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Review Article

Surgical management x recurrence of Odontogenic myxoma: Literature review and case reports

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ABSTRACT

Odontogenic Myxoma is a benign mesenchymal neoplasm probably originated from the ectomesenchyma. It presents a slow growth and at the beginning of its development the lesion is asymptomatic, what justify the challenging diagnostic and consequently choice of treatment.

Objective: The aim of this study is to review the literature in the past twenty years focusing on association between surgical management of Odontogenic Myxoma and their respective recurrence rates. We also report four cases treated in our Service.

Results and conclusions: A sample of 26 cases was analyzed. Our findings were similar when comparing our case series and literature. There was no statistical difference of recurrence rates between conservative and radical treatment modalities of Odontogenic Myxoma according to Fisher's exact test ($p = 0.431$). This finding would encourage adopting conservative modalities. However, due to low number of analyzed cases and heterogeneity of sample, data should be interpreted with caution. This conclusion does not diminish the importance of follow-up for all cases.

1. Introduction

Odontogenic myxoma (OM) is an uncommon intraosseous benign neoplasm, locally invasive, that occurs more frequently in young adults on the posterior region of mandible. The incidence of OM varies from 0.5% to 17.7% considering all the odontogenic tumors [1]. Radiographically, lesion exhibits a unilocular or a multilocular radiolucency with irregular or scalloped margins [2–5]. The lesions are usually asymptomatic, although some features are commonly present such as tooth displacement, extension into the maxillary sinus and obliteration of the inferior alveolar canal [2–6] and as it advances in size disturbing symptoms such as pain, dysesthesia, ulceration and tooth mobility may be found [7].

OM is originated from odontogenic ectomesenchyma of a developing tooth and/or periodontal ligament mesenchymal cells [8–11]. The theories around odontogenic origin are supported by proximity to the tooth-bearing areas of the jaws, frequent associated with missing or not erupted teeth, occasional presence of inactive odontogenic epithelium and histological similarity with pulpal ectomesenchyma [10]. OM is composed by stellate and spindle-shaped cells in an abundant myxoid extracellular stroma [9–12]. There are some molecular aspects of OM described: the expression of matrix metalloproteinases (MMPs) and antiapoptotic proteins; alterations in receptor activator of nuclear factor kappa B ligand (RANKL) and osteoprotegerin (OPG) system; and genetic alterations [13–15], however the invasive behavior of these lesions was not mechanistically defined.

Reports of surgical treatment of OM range from curettage to marginal or segmental resection with different rates of recurrence [16], at around 10–30%, especially when a more conservative approach is performed [17]. Until now, there is not a consensus about the best treatment protocol [18].Considering the importance on definition of treatment options for OM, the purpose of the present article is to report four cases of surgical management of OM. We also compared the data with a literature review and assessed the association between recurrence rates and surgical modalities.

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2. Material and methods

The construction of this article was divided in two stages cited bellow.

2.1. Stage 1: literature review

A review of the literature was carried out to retrieve studies on OM treatment modalities published from 1997 to 2017. The inclusion criteria were retrospective studies, case series and case reports. The following inclusion criteria were also used: (1) Population of patients of any age and sex with appropriately described history and submitted to surgical treatment of OM; (2) Cases of OM diagnosed by histopathological analysis; (3) Treatment modalities of OM specified and (4) Cases with description of the follow-up period and recurrence.

Exclusion criteria were studies in languages other than English, studies with no available full texts and with no specified sample and follow-up period < 12 months. PubMed (National Library of Medicine), Web of Science (Thomson Reuters) and Scopus (Elsevier), Cochrane Library and Medline Ovid electronic databases were examined to identify studies that could be included. The search was undertaken in March 2017 using the following descriptors "*Odontogenic Myxoma*", "*Treatment*". The retrieved references were exported to the EndNote software (Thompson Reuters, New York, NY, USA). After removal of duplicates, the selection of the studies was performed in two phases. In phase 1, titles/abstracts that met the eligibility criteria were included. If a title/abstract provided insufficient information for a decision about inclusion/exclusion, the full text was obtained and assessed in phase 2. Those who met the eligibility criteria were also included.

