REVIEW ARTICLE

DIFFERENT TREATMENT MODALITIES FOR THE MANAGEMENT OF AMELOBLASTOMA

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ABSTRACT:
Ameloblastoma is a benign but locally aggressive epithelial odontogenic neoplasm. It represents 1% of all tumours of the jaw bone. In 80% of cases, it is localized in the mandibular molar and ascending ramus area, mostly associated with an unerupted tooth. It occurs over a wide range of ages and with equal frequency in men and women. It can be treated by enucleation, bone curettage or wide resection. The rate of local recurrence is high when it is treated inadequately.
In this article, we are discussing various treatment modalitites protocols for ameloblastoma.
Key words- Ameloblastoma, Bone curettage, Enucleation, Recurrence.

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INTRODUCTION:

Ameloblastoma, from the English word "amel" which means enamel and the Greek word "blastos" which means germ[1], is a rare entity of benign odontogenic tumor. Ameloblastoma is reported to constitute about 1-3% of tumours and cysts of the jaws. The tumour is thought to originate from sources that include residual epithelium from tooth germ; epithelium of odontogenic cysts; stratified squamous epithelium; and epithelium of the enamel organ. The tumour is by far more common in the mandible than in the maxilla and shows predilection for various parts of the mandible in different racial groups.[2] The relative frequency of the mandible to maxilla is reported as varying from 80–20% to 99–1%. Clinically, ameloblastoma appears as an aggressive odontogenic tumour, often asymptomatic and slow growing, with no evidence of swelling. It can sometimes cause symptoms such as swelling, dental malocclusion, pain and paresthesia of the affected area.[2,3] It often presents as a slow growing, painless swelling, causing expansion of the cortical bone, perforation of the lingual and/or buccal plates and infiltration of soft tissue. There is often delay in the diagnosis because of its slow-growing nature.5 Aameloblastoma has a characteristic but not diagnostic radiographic appearance.2 The neoplasm usually appears as a unilocular radiolucent area or a multilocular radiolucent area with a honeycomb appearance.[4] Resorption of the adjacent tooth roots is not uncommon. In many cases an unerupted tooth, most often a mandibular third molar, is associated with the tumour.[4] Treatment of mandibular ameloblastoma continues to be controversial. It can change with clinicoradiologic variant, anatomic location and clinical behaviour of the tumour[5]. Also, the age and the general state of health of the patient are important factors. Treatment consists of wide resection, curettage and enucleation.[6] Rates of recurrence may be as high as 15% to 25% after radical treatment and 75% to 90% after conservative treatment. The aim of this article is to describe conservative treatment of ameloblastoma by

enucleation and bone curettage in cases where the lower border of the mandible is not affected by the tumour[7]. The aim of the present paper is to critically review the pertinent literature and determine the most appropriate method of treatment for ameloblastomas.

TREATMENT

Treatment of ameloblastomas is primarily surgical. There has been some debate regarding the most appropriate method for surgical removal of ameloblastomas. These range from conservative to radical modes of treatment. The conservative modalities include curettage, enucleation and cryosurgery; while the radical modalities are marginal, segmental and composite resections. There is a lack of consensus over the most appropriate treatment modality.[8,9]

SURGERY

Surgery is the standard treatment for ameloblastomas. Historically, the extent of resection has been controversial, comprising of two surgical options: ‘‘conservative’’ vs. ‘‘radical’’. The former involves enucleation/curettage of the bony cavity, while the latter involves a radical operation with appropriate margins.[10]

ADVANTAGES OF ENUCLEATION

1. It is an outpatient procedure able to be performed by many different service providers (Oral Surgeons and ENT), since it requires no reconstruction.
2. Furthermore, benign dentigerous cysts can mimic unicystic ameloblastomas and are cured with simple enucleation. To limit recurrence rates of unicystic ameloblastomas, oral surgeons have extended this procedure to include intra-operative adjuvant treatment of the bony margins with cryotherapy, tissue fixatives such as Carnoy’s solution, drilling and cautery.[11]

LIMITATIONS

1. Simple enucleation demonstrate recurrence rates 60–90 %.
2. It has limited role in the management of multicystic ameloblastomas.

