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Management techniques of ameloblastoma: a literature review

Técnicas de tratamento do ameloblastoma: uma revisão de literatura

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ABSTRACT

Ameloblastoma is a benign neoplasm essentially composed of epithelial tissue that has an invasive and infiltrative behavior at local level with a high recurrence rate. The prevalence of tumors and oral cysts is 1%, and the prevalence of odontogenic tumors is about 11%. The etiology is not yet fully known; however, one of the most accepted theories is that the lesion starts developing from remaining cells of the dental lamina, reduced enamel epithelium, Malassez's epithelial rests, or even from a basal cell layer of the epithelium surface. The literature does not report sex-and ethnicity-related occurrence; however, it is known that the most affected anatomical region is the mandible. It is essential to study oral lesions with the purpose of promoting early diagnosis and the most conservative intervention possible. This way, this study is a literature review of works published between 2006 and 2014 conducted to find the existing protocols for the treatment of ameloblastomas.

Indexing terms: *Ameloblastoma. Dentistry. Protocol. Therapeutics.*

RESUMO

O ameloblastoma é uma neoplasia benigna formada essencialmente de tecido epitelial que embora apresente benignidade tem um comportamento invasivo e infiltrativo a nível local, apresentando também o inconveniente de uma elevada taxa de recidiva. Sua prevalência é de 1% dos tumores e cistos orais e de cerca de 11% dos tumores odontogênicos. Ainda não se conhece totalmente a sua etiologia, contudo uma das teorias mais aceitas é que a lesão se origine de células remanescentes da lâmina dental, do epitélio reduzido do esmalte, restos epiteliais de Malassez, ou mesmo de uma camada de células basais componentes do epitélio de superfície. Na literatura não se encontra relatos de predileção quanto ao gênero ou etnia, mas sabe-se que a região anatômica mais acometida é a mandíbula. Sabendo-se da importância de se pesquisar e conhecer as lesões bucais, visando o seu diagnóstico precoce e intervenção mais conservadora possível, foi realizada uma revisão de literatura entre os anos de 2006 a 2014 com o objetivo de verificar os protocolos existentes para o tratamento dos ameloblastomas.

Termos de indexação: Ameloblastoma. Odontologia. Protocolo. Terapêutica.

INTRODUCTION

Ameloblastoma is a benign neoplastic lesion of the maxilla characterized by slow and usually asymptomatic growth[1]. When it is not diagnosed and evolves to a more advanced level, signs such as change of position, shift and/or mobility of next teeth, root resorption, and even paresthesia[2]. It can cause erosion of bone tissue, promote invasion into soft tissues, and appear in the future with cortical bone expansion[3].

There are four types of ameloblastoma according to the classification of the World Health Organization, namely: solid/multicystic; unicystic; peripheral; and desmoplastic. The variables accepted for treatment are: age; infiltration potential; affected site; radiographic aspect; and prognosis[4].

When proper diagnosis is carried out, it is crucial to establish a good treatment plan based on clinical and imaging examinations. In addition, it is essential to perform complementary tests, such as computerized tomography and radiographs[5].

These lesions have a unique clinical behavior; however, controversy about the choice of treatment is very common. There are several reports of various treatment methods for ameloblastomas, ranging from the most conservative to the most radical. Example are: curettage;

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cryotherapy; removal associated with cryotherapy; marsupialization; electrocauterization; sclerotherapy; and radiotherapy.

One of the most reported techniques is complete surgical removal of the lesion, including the extension of a security margin with at least 1- to 2-cm thickness to reduce the risk of recurrence[6-7]. There has been growing preference for more conservative methods over time, because radical procedures entail major problems for the patients. The disadvantages of radical methods are chewing problems, dysfunction of mandibular movements, and noticeable mutilation including facial deformity[8].

It is crucial to enhance and enrich knowledge by means of which the professionals will be aware of the largest possible number of procedures, thus expanding the options for choosing the most appropriate therapy for the patients. Therefore, the present study was conducted in order to bring together the information of the literature about treatment options for ameloblastomas. The purpose was to gather the knowledge dispersed in different productions and facilitate readers' access to information.