2.2. Study selection

The electronic searches yielded 907 references. Following the removal of 61 duplicates, inclusion and exclusion criteria were applied on 846 references. 26 articles reporting 66 cases of OM were selected and included in this review. No reference that met the eligibility criteria was identified in the hand searches. The flowchart depicts the search and the selection process (Fig. 1).

2.3. Data extraction and items

The following data were extracted from the articles included in the literature review: author and year of publication, number of cases reported, participants' gender and age, anatomical location of OM, treatment modalities, recurrence rates and follow up period. These studies and our case series were included in a table and the data were compared (Table 1). Conservative treatment (CT) included: curettage or enucleation associated or not with adjuvant therapy (peripheral osteotomy, cryotherapy). Radical treatment (RT) included marginal and segmental resection.

2.4. Stage 2: case reports

We also presented four OM cases from Clinical Hospital of the Federal University of Minas Gerais submitted to an incisional biopsy to confirm the diagnostic and then treated as described below.

2.4.1. Case 1 - E.F.R.O

A 22-year old male patient was referred for an evaluation of a mandible lesion. The patient looked for a dentist with a complaint of dental mobility. After radiographic examination the patient was referred to our service for evaluation. Extraorally, he presented a slightly facial asymmetry at the right submandibular region. Intraorally, he presented a buccal swelling at the right mandibular ramus, associated with dental mobility of both ipsilateral inferior third and second molars (Fig. 2A). Cone Beam Computerized Tomography (CBCT) revealed a hypodense, multilocular, poorly delimited image, at the right mandibular angle and ramus, causing tooth displacement and radicular resorption (Fig. 2B). After incisional biopsy, histological examination was consistent with the diagnosis of OM. Segmental resection was performed under general anesthesia. The whole grey-white was entirely removed, without fragmentation (Fig. 2C). Peripheral osteotomy was used as adjuvant therapy. The choice for segmental resection as a treatment modality, in this case, was based on the lesion size. A reconstruction plate (2.4 mm) was used to restore the mandibular contour (Fig. 2D). The patient recovery was uneventfully and 29 months after the procedure there is no clinical and/or radiographic signs of recurrence. Besides that, postoperative x-ray revealed considerable dimensions of neoformed bone. He will be submitted to a reconstructive surgery, followed by dental rehabilitation.

2.4.2. Case 2 – M.F.M

A 28-year old male patient was referred by another professional, after a routine radiography revealed a radiolucent image on the right mandibular angle. The patient was asymptomatic and systemically presented controlled diabetes. Clinically there were no signs of pathology and no facial asymmetry (Fig. 3A). On CBCT was possible to observe a hypodense, unilocular, poorly defined lesion, causing cortical erosion and the displacement of the right inferior third molar (Fig. 3B). The diagnosis of OM was achieved after incisional biopsy and the curettage of the lesion was conducted under general anesthesia. During the surgery, the lesion was removed in multiple fragments. Peripheral osteotomy was used as adjuvant therapy. The inferior border of the mandible was preserved despite its reduced thickness. After 10 months the patient returned with no complaints, but with tomographic signs of recurrence. Since the conservative treatment adopted as the first choice did not result in cure, the recurrent lesion was removed with security margins of approximately 10 mm under general anesthesia (Fig. 3C). There are no signs of recurrence 24 months after the second procedure.

