Conservative treatment of ameloblastoma: report of 2 cases and review of the literature

Tratamiento conservador de ameloblastoma: reporte de 2 casos y revisión de la literatura

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Abstract
Introduction: ameloblastomas correspond to one of the most prevalent odontogenic tumors in developing countries, they are mainly located in the mandible, and their treatment has been widely discussed over the years, using radical or conservative treatments depending on different variables. Clinical case: we present two cases of patients with ameloblastoma who underwent conservative treatment without the use of adjuvant therapy, obtaining satisfactory results at 36 and 48 months. Discussion: due to a possible recurrence with conservative treatment, radical management has been suggested, however, the choice of treatment should be based on a series of clinical, histological, and radiographic characteristics.

Keywords: ameloblastoma; odontogenic tumors; mandible; conservative treatment.

Caso clínico: se presentan dos casos de pacientes con ameloblastoma que fueron tratados con tratamiento conservador sin el uso de terapia adyuvante, obteniendo resultados satisfactorios a los 36 y 48 meses. Discusión: de un posible recurrencia con tratamiento conservador, se ha sugerido manejo radical, sin embargo, la elección de tratamiento debe ser en base a una serie de características clínicas, histológicas y radiográficas.

Palabras Clave: ameloblastoma; tumores odontogénicos; mandíbula; tratamiento conservador.

Introduction
The World Health Organization defines ameloblastomas as a locally invasive polymorphic neoplasm that commonly has a follicular or plexiform pattern, in a fibrous stroma, with characteristics of a benign but locally aggressive tumor, according to their characteristics, they are divided into conventional, unicystic, metastatic, peripheral, and adenoid (Díaz D et al., 2014; Cadavid et al., 2019). It represents approximately 1% of all oral tumors and about 9-11% of odontogenic tumors (Masthan et al., 2015; Almeida et al., 2016; Laborde et al., 2017). They show slow-growing tumors, with an affinity for bone tissue, not soft tissue, and have a high recurrence rate (60-80%) if they are not removed properly (Haq et al., 2016).

It corresponds to the most prevalent odontogenic tumor in developing countries. The worldwide incidence is 0.5 cases per million people per year, with a higher incidence in Africa and China. It has been observed that the African American population is five times more likely to develop it compared to the Caucasian population. Most patients with ameloblastoma are between the ages of 30 and 60. Only 10-15% of cases occur in the pediatric population (Effiom et al., 2018). In 88% of cases, this tumor occurs in the mandible, with a higher incidence in the mandibular ramus region (Hong et al., 2007).

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Ameloblastoma has a slow growth, without signs or symptoms in early stages, which in more advanced stages can cause cortical expansion, associated or not with pain or superinfections. In the literature, there have been reported cases of ulcerations in the mucosa, loss of dental mobility, and paresthesia of the inferior alveolar nerve (Pozo et al., 2011; Valls et al., 2012; Shi et al., 2014).

Radiographically, it appears as a cystic lesion that causes expansion and erosion of the cortical bone. There are 3 radiological patterns of this lesion: unilocular, multilocular, and honeycomb; however, no radiological correlation has been found with age, sex, histological type, or the behavior or aggressiveness of the tumor. Root resorption is highly suggestive of ameloblastoma; however, the definitive diagnosis is based on the histopathological study in correlation with the clinical and radiological features. (Valls et al., 2012; Laborde et al., 2017).

The treatment for ameloblastomas is widely debated, but in general, it can be grouped into two main currents, conservative or radical treatment. Conservative treatment includes enucleation, curettage, surgical excision in conjunction with peripheral osteotomy, or with adjuvant therapy through cryotherapy or Carnoy’s solution. On the other hand, radical treatment consists of bone resection. In the mandible, the resection can be completed through segmental osteotomy or a mandibulectomy or can be marginal, preserving the lower border of the mandible. (Pogrel & Montes, 2009; Almeida et al., 2016; Neagu et al., 2019).

We present two cases of male patients diagnosed with ameloblastoma, who were treated conservatively and with satisfactory results. This is to report the success that can be achieved with the conservative management of this pathosis, and thus be able to reduce the morbidity of patients.

**Clinical cases**

**Clinical case 1**
A 16-year-old male patient with no known systemic alterations. Consultation due to an increase in volume in the left posterior region of the mandible. Extraoral examination shows no findings. On intraoral examination shows swelling on the retromolar sector, posterior to tooth 3.7 of approximately 3 cm in diameter, unique, hard consistency, not adhered to soft tissues, without coloration changes, of defined limits, and painless.

In the radiographic examination, a radiolucent area, size 3 x 4 cm, is observed in relation to unerupted tooth 3.8, ramus, and left mandibular body, which produces cortical bone expansion and thinning, without alterations to adjacent structures.