This is a cross-sectional study and the literature review focused on the topic "treatment techniques for ameloblastoma". The data were collected from scientific articles published in reliable databases, such as: MEDLINE; SciELO; BIREME, Portal de Periódicos CAPES/MEC; and BBO. For the selection of the best publications, we used keywords in Portuguese and English, namely: protocolo; ameloblastoma; odontologia / protocol; ameloblastoma; dentistry. The selected articles had been published between 2006 and 2014. Initially, we found 57 articles that contained the keywords used in the search. After a careful selection, 36 articles were used in this literature review, because they contained the management techniques that we wished to address in the present study.

Literature review

According to the World Health Organization, ameloblastoma is a benign lesion of follicular or plexiform aspect with a fibrous stroma. It is usually characterized as a benign epithelial odontogenic tumor with no ectomesenchymal element. It also has a local invasive behavior and a high recurrence rate[9].

With respect to its pathogenesis, the literature reports that this lesion probably develops from residual cell proliferation of the enamel organ. It can also arise from the evolution of epithelium cells of an odontogenic cyst, as well as from the basal layer of the oral mucosa[10]. As for the profile of the patients, ameloblastoma makes no sex distinction; however, regarding age, there is a greater occurrence in patients aged 30 to 40 years[5].

With respect to the site affected, the lesions occur more commonly in the mandible. This fact has been reported to be four times greater when compared to the occurrence in the maxilla. The most affected regions are the mandible body and the ascending branch with 70 and 20% of the cases, respectively[11]. Still, 10% of the cases occur in the maxilla, and the posterior region is involved in 47% of patients; whereas, on average, the maxillary sinus and the nasal cavity floor are involved in 15% of the cases. The mandibular premolar and maxillary canine regions are affected in 18%, of the cases, and the palate is only affected in 2% of the cases[12].

Ameloblastomas have the ability to expand, which is very dangerous for the patients, since they usually occur in an asymptomatic and slow way, and they may also invade neighboring structures[13]. When an ameloblastoma evolves and reaches advanced stages, it acquires destructive capabilities. It can affect the tissues and even cause facial dissymmetry, pain, occlusal disorders, otalgia, ulcerations, paresthesia, and compromise dental health. There are also reports in the literature about a propensity of ameloblastomas to transform into malignant lesions, even though this event is very rare. Due to the absence of signs and symptoms during the first stages, early diagnosis of the lesion is rare. Early diagnosis often occurs because ameloblastomas are found during routine exams or those indicated for other procedures[14].

A fundamental step to choose the best treatment for ameloblastomas is the identification of the type of lesion, namely: peripheral; unicystic; multicystic; and even solid and desmoplastic[6].

Unicystic ameloblastomas are very similar to dentigerous cysts in both clinical and radiological aspects, especially when the ameloblastoma is associated with retained teeth[11]. This similarity is so strong that, many times, it is possible to differentiate them just by means of a histopathological examination, expecting the presence of a cystic cavity totally or partially covered by ameloblastic-type epithelium[14]. It has also been reported that some ameloblastic lesions may exhibit nodules within the cavity[13].

Even after the diagnostic hypothesis indicate a unicystic ameloblastoma, it is important to determine the subtype, which depending on the microscopic aspect can be: luminal; intraluminal; or mural[15]. A luminal

lesion exhibits a layer of fibrous tissue totally or partially covered by ameloblastic epithelium[16]. On the other hand, an intraluminal unicystic ameloblastoma exhibits characteristics similar to those of the plexiform type, especially due to the presence of projections of epithelium toward the cavity[13]. Finally, the mural lesion exhibits invasion of the fibrous tissue, where groups of epithelial cells derived from the parenchyma of the lesion reach the surrounding bone tissue. It is worth noting that unlike the other two types, this one requires a more invasive approach due to their increased risk of recurrence[14].

Through a radiographic exam, an ameloblastoma is observed as a single or multiple radiolucent lesion. It has clearly defined edges and may or may not exhibit sclerotic margins. It has been often reported in association with retained teeth[2].