2.4.3. Case 3 – V.G.S

A 29-yeard old female patient looked for dental treatment with a complaint of tooth pain and swelling at the maxillary left buccal gingiva. Another professional asked for an x-ray and referred the patient. Clinically, she presented a facial asymmetry on the left side of the face, with ocular dystopia. Intraorally it was observed a swelling of both buccal and palatine cortical of the left maxilla (Fig. 4A). Tomographic examination revealed a mixed image, measuring approximately 50 mm, on left side of the maxilla, causing displacement of the orbital floor and tooth displacement, associated with expansion of both buccal and palatine cortical (Fig. 4B). The patient was referred for an ophthalmological evaluation and no alterations were observed. The diagnosis of OM was achieved after incisional biopsy and the lesion was resected with security margins under general anesthesia (Fig. 4C), through an extraoral approach (Weber-Fergusson access). Despite the aesthetic impairment, we choose for segmental resection considering the anatomical localization of the lesion, which would make it difficult to perform more conservative approach. With the goals of reconstruct the orbital floor to give support to the ocular globe, a titanium ocular mesh was fixed at the residual infra-orbital border. The patient recovery was uneventfully and 24 months after the procedure there is no clinical and/or radiographic signs of recurrence. Ocular movements are present and no visual acuity was lost.

2.4.4. Case 4 – F.A.F

A 21-year-old male patient sought for the Service when he was 13 years-old. He was referred for evaluation of an asymptomatic swelling in the maxilla, with evolution time of 4 months, according to his mother report (Fig. 5A). At that occasion on physical examination, it was observed the presence of an asymptomatic swelling, on the anterior region of the maxilla, firm to the touch and covered by normal mucosa. A computed tomography exam was requested and revealed the presence

