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THERAPEUTIC APPROACH TO AMELOBLASTOMA: REHABILITATION PROTOCOLS AND RECURRENCE CONTROL

ABORDAGEM TERAPÊUTICA DO AMELOBLASTOMA: PROTOCOLOS DE REABILITAÇÃO E CONTROLE DE RECIDIVA

ABORDAJE TERAPÉUTICO DEL AMELOBLASTOMA: PROTOCOLOS DE REHABILITACIÓN Y CONTROL DE LA RECIDIVA

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ABSTRACT

In the context of stomatology and head and neck surgery, ameloblastoma plays a prominent role. Although defined by the World Health Organization (WHO) as a benign entity, it exhibits biologically aggressive behavior, characterized by an infiltrative growth pattern and high recurrence rates, which demands an in-depth understanding of its pathogenic and clinical aspects to achieve a favorable prognosis. Ameloblastoma is an odontogenic neoplasm of epithelial lineage that, despite being histologically benign according to the WHO, displays a biological phenotype marked by aggressive medullary infiltration, progressive expansion, and elevated recurrence rates. The complexity of clinical management lies in the dichotomy between complete eradication of tumor margins and preservation of the functional and aesthetic integrity of the stomatognathic system. The analysis of contemporary therapeutic modalities indicates that the transition between conservative interventions and radical resections should be based on rigorous mapping of the histopathological subtype and the cortical extent of the lesion. In parallel, the integration of molecular biomarkers and immediate prosthetic reconstruction techniques redefines prognosis, enabling an approach that goes beyond strict oncological control. Clinical resolution and mitigation of tumor recurrence depend on individualized management, with particular attention to patient age and specific tumor biology. It is

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imperative that therapeutic outcomes be supported by longitudinal surveillance protocols and multidisciplinary rehabilitation, ensuring morphofunctional restoration and long-term preservation of quality of life.

Keywords: Ameloblastoma. Mandibular Neoplasms. Local Recurrence. Oral and Maxillofacial Surgery. Oral Rehabilitation.

RESUMO

No cenário da estomatologia e cirurgia de cabeça e pescoço, o ameloblastoma assume papel de destaque, embora definido pela Organização Mundial da Saúde (OMS) como benigno, comporta-se de maneira biologicamente agressiva, com padrão de crescimento infiltrativo e alta recidiva, o que demanda uma compreensão aprofundada de seus aspectos patogênicos e clínicos para um prognóstico favorável. O ameloblastoma configura-se como uma neoplasia odontogênica de linhagem epitelial que, embora histologicamente benigna, como afirma a OMS, exibe um fenótipo biológico caracterizado por infiltração medular agressiva, expansão progressiva e elevados índices de recidiva. A complexidade do manejo clínico reside na dicotomia entre a erradicação completa das margens tumorais e a manutenção da integridade funcional e estética do sistema estomatognático. A análise das modalidades terapêuticas contemporâneas evidencia que a transição entre intervenções conservadoras e ressecções radicais deve ser fundamentada em um rigoroso mapeamento do subtipo histopatológico e da extensão cortical da lesão. Paralelamente, a integração de biomarcadores moleculares e técnicas de reconstrução protética imediata redefine o prognóstico, permitindo uma abordagem que transcende o controle oncológico estrito. A resolução do quadro clínico e a mitigação da recorrência tumoral dependem da individualização da conduta, com especial atenção à idade do paciente e à biologia tumoral específica. É imperativo que o desfecho terapêutico seja sustentado por protocolos de vigilância longitudinal e reabilitação multidisciplinar, assegurando a restituição morfofuncional e a preservação da qualidade de vida a longo prazo.

Palavras-chave: Ameloblastoma. Neoplasias Mandibulares. Recidiva Local. Cirurgia Bucomaxilofacial. Reabilitação Bucal.