An efficient clinical and imaging assessment is very important to determine the best treatment, given that unilocular cases are less aggressive. These cases have less chance of recurrence, thus allowing dental surgeons to perform a less invasive surgery. For example, they may choose enucleation and curettage. On the other hand, multilocular ameloblastomas require a more aggressive treatment to promote lesion resection, including security margins. This procedure often requires the reconstruction of the bone segment due to the amount of tissue removed[17]. Often, surgeons choose the combination of conventional surgery and ancillary methods, such as the application of Carnoy's solution, cryotherapy, or diathermy, in order to reduce the risk of lesion recurrence[3].

A desmoplastic ameloblastoma is characterized by a large amount of collagen in its stroma, which is permeated by ovoid-shaped islets, as well as strands of epithelial tumor cells of odontogenic origin[18]. This type of lesion usually occurs in the maxillary anterior region. A radiographic exam will show that it is very similar to a benign fibro-osseous lesion, but with more diffuse edges. These characteristics pose a problem at the time of planning the treatment, because it is difficult to establish the extension of the surgery, especially when there are signs of a more aggressive behavior[4].

A solid or multicystic ameloblastoma has a greater tendency to infiltrate into neighboring tissues. This characteristic raises the risk of lesion recurrence after the surgery, thus requiring a fast and accurate approach[7]. When multicystic ameloblastomas are submitted to radiographic examinations, they are usually radiolucent and multilocular. They are described in the literature as similar to "honeycombs" or even "soap bubbles". They can cause dental movements if they are too close to these structures, in addition to promoting root resorption or perforations on the lamina dura[16].

Methods of diagnosis

The most common method for detecting these lesions consists of imaging examinations. The tests include panoramic radiographs, computerized tomography imaging, and magnetic resonance imaging. These are indicative and guiding tests and histopathological examinations provide the definitive diagnosis.

Among the many imaging tests, computerized tomography is an important ally for the assessment of possible ameloblastomas. This test allows visualizing the cortical margins, measuring the extension of the lesion, and the possible involvement of neighboring structures. It also enables obtaining images without risk of overlapping or distortion errors[19-20].

Some of the pathologies that should be taken into consideration in the differential diagnosis of ameloblastomas are cherubism, keratocystic odontogenic tumor, myxoma, and central giant cell lesion, among others. This way, a reliable diagnosis cannot solely be based on imaging examinations. It requires a much more complex assessment with joint interpretation of clinical examinations and histopathological analyses.

When a histopathological examination is performed, it is necessary to consider some criteria that indicate the occurrence of ameloblastomas. Among them, it can be mentioned the presence of islets, nests, and strands composed of ameloblastic epithelial cells associated with a fibrous stroma. Ameloblastomas can be observed exhibiting different patterns, such as follicular and plexiform, which are the most common, although there are also reports of rarer types, such as acanthomatous with granular and basal cells[21].

It was observed that the most common pattern is the follicular, representing 64.9% of the cases studied. The plexiform type occupies the second place with 13%, followed by desmoplastic with 5.2%. The acanthomatous type was the least prevalent, with an occurrence of 3.9%. It is worth noting that these histological changes did not influence the clinical or biological behavior of the lesion and the degree of invasiveness or predisposition to the occurrence of metastases, which were only reported as differentials for diagnostic and research purposes[22].

Treatments

The choice of the best therapy is a very important step and should always be focused on the elimination of the lesion, taking into account the morbidity that the method chosen will cause, as well as the influence that it will have on the life and rehabilitation of the patients[1]. There are many options, ranging from curettage to extensive bone resections, and the reconstruction may be carried out using plates and pins[19].

Some factors to be considered are the histological subtype of the lesion and the presence of mural invasion. This specific situation requires a more aggressive surgery due to the high risk of recurrence[22-23]. Some studies suggest that marginal resection is the appropriate treatment for the minor lesions of multicystic ameloblastomas. However there are reports of recurrence in approximately 15% of the cases[24].