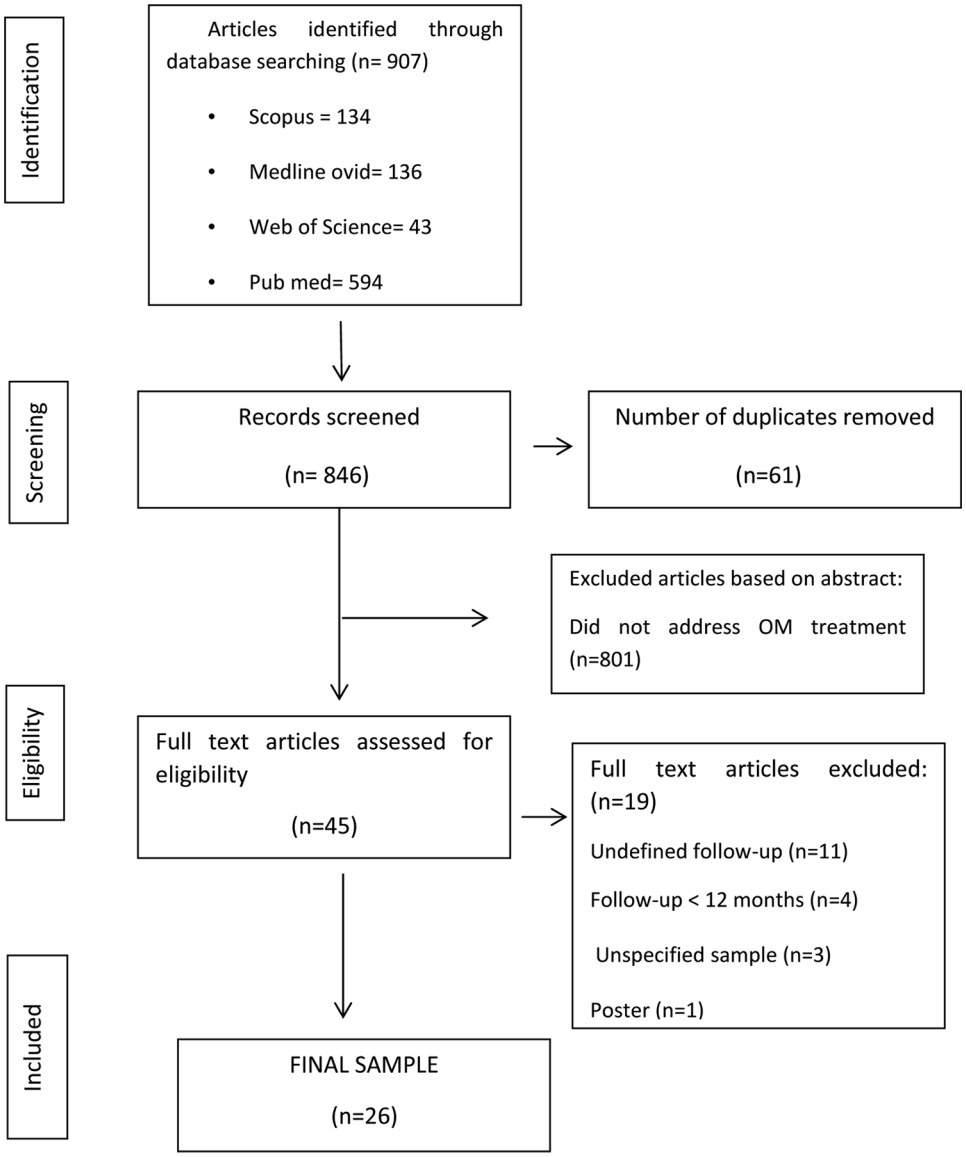

Fig. 1. Flowchart of the literature review. The process of literary search was organized in the four phases. The final sample consists of 26 articles about OM treatment modalities published in the last twenty years.

of a mixed poorly-defined lesion on maxilla, extending from the deciduous first right upper molar to the upper left deciduous canine (Fig. 5B). Incisional biopsy was performed under local anesthesia and histopathological examination confirmed the diagnosis of OM. The patient underwent a first surgical procedure under general anesthesia aiming the enucleation of the lesion. The lesion was removed in fragments due to its fragile consistency (Fig. 5C). The enucealtion were performed considering patient's age. After 8 years of follow up, the patient had no clinical or imaging signs of recurrence. Thus, a prosthetic rehabilitation was proposed, aiming first the reconstruction of atrophic maxillary ridge with a free autogenous bone graft, from the anterior iliac crest and insertion of dental implants four months after the reconstruction. Six months after implants placement, the prosthetic treatment was completed. Eight months later, the patient currently is rehabilitated morphological, functional and aesthetically, with no signs of recurrence of the lesion.

3. Results

3.1. Literature review

The process of literary search has been transformed into a flowchart (Fig. 1) and consisted of 26 papers containing 66 cases that describe surgical management of the OM. The selected articles were organized into a chart and related to the type of treatment performed and their corresponding recurrence rates (Table 1).

3.2. Clinical features

Considering the gender, OM was observed in 35 females, in 28 males and 3 cases do not specify patient's gender. The mean age of OM occurrence was 26.3 years. It was not possible to define a site predilection, since 35 cases were in the maxilla and 31 in the mandible. In our case reports (n = 4), the mean age of OM occurrence was 23 years, we neither find a gender or site predilection, 2 patients were male and 2 were female and 2 cases occurred in the maxilla and 2 in the mandible.

Table 1
Cases of OM included in the article.

