MULTIMODAL MANAGEMENT OF AMELOBLASTOMA: TWO CASE REPORTS OF SURGERY COMBINED WITH RADIOTHERAPY

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ABSTRACT

Introduction: According to the World Health Organization, ameloblastoma is a benign intraosseous epithelial odontogenic tumor that grows slowly but progressively, potentially reaching significant size and causing considerable morbidity. It has a high recurrence rate if not completely removed. Its management is challenging due to its impact on patients' quality of life. The purpose of this study is to present our institutional experience at the Radiotherapy Department of Salah Azaiez Institute in Tunisia through two cases of mandibular ameloblastoma.

Case presentation: The first case involves a 46-year-old man with no notable medical history, who consulted his dentist for a painless gingival swelling. A macrobiopsy revealed an ameloblastoma, leading to radical surgery. He underwent a hemimaxillectomy with removal of half of the palatal vault. Recovery was uneventful. Histopathological examination confirmed a follicular-type ameloblastoma. A follow-up CT scan three months later showed osteolytic lesions involving the right pterygoid and zygomatic processes, indicating residual tumor extension measuring 12 x 9 x 8 mm. A multidisciplinary team decided on adjuvant radiotherapy using IMRT at a dose of 60 Gy.

The second case concerns a 72-year-old woman who had surgery for a right mandibular ameloblastoma in 1987 without adjuvant radiotherapy. In 2006, imaging revealed a recurrence at the same site. Following additional surgery, progression was noted, and 3D-conformal radiotherapy at 50 Gy was administered. Unfortunately, the tumor continued to progress aggressively, and the patient received palliative care.

Conclusion: Ameloblastoma is a benign odontogenic tumor with aggressive behavior and a high risk of recurrence. While surgery remains the mainstay of treatment, radiotherapy has a key role in managing locally advanced, recurrent, inoperable, or metastatic disease

Key Words: Ameloblastoma, Surgery, Radiotherapy, Combined treatment.

INTRODUCTION

Despite its classification as a benign odontogenic tumor, ameloblastoma displays aggressive behavior due to its invasive nature. It constitutes approximately 1% of maxillary and mandibular tumors; however, excluding pseudotumors and cysts elevates this ratio to 11% [1-3]. First documented by Malassez et al. in 1885, ameloblastoma is believed to originate from epithelial remnants of the developing root sheath, although its precise etiology remains largely unclear. Typically affecting young adults with a median age of 35 years and a male predilection, ameloblastoma can be categorized into central or peripheral types[2]. Central ameloblastomas develop within the jawbone, whereas peripheral variants manifest on the gum surface without penetrating the underlying bone. Central ameloblastomas are further classified as multicystic/solid or unicystic, with the latter demonstrating greater aggressiveness [4-5].

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In rare cases, ameloblastoma can undergo malignant transformation, spreading hematogenously. Malignant forms include metastasizing ameloblastoma and the more aggressive ameloblastic carcinoma. Surgical intervention represents the cornerstone of treatment for these tumors, aiming to achieve clear margins to mitigate the risk of local recurrence. Radiotherapy is typically reserved for cases of locally advanced disease or when patients decline extensive surgical procedures. However, it is not the preferred initial treatment for operable tumors.

This study aims to present practical insights from the radiotherapy department at Salah Azaiez Institute in Tunisia concerning the management of mandibular ameloblastoma, elucidated through the analysis of two specific cases.

CASE PRESENTATION:

Case 1

A 46-year-old male, without significant medical history, was referred to the maxillofacial surgery department of our hospital for adjuvant radiotherapy following the diagnosis of an ameloblastoma in the right maxilla. The patient had presented with a painless gingival cystic swelling persisting for 6 months. A macrobiopsy confirmed the presence of an ameloblastoma. Subsequently, he underwent a hemimaxillectomy with hemipalatectomy (Fig. 1). The definitive histopathological analysis identified a follicular type ameloblastoma with clear surgical margins.

Histopathological examination revealed a follicular pattern characterized by islands of odontogenic epithelium surrounded by fibrous stroma. The epithelium displayed peripheral palisading cells with reverse polarization and central loosely arranged cells resembling stellate reticulum (Fig. 2). The patient experienced no significant postoperative complications. No major post operative complications were observed. The follow- up CT scan (9 months later) showed a right maxillary resection with densification of the fat in the tumor bed. Expansive osteolytic lesions centered on the body of the right pterygoid process and zygomatic process, measuring respectively 11 x 9mm and 12x8mm, suggesting a remnant of the maxillary and pterygoid extensions of the operated ameloblastoma.