When the ameloblastoma reaches a larger volume, compromising a great portion of cortical bone and anatomical structures, there is a need of more invasive procedures, such as segmental resection with the discontinuity of the bone piece, even removing the periosteum and overlaying soft tissue[25].

A factor of great importance is the multidisciplinary work of the professional teams involved in the treatment of the patients, who should be prepared during the preoperative period by being informed that they will have to live with the changes caused by the radical treatment. The aesthetic and functional rehabilitation of a segmental defect in the mandible is a challenge to be overcome by a multiplicity of combined procedures[26].

An example of this preoperative organization is the creation of trial models, which can provide guided access to anatomical regions, thus ensuring a more conservative and safe procedure with simulation of osteotomies and resections. It is possible to plan several different surgeries and choose the best one before the patients undergo it[27].

Radical surgical procedures are those characterized by the removal of large pieces of bone tissue, which, in some cases, involve soft tissues in order to eliminate the pathology. Some examples are: composite tissue resection; mandibulectomy or maxillectomy, both partial or total; and great ablative treatments or procedures that cause extensive anatomical loss. These procedures often require future reconstructions by means of bone grafting or use of biocompatible materials[25].

A negative aspect of treatments for ameloblastoma is social disorder resulting from surgical procedures or pathological conditions that cause deformities. Some patients, for example, are only diagnosed when the disease is at an advanced stage, with facial disfigurement, serious functional losses, and difficulty in eating and performing oral hygiene. This fact makes the approach difficult, because these patients are socially segregated, or they even refuse treatment[28].

The collaboration and awareness of the patients are necessary, since they will need more rigorous attention and care regarding their oral health, a specific diet, follow-up, and periodical examinations[29].

Treatment according to age

A 13-year follow-up study conducted with teenagers from Kenya revealed that, fortunately, this lesion was uncommon in children. In their conclusions, the authors reported that a big specific challenge of the treatment in young patients could produce changes in facial growth. This way, extensive procedures should be avoided, whereas conservative procedures are recommended[21]. In 2010, it was suggested that conservative surgeries would interfere less in facial developing[30].

In 2013, the concept about the importance of avoiding extensive procedures was reinforced, since they posed the risk of compromising facial structures that were essential for skeletal and dental development. It was recommended that more radical procedures should be performed when the patients exhibited recurrence, and that follow-up of patients should be conducted for at least 20 years[28].

Treatment depending on the anatomical site

Another factor to be taken into consideration when choosing the surgical protocol is the anatomical site of the lesion, which directly influences on the pre-and post-assessment of treatment. Alvarenga et al.[23] assessed 48 cases of this lesion. In these patients, 94.8% of the lesions were located in the mandible. This result was in line with that found by França et al.[29] in a group of 40 patients, in which mandibular prevalence was 92.5%.

Though less frequent, maxillary ameloblastomas are more aggressive and have more unfavorable prognosis in addition to the greater difficulty in treating them. Unlike compact bones that compose the mandible, the maxilla has a much thinner bone tissue, which facilitates faster advancement of the lesion. In that case, it is possible that she lesion reaches the orbital sinus area and the cranial base. This way, a more radical approach is necessary when

choosing the initial surgery[31].

When choosing between a radical or a conservative surgery, it is necessary to consider the size and the site of the tumor, as well as the clinical aspect of progression, the proximity with anatomical structures, histological characteristics, and systemic conditions of the patients. In the case of maxillary ameloblastomas, the choice of radical procedures is almost certain, because the spongy characteristic of maxillary bone facilitates the spread of the lesion[29].

It is also essential to take into consideration the relationship between the lesion and neighboring structures. Some studies have reported a very high risk of lesion recurrence when simple curettage is performed, and recommended post-operative follow-up of the lesions in the maxilla for the rest of the patients' lives[20].

Treatment based on histological varieties

There is certain divergence among authors with respect to histological and radiographic assessments of ameloblastomas. There is a contradiction in the fact that ameloblastomas are reported as highly recurrent lesions, and many studies suggest a conservative treatment. Authors have also suggested that ameloblastomas can be more harmful than many neoplasms in the maxillofacial region, indicating a radical treatment for this pathology considering the consolidation of facial reconstruction techniques[32].