Study	Treatment	Treatment Modality	Localization	Cases	Recurrence	Follow-up (years)
Rotenberg et al. [19]	Marginal resection	RT	Mx	5	No	2-14
Halfpenny et al. [20]	Condilectomy	RT	Md	1	No	3
Liu et al.4 [21]	Maxilectomy	RT	Mx	1	No	1
Murphy et al. [22]	Segmental resection	RT	Mx	1	No	2
Kansy et al. [23]	1: enucleation 2: hemimaxilectomy 1: marginal resection + hemimaxilectomy	1:CT, 3:RT	3:Mx, 1:Md	4	Yes (2: RT)	2-8
King et al. [24]	Enucleation + cryotherapy	CT	Mx	2	No	1.5 - 2
Boffano et al. [18]	3: Enucleation + curettage 7: Segmental resection	3:CT, 7:RT	8:Md, 2:Mx	10	No	1 - 13.5
Leiser et al. [11]	3: Segmental resection	RT	2:Mx, 1:Md	3	No	5
Toller et al. [25]	Curettage + peripheral osteotomy	CT	Mx	1	No	2
Kawase Koga et al. [26]	Enucleation + curettage	CT	Md	1	No	10
De Melo et al. [27]	Segmental resection	RT	Md	1	No	1.5
Rocha et al. [28]	Curettage + cryotherapy	CT	Md	1	No	10
Goel et al. [29]	Segmental resection	RT	Md	1	No	1
Lahey et al. [30]	Segmental resection	RT	Md	1	No	2
Zanetti et al. [31]	Marginal resection + curettage	RT	Mx	1	No	5
Andrews et al. [32]	4: Marginal resection 1: Incomplete excision 1: Debridement	4:RT, 2:CT	4:Md, 2:Mx	6	Yes (2:CT)	1.5- 6
Chaudhary et al. [33]	10: Enucleation + curettage 3: Resection	10:CT, 3:RT	9:Mx, 4:Md	13	Yes (2:CT)	6
Chiodo et al. [34]	Segmental resection	RT	Mx	3	No	2-5
Wachter et al. [35]	Marginal resection	RT	Mx	2	No	2
Souza et al. [36]	Segmental resection	RT	Md	1	No	6
Mittal et al. [37]	Enucleation + curettage	CT	Md	1	Yes	3
Reddy et al. [38]	1: Surgical excision 1: Segmental resection	1:CT, 1:RT	Md	2	No	2
Sarode et al. [39]	Enucleation + peripheral osteotomy	CT	Md	1	No	1
Shivashnkara et al. [40]	Enucleation	CT	Md	1	No	1
Guo et al. [41]	Segmental resection	RT	Md	1	No	1
Zainine et al. [42]	Marginal resection	RT	Mx	1	No	2.5
Case 1	Segmental resection	RT	Md	1	No	2.4
Case 2	Curettage + peripheral osteotomy	CT	Md	1	Yes	2
Case 3	Segmental resection	RT	Mx	1	No	2
Case 4	Enucleation	CT	Mx	1	No	8

Mx: maxilla; Md: mandible; RT: radical treatment; CT: conservative treatment.

3.3. Treatment modalities X recurrence

About treatment modalities, conservative treatment (n = 24) included: enucleation (n = 6), enucleation + curettage (n = 14), enucleation + peripheral osteotomy (n = 1), enucleation + cryotherapy (n = 2) and curettage + cryotherapy (n = 1). Aggressive modalities (n = 42) included marginal (n = 13) or segmental resection (n = 29). Recurrence was found in seven cases (10.6%), in which 2 of these were treated by aggressive treatment modalities. The other five ones were related to conservative management of the tumor.

In our case series, two patients underwent conservative treatment: enucleation (n = 1) and curettage + peripheral osteotomy (n = 1) and other two underwent aggressive treatment modality (n = 2) that consisted of segmental resection. Recurrence was found in 1 case, treated by conservative modality (curettage and peripheral osteotomy). It could be assigned to the fragile consistence of the tumor. A second surgery was performed and the choice was for marginal resection, and the patient remains free of disease for 24 months.

Considering patients in the review and our ones, we found 70 patients. In this sample (n = 70), recurrence was presented in 8 cases (11.42%). Whereupon, 43 patients (61.42%) underwent to radical treatment in which 2 cases (4.65%) presented recurrence and 27 patients (38.57%) underwent to conservative modalities, in which 5 cases (18.51%) presented recurrence. This data were analysed according to Fisher's exact test in a two tale contingency table which revealed a non-statistically significant difference (p = 0.060).