RESUMEN

En el ámbito de la estomatología y la cirugía de cabeza y cuello, el ameloblastoma ocupa un papel destacado. Aunque es definido por la Organización Mundial de la Salud (OMS) como una entidad benigna, presenta un comportamiento biológicamente agresivo, con un patrón de crecimiento infiltrativo y altas tasas de recidiva, lo que exige una comprensión profunda de sus aspectos patogénicos y clínicos para alcanzar un pronóstico favorable. El ameloblastoma se configura como una neoplasia odontogénica de estirpe epitelial que, a pesar de ser histológicamente benigna según la OMS, exhibe un fenotipo biológico caracterizado por infiltración medular agresiva, expansión progresiva y elevados índices de recidiva. La complejidad del manejo clínico radica en la dicotomía entre la erradicación completa de los márgenes tumorales y la preservación de la integridad funcional y estética del sistema estomatognático. El análisis de las modalidades terapéuticas contemporáneas evidencia que la transición entre intervenciones conservadoras y resecciones radicales debe fundamentarse en un riguroso mapeo del subtipo histopatológico y de la extensión cortical de la lesión. Paralelamente, la integración de biomarcadores moleculares y técnicas de reconstrucción protésica inmediata redefine el pronóstico, permitiendo un abordaje que

trasciende el control oncológico estricto. La resolución del cuadro clínico y la mitigación de la recurrencia tumoral dependen de la individualización de la conducta terapéutica, con especial atención a la edad del paciente y a la biología tumoral específica. Es imperativo que el desenlace terapéutico esté sustentado por protocolos de vigilancia longitudinal y rehabilitación multidisciplinaria, garantizando la restitución morfofuncional y la preservación de la calidad de vida a largo plazo.

Palabras clave: Ameloblastoma. Neoplasias Mandibulares. Recidiva Local. Cirugía Bucomaxilofacial. Rehabilitación Bucal.

1 INTRODUCTION

Ameloblastoma is defined as a benign odontogenic tumor of epithelial origin, characterized by locally aggressive behavior and a high propensity for recurrence (Gasparro et al., 2024). In addition, it is a tumor that can reach large proportions, which will possibly extend to the intracranial compartments, bringing several clinical implications (Amorcida et al., 2022). The locally aggressive character of ameloblastoma, evidenced by high recurrence rates, especially after conservative approaches, represents a central challenge in the surgical control of the disease and in the definition of appropriate therapeutic protocols (Gasparro et al., 2024; Armocida et al., 2022). Representing approximately 10% of all oral lesions, this neoplasm manifests predominantly in the mandible, especially in the body and mandibular angle regions (Xu et al., 2024), however, due to its aggressive local growth, it may extend to several regions, such as the skull base, paranasal sinuses, infratemporal fossa, pterygopalatine fossa, the parapharyngeal space, and the orbit (Amorcida et al., 2022). The 2022 World Health Organization (WHO) classification categorizes ameloblastomas into five main variants: conventional, unicystic, peripheral, adenoid, and metastatic, with the conventional type being the most frequent and biologically most aggressive (Quisiguiña-Salem et al., 2024). The estimated global incidence of ameloblastoma is approximately 0.92 cases per million inhabitants per year, mainly affecting individuals between the third and fourth decades of life, with a marked predilection for the mandible, responsible for about 80% of the cases described (Rayamajhi et al., 2022; Gasparro et al., 2024). This histopathological heterogeneity has direct implications for the therapeutic approach, since different variants of ameloblastoma have distinct patterns of invasiveness and risk of recurrence, requiring individualized approaches (Quisiguiña-Salem et al., 2024; Ouertani et al., 2024).

Among all cases, 53.2% are male and 46.7% female, occurring mainly in the third decade of life, impacting the patient's quality of life and health systems, requiring substantial resources for surgical interventions, long-term follow-up, rehabilitation, and continuous care (Gasparro et al., 2024). In this context, the predominance of ameloblastoma in young adults, associated with its locally destructive behavior, makes its functional, aesthetic, and socioeconomic sequelae more relevant, since it affects individuals in the middle of their productive phase and with longer life expectancy, reinforcing the need for therapeutic strategies that reduce the risk of recurrence without significant loss of function or quality of life (Gasparro et al., 2024).