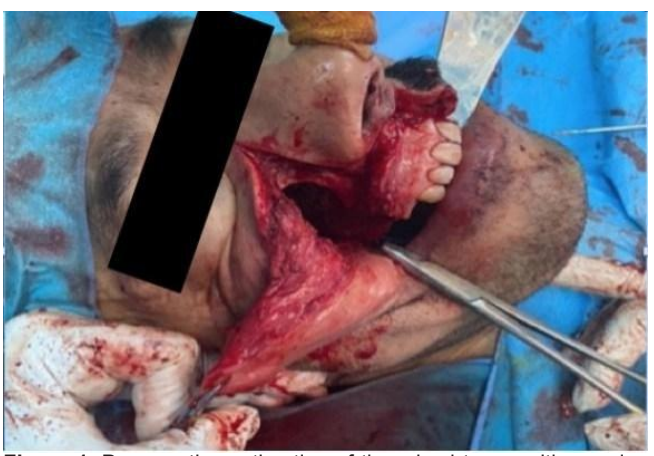

Figure 1. Peroperative extirpation of the mixed tumor with para-latero-nasal incision

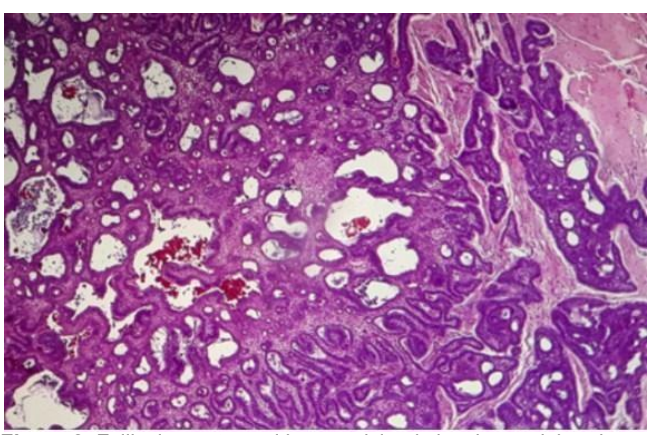

Figure 2. Follicular pattern with tumor island showing peripheral palisading and central cystic degeneration (x 40)

Following a multidisciplinary team review, the collective decision was to proceed with adjuvant radiotherapy at a dose of 60 Gy on the planning target volume (Fig. 3).

During radiotherapy, the patient developed only mild acute toxicity, consisting of grade 1 radiomucositis, without radiodermatitis, and maintained very good tolerance overall. He was reviewed weekly throughout the treatment. Follow-up was satisfactory, with a facial CT scan performed at six months showing no evidence of recurrence, and a subsequent scan at one year confirming persistent disease-free status. Clinically, the patient preserved good masticatory function, clear phonation, and an overall satisfactory quality of life, with no complaints of xerostomia or functional limitations. No late toxicity such as soft tissue fibrosis or osteoradionecrosis was observed during the follow-up period.

At two years post-treatment, clinical evaluation confirmed the patient's continued good oral function, quality of life, and absence of recurrence.

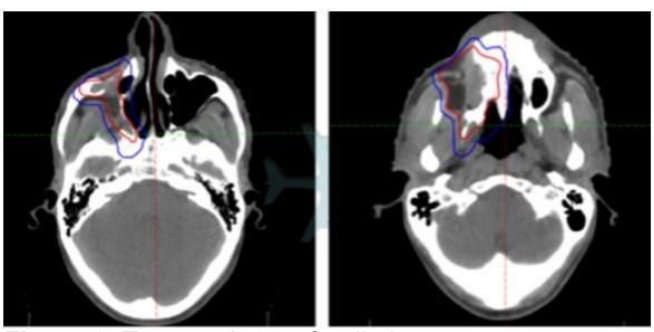

Figure 3. Target volume of radiotherapy
CTV: clinical target volume in red
PTV: planning target volume in blue