The authors suggest that the treatment of solid/multicystic ameloblastomas should firstly consider the assessment of anatomical barriers, such as cortical bone, periosteum, muscles, and mucous membranes that might have been affected. In case these tissues have been affected, there will be a need of resection. In addition, the authors propose that these resections should have a bone margin of at least 1.5 cm between the lesion and healthy tissue[32].

Bianchi et al.[4] have agreed with this ideas. Even if the treatment proposed for unicystic and peripheral ameloblastomas is similar to the treatment for dentigerous cysts by performing curettage therapy, these authors proposed a more radical intervention in cases of multicystic ameloblastomas. They have also indicated resection with security margin associated with vascularized grafting for more extensive lesions[4].

The management protocol proposed in 2010 recommends that unicystic ameloblastomas should initially be approached with marsupialization, followed by a careful radiological assessment to determine whether the lesion is decreasing. Otherwise, enucleation should be performed in the case of solid/multicystic ameloblastomas. On the other hand, in case of recurrence, the protocol indicates a radical treatment with security margins of 1.5 to 2 cm. Post-operative follow-up with annual assessments should be performed during the first five years, followed by biannual assessments during the next ten years[30].

The surgical methods are the prevailing procedures in the treatment of ameloblastomas. In many cases, the treatment includes total resection of the lesion and, in most cases, the resection is supraperiosteal with adequacy of free margins[33]. Desmoplastic ameloblastomas have some particularities, and more aggressive approaches are indicated in their treatment. They are usually treated by means of bone resection with security margins[34].

Treatment with auxiliary techniques

In order to reduce the extent of the surgery performed to remove the lesion, and decrease the risk of recurrence, some techniques can be associated with the final resolutive procedure[4]. Marsupialization is an example of a technique that has been used in some extensive ameloblastomas. This procedure is aimed at reducing the size of the lesion and ensuring a second surgical procedure which will be safe for anatomical structures. According to several authors, smaller and unicystic lesions can be treated with enucleation and curettage, which can also be associated with other ancillary procedures, such as peripheral osteotomy, application of Carnoy's solution, and cryotherapy[35].

Peripheral osteotomy is another example of complementary procedures especially performed in combination with enucleation and curettage. One of its advantages is the definitive removal of the lesion, avoiding arbitrary removal of bone margins and preserving the bone contour and stability of maxillamandibular bones. According to most protocols, an osteotomy with a maximum of three millimeters in extension beyond the visible bone margins is performed after removing the lesion by enucleation and curettage[26].

An alternative to facilitate the visualization of the lesion margins is to apply 2.5% gentian violet solution to the bone in order to dye the walls of the cavity. The inner part of the cavity is dyed with a cotton swab soaked in the solution. This way, during the osteotomy, it is possible to distinguish the edges of the portions that were treated or not[5].

There are other adjuvant treatments for ameloblastomas, such as radiotherapy, although this

technique has been discouraged by many authors and reported to cause hemifacial atrophy. Its use is restricted to cases in which the lesions are inoperable or exhibit a very fast growth pattern[34].

With respect to radiotherapy for the treatment of ameloblastomas, Koukourakis et al.[35] pointed out that this is an alternative that should only be used in certain patients with lesions in which resection margins cannot be performed and the tumors cannot be completely removed. These authors have also reported the need of multicenter studies for the determination of standards to be applied in the use of radiotherapy to treat these tumors.

Hammarfjord et al.[33] argue that radical resection is still the best method for ameloblastomas, because the results have shown the lowest rates of recurrence. Still, the authors recommend radical recession for cases in which the lesions are considerably extensive. However, they affirm that this procedure should be avoided in case that other healthy areas are unnecessarily involved.

In the same study, the authors mention the possibility of using a more conservative treatment for minor lesions. They claim that, even with recurrence rates of around 60%, it is possible to perform this conservative procedure and, if necessary, an extensive treatment can be subsequently performed when the recurrence is confirmed[33].