4. Discussion

Since its first report in the literature by Thomas in 1954, still there is no consensus about surgical management of OM. OM can be treated conservatively or radically and the choice will depend on lesion size, age of the patient, previous treatment and history of recurrence. To determinate if there is a best treatment modality for OM, we performed

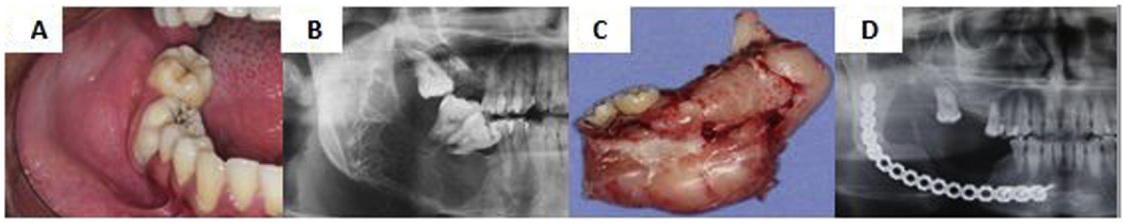

Fig. 2. Case 1 general features. A: The patient presented a buccal swelling at the right mandibular ramus. B: Radiographic image revealed a hypodense, poorly delimited image at mandibular right posterior body and ramus. C: after OM final diagnosis, segmental resection was performed under general anesthesia. D: A reconstruction plate (2.4 mm) was used to restore the mandibular contour.

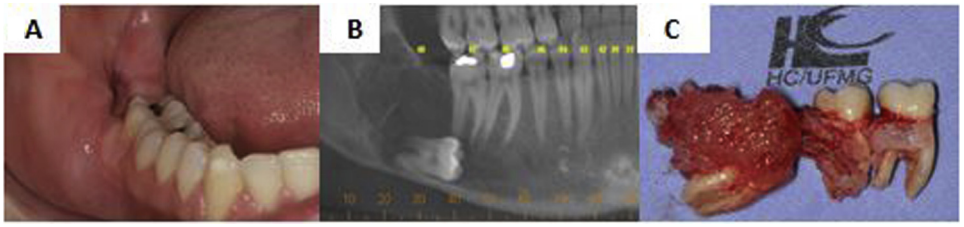

Fig. 3. Case 2 general features. A: The patient did not present any clinical alterations. The element 48 was absent. B: Cone Beam computed tomography revealed a hypodense unilocular lesion causing the displacement of the right inferior third molar. C: Marginal resection after OM recurrence.

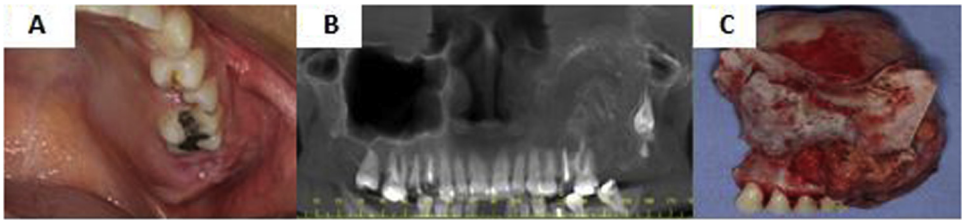

Fig. 4. Case 3 general features. A: The patient presented a swelling at the maxillary left buccal gingiva. B: Tomographic examination revealed a mixed image, measuring approximately 50 mm, on left side of the maxilla, causing displacement of the orbital floor and tooth displacement. C: The lesion was resected with security margins under general anesthesia, through an extraoral approach.

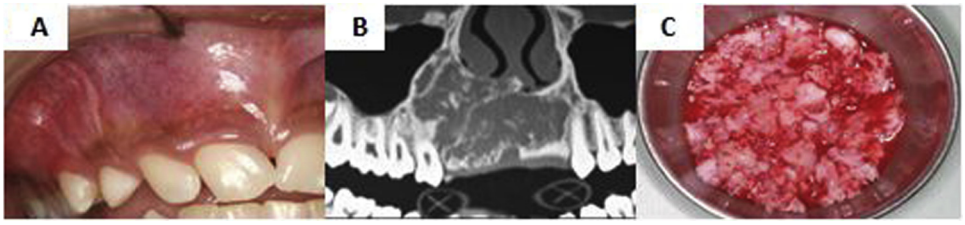

Fig. 5. Case 4 general aspects. A: Clinical examination showed an asymptomatic swelling in the anterior maxilla. B: Tomographic evaluation showed the presence of a mixed poorly-defined lesion on maxilla, extending from the deciduous first right upper molar to the upper left deciduous canine. C: The lesion was removed surgically in fragments due to its fragile consistency.

a critical review in the literature to report treatment modalities with its respective recurrence rates. We additionally reported four OM cases treated in our institution.

