation to the bone is inserted for the procedure. Osteotomy is made in curvilinear fashion along the predetermined line with copious irrigation. If in conjunction with neck access such as a neck dissection, the transcervical approach can be used for part or all of the osteotomy.

Segmental resection

Segmental resection is indicated in the treatment of benign or malignant mandibular pathology requiring bony margins involving the entire vertical height of the mandible or when a marginal resection would compromise the structural integrity of the mandible. The method is contraindicated in cases of cysts or small tumors that can be adequately treated by marsupialization, enucleation, or marginal resection, thereby preserving the structural integrity of the mandible.

Teeth involved in the proposed resection should be included in the specimen. One tooth on either side of the proposed resection is typically removed to allow for adequate margins and to facilitate the osteotomy. If the dissection is subperiosteally or only a thin layer of tissue is to be included with the resection, the reconstruction plate can be pre-adapted to the mandible with holes for fixation screws drilled. At this point the plate is removed, and the lingual tissues are dissected subperiosteally at the sites of the proposed osteotomy and protected using a broad malleable retractor [9].

Maxillectomy

The primary indication for maxillectomy is ablation of malignant and specific benign diagnoses. Advanced fungal disease such as mucormycosis and aspergillosis, bisphosphonate osteonecrosis, and osteoradionecrosis also require the procedure. Variations of the maxillectomy include the extraoral approach via a Weber-Ferguson incision. Resection margins for locally aggressive benign odontogenic lesions such as ameloblastoma or myxoma traditionally include 1 cm of bone and 1 cm of intact anatomic barrier [10].

This technique is limited primarily due to anatomic features of the individual lesion. Careful preoperative radiographic evaluation in all three planes is required, with particular attention to possible extension beyond the confines of the maxilla in the region of the nasal floor, orbital floor, and posterior maxilla.

With the completion of soft tissue dissection, the planned bone margins are defined. A reciprocating saw is used to create vertical anterior and posterior osteotomies across the alveolus. In the dentate patient, teeth may be extracted at the site of the osteotomies. Preoperative imaging determines the superior extent of the osteotomies. A buccal horizontal osteotomy is then completed to connect the anterior and posterior vertical osteotomies followed by a sagittal palatal osteotomy to connect the vertical osteotomies on the medial resection margin. For lesions extending anteriorly or to the midline, the lateral nasal wall must be osteotomized with a guarded osteotome. The junctions of the osteotomies are then connected with an osteotome or saw.

If the resection includes the tuberosity, the pterygoid plates should be osteotomized last. A broad curved osteotome is placed below the pterygomaxillary fissure and directed in an infero-medial direction. Palpation with the opposite hand in the hamular notch assists in correctly placing and orienting the osteotome.

For more extensive lesions, which involve the orbital floor, a Weber-Ferguson incision is indicated. The Weber-Ferguson surgical approach is indicated for access to maxillary tumors that either extend superiorly toward the orbital floor or involve the orbit or for tumors that extend posteriorly toward the posterior wall of the maxillary antrum. This approach provides a wide access to all areas of the maxilla and orbital floor [11].

Mandibular Recontruction

The fibular free flap is the most popular and has the added advantage of reconstructing long segment mandibular defects. Hidalgo, in 1989, introduced the osteocutaneous fibula free flap for use in mandibular reconstruction when he presented 12 cases of segmental mandibular defects averaging 13.5 cm[12]. Since then, the fibula free flap has become the gold standard for reconstruction of a large variety of mandibular defects due to its consistency in size, vascular pedicle length, vessel diameter as well as the ability to incorporate a reliable skin paddle with the bone flap.

Alternatives to the fibula free flap are also available; including nonvascularized corticocancellous bone grafts, vascularized scapula free flaps, osteocutaneous radial forearm free flaps, as well as the vascularized iliac crest free flap.