Ueno et al suggested that that ‘excessive resection’ of the mandible constituted excessive treatment, and Feinberg and Steinberg noted that this might be particularly true in young patients, in whom an interruption in growth and development could interfere with future function and aesthetics. Sammartino et al also advocated for conservative treatment of large ameloblastoma due to ‘low morbidity’ associated with these procedures. According to the authors radical treatment is associated with serious cosmetic, functional and aesthetic problems.[12]

The **‘‘radical’’** surgical option is the current standard of care for ameloblastoma and includes en bloc resection with 1–2 cm bone margins and immediate bone reconstruction to help with speech and swallowing.[13] Proponents of radical approach to the treatment of ameloblastomas are of the opinion that, although, these tumours are histologically benign in nature, they are locally aggressive and the clinical behavior may be regarded as lying somewhere between benign and malignant lesions. Enucleation and curettage of ameloblastoma result in unacceptable recurrence rates. The recurrence rates of 55% to 90% for solid or multicystic lesions treated by enucleation or curettage have been reported. Metastases following conservative management have also been reported.[14]

The cost-benefit analysis of the conservative management is another topical issue. Treatment of large ameloblastoma with less than radical approach, only to wait for recurrence before radical treatment is instituted is expensive in terms of cost to the patient and extensive follow-up required.[15] It has been reported that the recurrence of an ameloblastoma in large part reflects the inadequacy or failure of the primary surgical procedure. Satkin and Hoffmeister in looking at early data from 1918 onward showed that continued under-treatment of ameloblastoma can lead to extensive and at that time unresectable recurrences. They reported a mortality of 30% from recurrent ameloblastoma in an early series of 13 cases.[16]

Chidzonga stated that the recommended treatment for ameloblastoma in children should be radical resection 0.5 to 1 cm past what appears to be normal bone. Radical treatment was also the method of choice employed by Arotiba et al.[17,18] Other studies have also shown that when a diagnosis of ameloblastoma is made, the treatment must be aggressive and radical. For solid-multicystic ameloblastoma of the mandible, a resection of the jaw should be approximately 1.5–2 cm beyond the radiological limit, in order to ensure that all the ‘microcysts’ and ‘daughter cysts’ are removed.[19]

Table 1: Reported recurrence rates by type of surgical treatment

Treatment	Patients (n)	Recurrence (%)	Reference
Conservative surgery	43	93	
Radical surgery	38	13	Sehdev et al[20]
Conservative surgery	13	86	
Radical surgery	7	14	Shatkin et al[21]
Conservative surgery	96	73	
Radical surgery	26	21	Mehlisch et al[22]
Conservative surgery	68	46	
Radical surgery	23	9	Uneno et al[23]
Conservative surgery	42	33	
Radical surgery	36	7	Nakamura et al[24]

RADIOTHERAPY

Earlier it was considered that Ameloblastomas are radio resistant. Although several studies have reported on adjuvant radiation for positive margins (gross and microscopic) and for recurrent and unresectable ameloblastomas, the outcomes are poor. As these patients are often young, the possible efficacy of radiotherapy must be weighed against the risk for future radiation-induced malignancies and other long term sequelae of radiation therapy. More work is needed to validate this treatment option. Despite these experiences, some studies advocate for adjuvant radiation in ameloblastic carcinoma, though the data are mixed. Complicating matters, there is no animal model of ameloblastoma, making it difficult to determine the biological effects of radiotherapy on ameloblastoma.[19,20]

There are relatively few data pertaining to the efficacy of RT. Robinson reported one of the first series, in which 18 patients were treated with RT alone; 13 patients (72%) developed a local recurrence. RT consisted of orthovoltage external beam RT, radium needles, or radon seeds.1 Sehdev et al reported on 11 patients treated at the Memorial Sloan Kettering Cancer Center with RT between 1921 and 1951.[20,21] Although the tumour initially responded in some patients, all eventually experienced progression of persistent disease or a local recurrence. Recently published studies analyzing the efficacy of megavoltage therapy in the management of ameloblastoma have questioned the proposition that these tumours are inherently radioresistant.[22-25]. Gardner reported on 3 patients treated with megavoltage RT (40, 45 and 55 Gy, respectively); all 3 responded initially but later recurred. Based on these results, Gardner concluded that RT can produce regression of an ameloblastoma, particularly the part which causes expansion of the jaw or has invaded the adjacent soft tissues but that it is not appropriate treatment for ameloblastomas and should be reserved for unresectable tumours.[26]

If radiotherapy is to be considered, then more data are needed to better understand its effectiveness.