After confirming the diagnosis with an incisional biopsy, under general anesthesia, enucleation, curettage, and extraction of teeth 3.8 and 3.7 were performed. The lesion was sent for histopathological study, and the patient had a postoperative recovery without complications.

The histopathological study reported a fibro conjunctive tissue lesion and bone trabeculae, compromised by an ameloblastic neoplasm partly cystic and partly solid that is made up of epithelial islets with palisade cells, with a stellate reticulum-like appearance in the center, and some microcystic formations, with peripheral hyalinization. Lesion consistent with conventional ameloblastoma follicular and plexiform subtype.

No signs of recurrence or other complications were observed after clinical and radiographic follow-up at 12, 24, and 36 months.

**Clinical case 2**
A 22-year-old male patient with no known systemic alterations. Consultation due to a radiographic finding of a right mandibular lesion. The extra and intraoral examination does not present relevant findings.

In the radiographic examination, radiolucent areas were observed, measuring 1 x 1 cm and 2 x 2 cm in relation to the right mandibular
body and ramus, with defined limits, corticalized, does not produce expansion or thinning of the tables, and without alterations to adjacent structures.

**Figure 3:** Radiographic examination. Radiolucent areas were observed, measuring 1 x 1 cm and 2 x 2 cm in relation to the right mandibular body and ramus, with defined limits, corticalized, does not produce expansion or thinning of the tables, and without alterations to adjacent structures.

After confirming the diagnosis with an incisional biopsy, under general anesthesia, enucleation, curettage, and extraction of teeth 4.7 were performed. The lesion is sent for histopathological study, and the patient had a postoperative recovery without complications.

The histopathological study reported a lesion of collagenized fibrous connective tissue, with a cystic cavity lined by thickened squamous epithelium, with cells in upper layers resembling a stellate reticulum, and in several parts’ epithelial islets with the formation of microcysts, some with palisade epithelium like ameloblasts, and in others compact epithelial islets. Lesion consistent with conventional ameloblastoma follicular subtype.

No signs of recurrence or other complications were observed after clinical and radiographic follow-up at 12, 24, 36, and 48 months.

**Figure 4:** Radiographic follow-up at 48 months. No signs of recurrence or other complications were observed.

**Discussion:**

The treatment of Ameloblastomas is surgical, but the use of a conservative or a radical approach, based on the clinical, histological, and radiographic characteristics, is controversial and widely discussed in the literature (McClary *et al*., 2016; Neagu *et al*., 2019). Regarding the choice of treatment, Hong *et al*., 2007 describe that when there is a diagnosis of Ameloblastoma, the treatment must be aggressive and radical, with resection of the mandible of approximately 1.5 – 2 cm beyond the radiographic limit, to avoid recurrences.

Although radical treatment is suggested, a thorough evaluation of several factors that may influence the choice of treatment, such as the clinical presentation and age of the patient, must be carried out. In children, conservative treatment is preferred to not impair facial growth and to avoid postoperative psychological, functional, and aesthetic complications (Samuel *et al*., 2014; Hendra *et al*., 2019).

Other authors suggest that the treatment modality should be determined based on size (≤ 5 cm, 5 to 13 cm, ≥ 13 cm), anatomical location, histological variant, and anatomical involvement (Singh *et al*., 2014).

In relation to the histological characteristics of ameloblastoma, it has been reported that some variants, such as the follicular, granular cell, and acanthomatous type, have a greater possibility of recurrence. Therefore, with these types of variants, it is necessary to carry out radical treatment and continuous monitoring of the patient. While other variants, such as peripheral desmoplastic, plexiform, and unicystic, have a low recurrence potential. (Hong *et al*., 2007; Haq *et al*., 2016). On the other hand, a higher recurrence rate of approximately 7-25% has been reported when conservative treatment is used in the treatment of unicystic ameloblastomas (Samuel *et al*., 2014).

Many authors prefer to perform a marginal or segmental resection, due to the high recurrence rate compared to conservative treatment. Hong *et al*., 2007, report an analysis where if the factors to be considered for treatment (age, location, size, etc.) are the same, using a radical or aggressive treatment the relative risk of recurrence decreased by 20%. However, despite the effectiveness of radical treatment, it is necessary to consider that this approach has great consequences for the patient, both aesthetic and functional, which can affect their quality of life (Laino *et al*., 2020).
Due to the fact that an increase in recurrence has been observed with the use of conservative therapy with curettage, adjuvant therapies are usually used, in order to cause the lysis of residual tumor cells and reduce the recurrence rate, such as Carnoy’s solution and cryotherapy, allowing less functional and aesthetic compromise, however, they can result in an increase in recurrence if they are not performed properly (Valls et al., 2012; Titinchi & Brennan, 2022).