Considering the lesion size, Boffano et al [18], recommended a conservative treatment for small lesions (diameter less than 3 cm) consisting of enucleation/curettage and segmental resection with immediate reconstruction for larger tumours. Andrews et al [32], considered that conservative approach should be indicated for any lesion in close proximity to vital structures, especially in young patients. Localization of tumour, particularly in paediatric population is another important factor in determining the excision's extent to follow a less radical approach to limit transfacial access, surgical morbidity, and potential growth disturbance [33]. Therefore, it is important to balance the use of the radical approach with maintaining the presence of vital or uninvolved structures to preserve function as fully as possible [20]. An alternative adjuvant approach for enucleation and curettage includes peripheral osteotomy to remove a circumferential margin of bone around the tumor [35]. This adjuvant approach has a lower associated morbidity, but only can be considered in cases with sufficient bone support [43].We presented a case of a young patient (case 4), where a surgical conservative approach was performed. The maintenance of palatine bone was fundamental, permitting the delayed rehabilitation of our patient.

OM has a recurrence rate between 10 and 43%, according to Liu et al [21], in a study published in 2014. Regarding previous treatments and recurrent lesions, the majority of the studies agree on the choice for more radical treatment. The recurrence rate after simple enucleation and curettage has been reported to be as high as 25% [26], and appears to have been described over 30 years after original surgery [20]. According to Murphy et al [22], to prevent recurrence, complete surgical resection with a 1 cm bony margin is advocated. If the lesion has less than 5 cm, it can be reconstructed immediately using bone graft or buccal fat pad in maxilla whereas the larger defects of size more than 5 cm require prosthetic reconstruction by obturator in maxilla and reconstruction plate followed by immediate or delayed vascularized fibular free flap are required [37–42].

The unencapsulated and infiltrative nature of OM can predispose to leave remaining fragments in the surgical wound. However, the well delimited and solid nature of the tumor can contribute to low recurrence rates. We believe that OM should be treated by means of more conservative curative surgery whenever possible, especially when supporting techniques are available (cryotherapy, peripheral osteotomy and chemical cauterization with Carnoy's solution). This finding was similar to that found in the case that was submitted to enucleation and curettage in our service (case 4). This less aggressive approach can avoid extensive surgical defects and physical, functional or psychological sequels and still facilitate the rehabilitation process.

With the purpose of minimizing relapses, when the bone involved by tumor is inviable to reconstruction procedures and the extension of the lesion does not contraindicate this treatment option, surgical resection with a safety margin is recommended [22–24,1–11].

Our analysis of recurrence comparing radical with conservative treatments revealed no significant difference. This finding would encourage adopting conservative modalities. However, we observed a tendency to higher recurrence when OM was conservatively treated. Moreover, due to low number of analyzed cases and heterogeneity of sample, data should be interpreted with caution. The importance of follow up in all studies is unanimous. According to some authors, two years is the most likely time for recurrence [11–31]. Halfpenny et al [20], in 2000, related that recurrence has been described 30 years after original surgery. In our department, our protocol involves a minimum follow-up period of 10 years. However, reconstruction and rehabilitation procedures should be offer to patient as soon as the wound repair is detected.

5. Conclusion

When analyzing the management of odontogenic myxoma adopted in the last 20 years and their respective forms of relapse, we conclude that there was no statistically significant difference when comparing conservative therapeutic options with radical ones. This finding would encourage adopting conservative modalities with adjuvant therapies

without forget that we have an obligation to offer the patient a better chance of healing. A strict follow-up should not be overlooked.

Ethical approval

Not required.

Conflict of interest

There is no conflict of interest in this article. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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