Cryotherapy is also an alternative procedure used to destroy possible cellular remains invisible to the naked eye, thus reducing the risk of recurrence. Through necrosis, this procedure eliminates possible cell infiltrations that would be unnoticed beyond the security margin, On the other hand, it has high cost and poses difficulty in handling and risk to healthy tissues[3].

In brief, ameloblastoma is one of the most worrying lesions that dental surgeons may have to deal with in their clinical practice. Even though it is a rare disease, it should be detected and diagnosed as early as possible. Given that this lesion is potentially expansive, destructive, and aggressive, it is essential that these professionals learn how to detect and treat it. They should also know the best treatment for the patients as soon as the lesion is detected.

The diagnosis in the early stages of the lesion is difficult, because it develops slowly and without apparent symptoms. Its clinical visualization is only possible when the lesion is at an advanced stage. It may be detected accidentally during routine exams or tests intended for other types of treatments. This way, the professionals should cogitate its existence at the time of performing differential diagnoses for other possible lesions[35].

A proper diagnosis can lead to an early intervention that will be very important for the patients, because, as described in the studies assessed, the type of lesion, extent, and involvement of neighboring structures are factors that have a strong influence at the time of choosing the type of treatment.

Treatment options vary with respect to how invasive they are. The number of surgical interventions and the approach adopted have specific indications and range from simple procedures to more radical surgeries, which can lead to facial deformities and functional disability in the patients.

It is essential that the chosen procedures result in the total elimination of the lesion, because it has a potential role for recurrence and progression to malignancies. This way, the professionals who deal with the cases should always balance the cost-benefit relationship to ensure the resolution of the problems. This relationship should be the least traumatic as possible for the patients, and the resolution option should always be the less invasive.

The surgical possibilities range from marsupialization and enucleation to radical resection. There is a consensus in the literature that although resection is destructive, it is the first choice for cases in which the lesion is at a very advanced stage. The advantage of this procedure is the removal of the ameloblastoma in a single surgical section, even though it poses the inconvenience of causing a significant loss in the patients.

When such removal may jeopardize important structures, such as the maxillary sinus or the mandibular channel, it is possible to choose a less invasive intervention with more than one surgical procedure, as is the case of marsupialization or decompression. These procedures will allow the regression of the lesion before its final removal. The lesion will stay apart from the structures that could be compromised and the advantage will be a smaller loss for the patients, even though it requires a longer period of time, careful follow-up, and there is a greater risk of infections between the surgical procedures.

Even with the purpose of avoiding recurrences of the lesion, it is possible to combine procedures such as cryotherapy or radiotherapy with the main intervention. Cryotherapy promotes the destruction of the cells infiltrated in neighboring tissues, and radiotherapy also has the function of removing cellular remnants.

Knowing the range of procedures that are available for the resolution of this issue, the professionals who assists patients with ameloblastoma should have the

sensitivity needed to consider the pros and cons. They should also consider the needs and possibilities of each patient, so that it is possible to draw the best plan that will solve the case with minimal tissue removal.

After an extensive review of the literature on treatments of ameloblastomas, we concluded that: (a) the best treatment for ameloblastoma is still its total resection, given that recurrence rates are low when this technique is used; (b) even though total resection of the lesion is the most appropriate treatment, it can lead to irreversible sequelae; (c) conservative treatments, such as decompression and marsupialization, have been proposed in the literature to avoid sequelae, followed by radical surgical treatment. The indication of conservative or radical treatments will depend on several factors, such as age, site of the lesion, histological type, extent, and involvement of neighboring structures; (d) a radical surgical treatment can be combined with techniques such as: vigorous curettage; peripheral osteotomy; resection followed by application of Carnoy's solution; resection followed by cryosurgery; and resection followed by electrocauterization, in order to further decrease recurrences; and (e) radiotherapy is only indicated for exceptional and extensive cases, in which the surgery would be mutilating, and unresectable lesions.

Collaborators

All authors participated in the preparation and revision of the article.

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