Carnoy’s solution has been described as a sclerosing agent for the treatment of cysts and fistulas and a fixative agent, applied for the treatment of ameloblastomas seeking to reduce the risk of recurrence (Lee et al., 2021). However, studies have described that, due to the original composition of this solution, which contains chloroform, there is an associated carcinogenic potential. (Forteza-López et al., 2019).

On the other hand, the use of cryotherapy has reduced the recurrence rate by 30%. It is believed to have the ability to devitalize bone to a depth of 1 to 2 cm, as well as causing less postoperative morbidity (López et al., 2010).

Recent reports have demonstrated high rates of mitogen-activated protein kinase (MAPK) pathway mutations in ameloblastoma, particularly ameloblastomas located in the mandible with a BRAF mutation (Faden & Algazi, 2017). Faden & Algazi, 2017, report a favorable outcome with a 75% tumor reduction at 12 months of a patient treated with a single agent BRAF inhibitor (BRAFi) dabrafenib. These results suggested that some of the ameloblastomas may be suitable for nonsurgical treatment or that the use of these therapies can achieve a more conservative treatment.

In this review, there was a total of 389 patients, out of this 222 were males and 169 females, with a mean age of 35.4 years, most of the reported cases were in the posterior mandible, mainly ramus and angle. Radiographically there was a variable presentation, with most of the cases with teeth involvement. Out of the conventional ameloblastoma, the most prevalent variants were the follicular and plexiform. There was no predilection for conservative or radical treatment, but most of the recurrences reported were treated with conservative treatment (Table 1) (Hasegawa et al., 2013; Singh et al., 2015; Haq et al., 2016; Laborde et al., 2017; Laino et al., 2019; Menon et al., 2019; Caroli et al., 2021; Hresko et al., 2021; Lee et al., 2021; Dandriyal et al., 2022).

In the reported cases, the age of presentation was not within the ranges of highest incidence, which is established between 30 and 60 years (Effiom et al., 2018) and was 35.4 years in the present review. With respect to the area of development, presentation, and histological characteristics it was according to what is described in the literature.

The conservative treatment of the described patients shows a favorable evolution, with no evidence of recurrences, at 36 and 48 months, and continues in close follow-up. In this review, recurrences have been reported ranging from, 7% to 48.7%, most treated with conservative treatment, however, the follow-up time was highly variable, due to which differences are observed in terms of recurrence. The literature indicates that 95% of ameloblastoma recurrences are detected during the first 5 years after the initial intervention, although 50% of these appear in the first year (Morales, 2009). Thus, it is highly recommended that the clinical and radiological follow-up is > 10 years, to evaluate possible recurrences.

Conclusion

Ameloblastomas correspond to one of the most prevalent odontogenic tumors in developing countries, so having the tools to carry out adequate management, whether conservative or radical, is essential to achieve not only avoiding the recurrence of the lesions but more important still, the well-being of the patient. It is in this sense that the case-by-case analysis becomes fundamental, considering the individual characteristics and needs of each patient such as age, systemic condition, sociocultural-labor factors, and previous experience, in order to offer a treatment plan that reduces the patient’s morbidity, and achieves a simpler rehabilitation, impacting on the quality of life of the patient in a positive way, establishing a system of long-term controls in search of this objective. Furthermore, a previously guaranteed clinical follow-up is essential, when treating odontogenic tumors. Based on what has been exposed through these reports, we can indicate that the conservative therapeutic option without the use of adjuvants delivers good long-term results; however, we recommend the analysis of more cases and long-term follow-up to establish accurate conclusions.
Table 1: summary table of articles reporting characteristics and treatment of ameloblastoma.