Maxillary Reconstruction

From regional soft tissue and bone containing flaps to free flaps with either soft tissue alone or with bone or combinations of soft tissue flaps and alloplastic implants are the options available for reconstruction. The regional soft tissue flaps include temporalis myofacial flaps [13], Facial artery myomucosal flaps (FAMM) [14] buccal pad of fat [15] and reverse submental flaps [16]. Of these, the buccal pad of fat flaps and the FAMM flaps are found to be useful in small and relatively lateral defects. The temporalis flap which served as the workhorse in several initial publications [17] on maxillary reconstructions is still useful and popular but there is a risk of flap dehiscence in larger defects more than 4 cm and immediate or late trismus. The reverse submental artery flap based on the distal facial artery was reported to be successful in a series of 13 cases by Wang *et al. [*18]. The flaps were de-epithelialised and used to cover defects of inferior maxillary defects and allowed to epithelise similarly to the temporalis myofacial flaps. These flaps undergo a phase of inflammation, granulation tissue re-formation followed by epithelisation. But, all these flaps allowing epithelisation could lead to contraction and obliteration of the sulcus, making dental rehabilitation difficult.

Dental implants after reconstruction

Implant placement can be performed simultaneously with the primary reconstruction or delayed as a secondary procedure after healing of the flap and completion of any indicated adjuvant therapy, such as radiation treatment. Investigators have reported successful outcomes with dental implants placed at the time of tumor ablation and reconstruction, as well as with delayed placement of fixtures [19].

Some investigators have also suggested a higher probability for successful integration, if the implants are placed at the time of the initial reconstruction and radiation is delayed for 6 weeks after reconstruction. Despite this hypothesis, Fenlon and collegues [20] compared immediate versus delayed (3 months) placement and found a significant loss of one-third of implants placed in before irradiation. Delayed placement overcomes some of these shortcomings but does lengthen treatment time. An important advantage of delayed placement of implants is the opportunity that it provides the prosthodontist to assess the exact needs for reconstruction and make recommendations for placement. Finally, if the reconstruction is for oncologic reasons, some consideration must be given to prognosis of the patient. It is important to match reconstructive efforts to prognosis, and this is especially true regarding dental implants.

Radiotherapy and chemotherapy

Chemotherapy may occasionally transform post-radiotherapy. Chemotherapy may also have a role in improvement of clinical symptoms in non-surgical patients. Much like radiotherapy, however, only with

continuous reporting of empirical case based data will the role of systemic chemotherapy be evaluable in this rare entity. Furthermore, with advances in the understanding of the molecular pathogenesis of ameloblastoma, targeted agents with fewer systemic side effects may prove more useful than traditional chemotherapeutic regimens.

Adjunctive Treatment

Cryotherapy

Treating ameloblastomas with cryosurgery offers advantages such as the ease of performing the procedure and maintaining a large margin of healthy bone that can be devitalized without a resection surgery, providing aesthetic and functional benefits. Furthermore, the use of liquid nitrogen cryosurgery for treating locally aggressive lesions of the jaw appears to be effective in preventing recurrence. Curi *et al*. [21] performed a study involving 36 patients with solid ameloblastomas of the jaw; they suggested that curettage followed by cryosurgery may decrease the local recurrence rate and also reduce the initial indication of resection with continuity defect.

Chemical fixation

Carnoy's solution, composed of 3 ml of chloroform, 6 ml of absolute ethanol, 1 ml of glacial acetic acid, and 1 g of ferric chloride, is often used as a complementary treatment of lesions with high recurrence rates [22]. Based on the review by Lau *et al*. [23] of treatment of unicystic ameloblastoma, only 16% of all unicystic ameloblastomas recur with enucleation and application of Carnoy's solution, although that review did not differentiate the subtypes of unicystic ameloblastomas. Use of Carnoy's solution may be more effective than enucleation alone for luminal and intraluminal types of unicystic ameloblastoma

Cautery

Mehilisch and coworkers [24] state that cautery if properly applied, increases the effectiveness of other types of therapy. In general, the use of cautery is empirical because of our lack of knowledge as to (1) how far the ameloblastoma in an individual case has infiltrated the surrounding cancellous bone, (2) in some cases how far the caustic agent penetrates into the cancellous bone, and (3) how effective the agent is an eradicating the tumor cells. Moreover, the possible harmful effects to normal tissue have to be considered.

The depth of penetration is known in the case of Carnoy's solution; however it penetrates cancellous bone up to 1.5mm after 5 minutes and up to 1.8mm after 1 hour.

Because unicystic ameloblastomas have such good prognosis after enucleation, the potential value of cautery is more as an adjunct to the treatment of typical intraosseous ameloblastomas(i.e. the solid or multicystic type) after curettage. Although Carnoy's solution is being used for this purpose in some centers, there appears to be no information in the literature concerning its efficiency.