Case 2

We present the case of a 72-year-old female patient with a significant medical history. In 1987, she underwent a right hemi-mandibulectomy with nodal dissection in the triangular area for a mandibular tumor, which histopathological examination confirmed as ameloblastoma. Adjuvant radiotherapy was not administered. After a period of lost follow-up, she returned in 2006 with a painful nodule measuring 35 mm at the original site, the right mandibular angle. A cervico-facial MRI revealed a tissue mass measuring 35 x 18 x 17 mm at the prior tumor bed, indicative of ameloblastoma recurrence, along with a 26 mm mass in the infratemporal fossa. In March 2006, she underwent a right hemimandibulectomy, confirming a 3 cm ameloblastoma upon histopathological examination. Subsequent imaging showed signs of tumor progression, prompting a recommendation for radiotherapy. The patient received 50 Gy of radiation targeting the right mandibular area. Unfortunately, follow-up imaging demonstrated persistent tumor growth despite treatment. Consequently, the patient transitioned to palliative supportive care.

DISCUSSION

Ameloblastoma is a prevalent benign odontogenic tumor primarily affecting the jaw, known for its slow growth and tendency to locally invade surrounding tissues [5] . It typically presents as painless swelling in either the mandible or maxilla. Diagnosis is often delayed, commonly identified through dental manifestations such as tooth mobility or loss, along with noticeable bone swelling in the affected jaw. In advanced cases involving the maxilla, symptoms may include nasal obstruction and diplopia. On dental panoramic radiographs, ameloblastomas typically exhibit a characteristic “soap bubble” appearance [6]. Diagnosing ameloblastoma can pose challenges due to its diverse clinical and radiographic presentations, which may resemble other odontogenic and non-odontogenic lesions. Achieving a definitive diagnosis typically involves a comprehensive approach combining clinical evaluation, radiographic imaging, and histopathological examination [6]. Incisional biopsies are crucial but require careful execution to minimize potential complications and diagnostic errors. The application of advanced imaging modalities has significantly enhanced the accuracy of ameloblastoma diagnosis, providing detailed insights into its extent and invasiveness[3] .

Radiologically, there are three classic varieties of ameloblastoma: solid/multicystic, unicystic and peripheral (extra-osseous). Solid/multicystic and unicystic types have several histologic variants that can have different shapes biological behavior [7].

Rapid detection of ameloblastoma plays a crucial role for prognostic evaluation and the preservation of oral function and aesthetic outcomes. In fact, early identification can help prevent significant bone destruction and facial deformities and allows for less aggressive treatment options.

Management of ameloblastoma depends on various factors, including size, location, histologic subtype, and patient age. Surgery remains the cornerstone of treatment for operable ameloblastomas, and the choice of surgical method may vary depending on the surgeon and the specific characteristics of the tumor [3-5].

Primary treatment options encompass a range of surgical techniques, from conservative approaches such as enucleation, curettage, and cryosurgery to more radical procedures including marginal, segmental, and composite resection[8-9].

The treatment of ameloblastoma presents challenges as it is often perceived as benign, yet it is locally invasive with a significant recurrence risk if not thoroughly eradicated. Numerous studies have compared conservative versus radical surgical approaches, with findings consistently indicating a higher local recurrence rate—approaching 100% in some cases—among patients treated conservatively[10]. Consequently, the prevailing recommendation among authors is to opt for radical treatment without delay as the case for our two patients described bellow.

Radiotherapy may be considered as an alternative treatment option for some cases of ameloblastoma, particularly in situations where surgery is not feasible or the tumor is localized advanced[11]. In addition, radiotherapy may be offered to patients who refuse surgery. The study conducted by Atkinson in 1984, which included a series of 10 cases of ameloblastomas treated with radiotherapy, provides valuable information on the potential effectiveness of radiotherapy as a treatment option for this condition. According to the results of this study, 90% of cases showed favorable results after radiotherapy, indicating a positive response to treatment [12]. It is important to note that three of the cases in the study involved a combination of surgery and radiotherapy, while the remaining cases were treated with radiotherapy alone. Despite the small sample size, the study results suggest that radiotherapy, either alone or in combination with surgery, could be effective in the management of ameloblastomas. Long-term follow-up of patients participating in the study also provides valuable information on the durability of treatment response. Only one surgically treated patient experienced a recurrence after 9 years, with an overall survival of 14 years from the last day of radiotherapy. This indicates that radiotherapy can lead to long-term disease control and satisfactory survival rates in some cases of ameloblastoma. Based on his experience and a review of the literature, Atkinson concluded that ameloblastomas are radiosensitive [13].

