

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.

Resumen

Introducción: Los ameloblastomas corresponden a uno de los tumores odontogénicos más prevalentes en los países en desarrollo, se ubican principalmente en la mandíbula, y su tratamiento ha sido ampliamente discutido a lo largo de los años, utilizando tratamientos radicales o conservadores dependiendo de distintas variables. **Caso clínico:** se presentan dos casos de pacientes con un ameloblastoma a quienes se les realizó tratamiento conservador sin uso de terapia coadyuvante, obteniendo resultados satisfactorios a los 36 y 48 meses. **Discusión:** Debido a una posible recurrencia con un 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.

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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 are 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 (Figure 1), 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.



Figure 1: 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. (Figure 2).



Figure 2: Radiographic follow-up at 36 months. No signs of recurrence or other complications were observed.

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 (Figure 3), radiolucent areas were observed, measuring 1 x 1 cm and 2 x 2 cm in relation to the right mandibular

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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)



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 (\leq 5 cm, 5 to 13 cm, \geq 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).

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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; 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.

Author/year	Age/Gender	Location	X-rays	Histopathology	Treatment	Recurrence	Follow-up	Complications
Dandriyal <i>et</i> al., 2022	102 patients, 61 males and 41 females, mean age 30.35 years	93.1% in the mandible, with a prevalence on the left side, most located on the ramus.	66.4% of multi- locular lesions, with most in- volved impact teeth the man- dibular third molar	63.8% conven- tional type, with the most seen the follicular fo- llowed by plexi- form	69.7% radical treatment, 30.3% conser- vative treat- ment	20.6%, mainly with conserva- tive treatment	Up to 9 years, with mean duration of 5.29 years	Fracture of recons- truction, wound dehiscence, post operative infection, and hardware re- moval
Hresko <i>et al.,</i> 2021	64 patients, 26 males and 38 females, mean age 42.95 years	87.5% in the m a n d i b l e , most located on the ramus and angle	50% of multi- locular lesions, with teeth in- volvement in 53.1% of the cases	90.6% conven- tional type, with the most seen the follicular fo- llowed by plexi- form	53.1% conser- vative treat- ment, 46.9% radical treat- ment	32.8%, mainly with conserva- tive treatment	Ranged from 2 to 10 years, with mean duration of 4.28	Facial asymmetry and disfigurement, transitory and per- manent paresthe- sia, infection and swelling
Lee <i>et al.,</i> 2021	2 patients, 1 male and 1 fe- male, mean age 17.5 years	100% in the mandible, loca- ted on ramus, angle and body	50% of multi- locular lesion, with teeth invol- vement in 100% of the cases	50% conventio- nal type, plexi- form variant	100% conser- vative treat- ment	No recurrence	Ranged from 8 to 10 months, with mean duration of 9	Not reported
Rocha <i>et al.,</i> 2021	53 patients, 25 males and 28 females, mean age 27.1 years	92.5% in the mandible, most located on the posterior area	67.3% of multi- locular lesions, with vestibu- lar and lingual osseous plates compromised	88.8% conven- tional type, with the most seen the follicular and plexiform	90.5% conser- vative treat- ment, 9.5% radical treat- ment	9.4%, mainly with conserva- tive treatment	Ranged from 24.4 to 128.9 months, with mean du- ration of 65.8 months	Dehiscence, infec- tion, transitory and permanent pares- thesia, pathologic fracture, bone se- questrum, facial asymmetry
Laino <i>et al.,</i> 2019	1 patient, fema- le, 47 years	Mandible, lo- cated on the body	Multilocular le- sion, with teeth involvement	Conventional type	Conservative treatment	No recurrence	5 years	Not reported
Menon <i>et al.,</i> 2019	45 patients, 30 males and 15 females, mean age 36 years	100% in the m a n d i b l e, most located on the ramus and angle	Not described	60% conventio- nal type, with the most seen the plexiform followed by fo- llicular	57% radical treatment, 43% conservative treatment	7%, treated with conserva- tive treatment	Ranged from 2 to 4 years	Not described
Laborde <i>et al.,</i> 2017	27 patients, 16 males and 11 females, mean age 46.3 years	74.1% in the mandible, lo- cated in the ramus, angle and body	37% of multi- locular lesions, with teeth in- volvement and bone invasion	89% conventio- nal type, with the most seen the fo- llicular followed by plexiform	56% conserva- tive treatment, 44% radical treatment	31%, mainly with conserva- tive treatment	Mean duration of 44.2 months	Not described
Haq et al., 2016	31 patients, 13 males and 18 females	100% in the mandible, lo- cated in the ramus, angle, and body	16% of multi- locular lesions, with teeth in- volvement	68% conventio- nal type, with the most seen the follicular and plexiform	87% conserva- tive treatment, 13% radical treatment	11% treated with conserva- tive treatment	Ranged 3 to 156 months, with mean duration of 38 months	Not described
Singh <i>et al.</i> , 2015	41 patients, 26 males and 15 females, mean age 43 years	80.5% in the mandible, most located on the posterior area	Not described	81% conventio- nal type	85.3% radical treatment, 14.7% conser- vative treat- ment	14.7% mainly with conserva- tive treatment	Mean duration of 8.5 years	Postoperative in- fection, complete failure of the flap
Hasegawa <i>et</i> al., 2013	23 patients, 12 males and 11 females, mean age 28.5 years	100% in the mandible, most located on the ramus and angle	47.8% of multi- locular lesions, with teeth in- volvement	100% conven- tional type, with the most seen the follicular and plexiform	100% conser- vative treat- ment	48.7% mainly with enuclea- tion without adjuvant treat- ments	Ranged 8 to 130 months	Not reported

Table 1: summary table of articles reporting characteristics and treatment of ameloblastoma.

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