Prognosis and recurrence rate

Prognosis for ameloblastoma depends on the age of the patient, tumor size, extent of disease, location of tumor, and histological type. Recurrence rates are dictated by the adequacy of the surgical margins and extension of maxillary ameloblastoma into vital structures (skull base, orbit, paranasal sinuses)[25]. Maxillary ameloblastoma is more aggressive in terms of disease extent and recurrence, with a common hypothesis for this relative difference being that the relative thinness of maxillary cortical bone provides a weaker barrier for loco-regional spread of tumor. Additionally, recurrence and reoperation may lead to increased risk of surgical complications [26].

Kim and Jang[27] and Escande *et al. [*28] reported an overall recurrence rate of 21.1% and 45%, respectively. Attempts have been made to use various markers to differentiate the types of ameloblastoma and prevent recurrences, although this has not yet yielded encouraging results. At present, the prognosis of recurrence appears to be associated with the surgical planning prior to evaluation of the histological subtype.

Follow-Up Care

Due to the slow-growing nature of the ameloblastoma, many recurrences occur after 5 years, and as long as 30 years after the initial diagnosis. Tumor surveillance in asymptomatic patients should consist of clinical exams and orthopantomograms every 6 months for 1 year, then once per year for a minimum of 10 years. Routine use of computed tomography (CT) scans for monitoring of maxillary ameloblastomas is reasonable, due to anatomic overlap of structures in this region. Due to the potential for late recurrence with all types of ameloblastoma and the importance of long-term and vigorous follow-up, patients unable or unwilling to follow such recommendations may be candidates for initial radical resection, regardless of histologic variant of ameloblastoma, to minimize the risk of recurrence.

Special Considerations for Treatment of the Recurrent Ameloblastoma

As noted, inadequate initial surgical treatment of ameloblastoma yields a high chance of local recurrence. Muller et al reported on 84 patients who underwent a total of 186 procedures for tumor clearance [29]. Many patients required multiple operations, more extensive surgery, and greater difficulty in reconstruction, increased morbidity, and potential for mortality. Also, there was increased chance of malignant change and metastasis. A minimum follow-up period of 10 years is recommended, especially after treatment of a recurrent ameloblastoma. Only 80% of

recurrent ameloblastomas are cured with resection. Table 1 shows appropriate treatment options for different type of lesions.

Table-1: Algorithm showing appropriate treatment options for different lesions

Lesion	Treatment options
Small lesion	Excisional biopsy [5]
Unilocular or multilocular cyst	Marsupilization followed by enucleation or Curettage [5]
Lesions not involving marrow space of the mandible	Marginal mandibulectomy [8]
Lesions involving entire height of mandible	Segmental mandibulectomy [9]
Malignant lesion and fungal diseases of maxilla	Maxillectomy [10]
Extensive lesions involving orbital floor	Maxillectomy with Weber-Ferguson incision [11]
Peripheral ameloblasoma	Conservative approach with supraperiosteal incision [30]
Metastatizing malignant ameloblastoma	chemotherapy and radiation for palliative therapy and an aggressive surgical approach (Radical resection with primary reconstruction of mandibular ameloblastomas) [31]
Ameloblastic carcinoma	Radical surgery with neck dissection [32]

CONCLUSION

- Numerous important aspects ought to be measured in scheduling the treatment of ameloblastoma:
- It is vital to distinguish among the three clinical types of ameloblastoma: the intraosseous solid or multicystic lesion; the well-circumscribed unicystic type; and the rare peripheral (extraosseous) ameloblastoma as they require different forms of treatment.
- Unicystic ameloblastomas extending into the lumen of the cyst or involving only the cystic lining can be removed completely by enucleation, whereas this treatment is inadequate if the tumor has annexed the outer part of the fibrous connective tissue wall of the cyst.
- Ameloblastomas may invade the inter-trabecular spaces of cancellous bone not invading the compact bone but eroding it. This feature has a direct bearing on the treatment.
- Ameloblastomas in the posterior maxilla should be treated more extensively than similar lesions in the mandible because of its proximity to vital structures and the difficulty in treating any recurrences.

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