Table 2: Recurrence rates after radiation treatment

Treatment	Patients (n)	Recurrence (%)	Reference
XRT	11	100	Sehdev et al[20].
XRT	2	100	Shatkin et al[21].
XRT	10	20	Atkinson et al[25]
XRT	5	40	Gardner[26]
XRT	1	0	Miyamoto et al[27].
XRT	8	50	Pinsolle et al[28]
XRT	1	0	Ueda et al[29]

XRT- radiation therapy

CHEMOTHERAPY

Systemic chemotherapy has been attempted a number of times, with numerous agents and combinations being employed. Reports have suggested that ameloblastoma may be sensitive to platinum-based agents, though occasional reports highlight lengthy survival without chemotherapy. Gall tested cyclophosphamide and methotrexate 5-fluorouracil therapy in a patient with lung metastases that occurred nine years after initial therapy. He noticed that the functional outcome was good although no objective response was seen.[24,25] Ramadas obtained partial response after 13 cycles of combination chemotherapy-associating cisplatin and cyclophosphamide administrated for lung metastases. Some other therapies have also shown activity, including vinblastine, bleomycin, paclitaxel and carboplatin.[26]

A review of the literature made by Lanham concluded that chemotherapy failed to show any antitumoral activity, including doxorubicin, methotrexate, prednisolone, bleomycin, 5-fluorouracil and dacarbazin. Moreover, the literature reports some patients with metastases showing long survival without receiving chemotherapy. Chemotherapy may also have a role in improvement of clinical symptoms in non-surgical patients.[27] 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. Experience with chemotherapy is minimal in the treatment of ameloblastoma and is largely limited to isolated cases. Lanham described a case report of ameloblastoma metastatic to the lungs and submandibular nodes treated with doxorubicin, cisplatin, cyclophosphamide, dacarbazine, and 5-fluorouracil; the tumour failed to respond. Duffey et al reported a case of ameloblastoma with dissemination to cervical lymph nodes, liver, and lungs treated with multi-agent chemotherapy. The tumour did not respond to treatment.[30] In contrast, Grunwald et al described a case of ameloblastoma metastatic to the lungs and pleura, which exhibited response to paclitaxel and carboplatin. 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.[31]

CONCLUSION

Ameloblastoma is considered to be a benign, but locally invasive odontogenic tumour with a high rate of recurrence. Essentially, most studies showed that the prognosis for ameloblastoma is more dependent on the method of surgical treatment rather the histologic type of tumour. Resection with some safe margin (marginal, segmental or composite resection depending on the site and size of the lesion) is the best primary method for treating solid/multicystic ameloblastomas to avoid recurrence.

Despite the 'radical' nature of a surgical resection, it may actually involve less morbidity than extensive hard and soft tissue resection with associated extensive morbidity that may be warranted in case of recurrence following inadequate primary treatment. However, a conservative (curettage, not enucleation) method may be considered in case of unicystic ameloblastoma of the anterior mandible without soft tissue involvement, for patients in their first decade of life.

Before 1980s, Ameloblastomas were considered to be radio resistant. Although several studies have reported on adjuvant radiation for positive margins and for recurrent and unresectable ameloblastomas, the outcomes are poor. The possible efficacy of radiotherapy must be weighed against the risk for future radiation-induced malignancies and other long term sequelae of radiation therapy. More work is needed to validate this treatment option.

Systemic chemotherapy has been attempted a number of times, with numerous agents and combinations being employed. Reports have suggested that ameloblastoma may be sensitive to platinum-based agents, though occasional reports highlight lengthy survival without chemotherapy. However more research is required to before finally accepting the role of chemotherapy in management of ameloblastoma. Author conclude that as there is a lack of consensus on the most appropriate treatment modality for ameloblastomas, there is a need to conduct more evidence-based clinical studies for clinical practice guidelines in the management of ameloblastomas of the jaws.

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