<table>
<thead>
<tr>
<th>Author/year</th>
<th>Age/Gender</th>
<th>Location</th>
<th>X-rays</th>
<th>Histopathology</th>
<th>Treatment</th>
<th>Recurrence</th>
<th>Follow-up</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dandriyal et al., 2022</td>
<td>102 patients, 61 males and 41 females, mean age 30.35 years</td>
<td>93.1% in the mandible, with a prevalence on the left side, most located on the ramus.</td>
<td>66.4% of multilocular lesions, with most involved impact teeth the mandibular third molar</td>
<td>63.8% conventional type, with the most seen the follicular followed by plexiform</td>
<td>69.7% radical treatment, 30.3% conservative treatment</td>
<td>20.6%, mainly with conservative treatment</td>
<td>Up to 9 years, with mean duration of 5.29 years</td>
<td>Fracture of reconstruction, wound dehiscence, post operative infection, and hardware removal</td>
</tr>
<tr>
<td>Hresko et al., 2021</td>
<td>64 patients, 26 males and 38 females, mean age 42.95 years</td>
<td>87.5% in the mandible, most located on the ramus and angle</td>
<td>50% of multilocular lesions, with teeth involvement in 53.1% of the cases</td>
<td>90.6% conventional type, with the most seen the follicular followed by plexiform</td>
<td>53.1% conventional treatment, 46.9% radical treatment</td>
<td>32.8%, mainly with conservative treatment</td>
<td>Ranged from 2 to 10 years, with mean duration of 4.28</td>
<td>Facial asymmetry and disfigurement, transitory and permanent paresthesia, infection and swelling</td>
</tr>
<tr>
<td>Lee et al., 2021</td>
<td>2 patients, 1 male and 1 female, mean age 17.5 years</td>
<td>100% in the mandible, located on ramus, angle and body</td>
<td>50% of multilocular lesion in 100% of the cases</td>
<td>50% conventional type, plexiform variant</td>
<td>100% conservative treatment</td>
<td>No recurrence</td>
<td>Ranged from 8 to 10 months, with mean duration of 9</td>
<td>Not reported</td>
</tr>
<tr>
<td>Rocha et al., 2021</td>
<td>53 patients, 25 males and 28 females, mean age 27.1 years</td>
<td>92.5% in the mandible, most located on the posterior area</td>
<td>67.3% of multilocular lesions, with vestibular and lingual osseous plates compromised</td>
<td>88.8% conventional type, with the most seen the follicular and plexiform</td>
<td>90.5% conventional treatment, 9.5% radical treatment</td>
<td>9.4%, mainly with conservative treatment</td>
<td>Ranged from 24.4 to 128.9 months, with mean duration of 65.8 months</td>
<td>Dehiscence, infection, transitory and permanent paresthesia, pathologic fracture, bone seq ues trum, facial asymmetry</td>
</tr>
<tr>
<td>Laino et al., 2019</td>
<td>1 patient, female, 47 years</td>
<td>Mandible, located on the body</td>
<td>Multilocular lesion, with teeth involvement</td>
<td>Conventional type</td>
<td>Conservative treatment</td>
<td>No recurrence</td>
<td>5 years</td>
<td>Not reported</td>
</tr>
<tr>
<td>Menon et al., 2019</td>
<td>45 patients, 30 males and 15 females, mean age 36 years</td>
<td>100% in the mandible, most located on the ramus, angle and body</td>
<td>Not described</td>
<td>60% conventional type, with the most seen the plexiform followed by follicular</td>
<td>57% radical treatment, 43% conservative treatment</td>
<td>7%, treated with conservative treatment</td>
<td>Ranged from 2 to 4 years</td>
<td>Not described</td>
</tr>
<tr>
<td>Laborde et al., 2017</td>
<td>27 patients, 16 males and 11 females, mean age 46.3 years</td>
<td>74.1% in the mandible, located in the ramus, angle and body</td>
<td>37% of multilocular lesions, with teeth involvement and bone invasion</td>
<td>89% conventional type, with the most seen the follicular followed by plexiform</td>
<td>56% conservative treatment, 44% radical treatment</td>
<td>31%, mainly with conservative treatment</td>
<td>Mean duration of 44.2 months</td>
<td>Not described</td>
</tr>
<tr>
<td>Haq et al., 2016</td>
<td>31 patients, 13 males and 18 females</td>
<td>100% in the mandible, located in the ramus, angle and body</td>
<td>16% of multilocular lesion, with teeth involvement</td>
<td>68% conventional type, with the most seen the follicular and plexiform</td>
<td>87% conservative treatment, 13% radical treatment</td>
<td>11% treated with conservative treatment</td>
<td>Ranged 3 to 156 months, with mean duration of 38 months</td>
<td>Not described</td>
</tr>
<tr>
<td>Singh et al., 2015</td>
<td>41 patients, 26 males and 15 females, mean age 43 years</td>
<td>80.5% in the mandible, most located on the posterior area</td>
<td>Not described</td>
<td>81% conventional type</td>
<td>85.3% radical treatment, 14.7% conservative treatment</td>
<td>14.7% mainly with conservative treatment</td>
<td>Mean duration of 8.5 years</td>
<td>Postoperative infection, complete failure of the flap</td>
</tr>
<tr>
<td>Hasegawa et al., 2013</td>
<td>23 patients, 12 males and 11 females, mean age 28.5 years</td>
<td>100% in the mandible, most located on the ramus and angle</td>
<td>47.8% of multilocular lesions, with teeth involvement</td>
<td>100% conventional type, with the most seen the follicular and plexiform</td>
<td>100% conservative treatment</td>
<td>48.7% mainly with enucleation without adjuvant treatment</td>
<td>Ranged 8 to 130 months</td>
<td>Not reported</td>
</tr>
</tbody>
</table>