In our study, the first case, which underwent surgery followed by adjuvant radiotherapy, showed effective local control without recurrence during the one-year follow-up period. This outcome underscores the potential importance of radiotherapy in managing ameloblastoma, particularly in situations where surgical treatment poses challenges or potential risks.

Since then, few cases have been reported in the literature regarding the role of radiotherapy as a viable treatment modality for ameloblastomas[14-15]. It is important to note that while radiotherapy can be effective in specific situations, it is not without potential risks and side effects. The decision to pursue radiotherapy should be individualized, considering factors such as the patient’s medical history, overall health, tumor characteristics, and personal preferences.

It’s crucial to recognize that local recurrences can still occur despite successful primary surgical treatment [15-16]. Moreover, in some cases, ameloblastomas can exhibit aggressive behavior with the potential for distant metastases following multiple surgical resections, similar to the experience of our patient in the second case.

Our first patient was treated with adjuvant radiotherapy using IMRT (Intensity-Modulated Radiation Therapy) on a linear accelerator. Target volumes were carefully delineated, and surrounding organs at risk were systematically protected to minimize radiation exposure and reduce potential toxicity.

A critical evaluation indicates that the contribution of radiotherapy in ameloblastoma is limited and should not

be overstated. The available evidence, mainly based on small case series, remains insufficient and lacks robust comparative trials. Complete surgical excision continues to represent the standard of care, providing the best long-term local control. Thus, radiotherapy should be reserved for specific indications—such as unresectable tumors, patients unfit for surgery, or those refusing operative management—although its efficacy appears lower than surgery alone. Although generally well tolerated, late adverse effects including xerostomia, osteoradionecrosis, and soft tissue fibrosis must be carefully considered

Several advanced radiotherapy techniques have emerged as alternatives or adjuncts to conventional radiotherapy in selected ameloblastoma cases. Among these, Gamma Knife radiosurgery and Proton Beam Therapy (PBT) have shown promising results in tumor control with acceptable safety profiles.

Gamma Knife radiosurgery is a precise form of stereotactic radiotherapy that delivers highly focused gamma rays to tumors while sparing surrounding healthy tissue. Its accuracy makes it particularly suitable for head and neck lesions near critical structures. Two reported cases illustrate its potential: a 35-year-old male with recurrent maxillary ameloblastic carcinoma achieved local control at treated sites with 16–24 Gy, although distant recurrences occurred later, and a 26-year-old female with unresectable cavernous sinus involvement showed significant tumor reduction and remained stable at three-year follow-up[17-18].

Proton beam therapy (PBT) offers another advanced option, utilizing the Bragg peak to deliver high radiation doses directly to the tumor while minimizing exposure to surrounding tissues. Reported cases include elderly or unresectable patients achieving complete tumor regression and long-term disease-free follow-up [19].

These findings suggest that Gamma Knife and PBT can provide effective tumor control with minimal side effects, although long-term efficacy and standardized treatment protocols require further investigation.

CONCLUSION

Ameloblastoma represents a challenging entity in oral and maxillofacial pathology due to its benign yet locally aggressive nature. Prompt and appropriate management is essential to achieve favorable outcomes and minimize the risk of recurrence. Surgery remains the cornerstone of treatment for operable cases, with both conservative and radical approaches tailored to individual patient factors and tumor characteristics.

For cases where surgical intervention is not feasible or complete, radiotherapy plays a significant role, especially in managing locally advanced or metastatic disease stages. While radiotherapy can provide effective tumor control, its use requires careful consideration of potential risks and benefits, emphasizing the importance of personalized treatment decisions.

Moving forward, continued research and collaboration among healthcare professionals are essential to further refine treatment protocols and improve patient outcomes in the management of ameloblastoma. Comprehensive long-term follow-up remains critical to monitor for recurrence, assess treatment efficacy, and ensure the best possible quality of life for patients affected by this complex condition.

Informed consent

Written informed consent was obtained from the patients for their anonymised information to be published in this article.

Conflict of interest: The authors declare that they have no conflict of interest related to this article.

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