Ameloblastoma commonly manifests as a painless swelling or expansion of the jaw, which is more frequently affected than the maxilla. This increase in volume tends to become progressively noticeable with tumor growth, which can lead to facial asymmetry. Although usually asymptomatic in the early stages, tumor enlargement can cause pain, discomfort, and dental changes, such as displacement and mobility, especially when there is involvement of adjacent structures (Gasparro et al, 2024). The indolent and often asymptomatic nature of ameloblastoma in the early stages contributes to late diagnosis, allowing the lesion to reach large dimensions before the intervention, which increases surgical complexity and, consequently, the risk of functional sequelae (Xu et al., 2024; Gasparro et al., 2024).

The differential diagnosis of ameloblastoma is complex, as various lesions and tumors of the mandible may exhibit similar clinical and radiographic aspects. Among the main pathologies that should be considered in the differential diagnosis are odontogenic keratocyst, dentigerous cyst, adenomatoid odontogenic tumor, and central giant cell granuloma (Gasparro et al, 2024). This clinical and radiographic overlap with other odontogenic lesions increases the risk of underdiagnosis and inappropriate initial approaches, particularly in single-member cases associated with impacted teeth, which can compromise disease control (Xu et al., 2024; Ouertani et al., 2024).

Although it is a slow-growing pathology and is often asymptomatic in early stages, progressive development can result in marked bone expansion, facial deformity, occlusal disorders, and pathological fractures (Xu et al., 2024). More severe cases, especially involving the maxilla, may present intracranial extension, invading the skull base and cranial fossae, representing a critical surgical challenge (Armocida et al., 2022). Therapeutic management is widely debated in the literature, establishing a dilemma between radical approaches, which seek to minimize recurrence, and conservative interventions, focused on functional preservation and the patient's quality of life (Gasparro et al., 2024).

Despite the extensive knowledge about the behavior and recurrence of ameloblastoma, a controversy persists between maximizing tumor control and preserving function, aesthetics, and quality of life. At the same time that radical approaches reduce recurrence, they impose greater morbidity, while conservative protocols favor functional and aesthetic rehabilitation, but at the price of a higher risk of recurrence. This dilemma

underpins the main therapeutic challenge of the disease and justifies an integrated analysis of treatment and rehabilitation protocols.

2 METHODOLOGY

The present study is a narrative literature review, structured with the purpose of synthesizing and examining contemporary scientific evidence on the therapeutic approach to ameloblastoma, with a focus on rehabilitation and recurrence. Data prospecting was based on the analysis of high-impact scientific articles, using the descriptors "Ameloblastoma", "Surgery" and "Treatment" as thematic axes. The documentary selection prioritized studies published in recent years that addressed surgical protocols, from conservative techniques such as decompression and enucleation to radical resections with safety margins. The inclusion criterion included fully available studies that directly discuss the central theme, while studies with low methodological rigor or without direct relevance to the proposed clinical management were disregarded. The analysis of the information followed a descriptive logic for the organization of the protocols and results observed.

3 RESULTS AND DISCUSSION

The invasive behavior of ameloblastoma is directly related to specific molecular alterations, highlighting mutations in the BRAF genes, especially the V600E mutation, and SMO, associated with the MAPK and Hedgehog signaling pathways, respectively. These mutations contribute to uncontrolled cell proliferation, bone resorption, and increased potential for tumor recurrence (Fuchigami et al., 2021). In addition, the interaction between tumor cells and the adjacent stroma plays a central role in the progression of ameloblastoma, favoring the remodeling of the extracellular matrix and the invasion of surrounding bone tissues, explaining, in part, the difficulty in complete eradication of the lesion by conservative methods (Fuchigami et al., 2021).

The analysis of the evidence indicates that the recurrence rate is the main differential factor between surgical modalities. Systematic reviews have shown that recurrence in conservative treatments (enucleation and curettage) is significantly higher, reaching up to 41% in the multicystic type, compared to about 8% in radical resections (Gasparro et al., 2024). For unicystic ameloblastoma, decompression followed by enucleation has shown favorable results , especially in children, where the capacity for

bone formation is high, where clinically and radiographically, it can present as a unilocular lesion, often associated with unerupted teeth, which can make it difficult to make the differential diagnosis with other cystic odontogenic lesions (Xu et al., 2024; Guo et al., 2022).

Radical treatments have a lower recurrence rate when compared to conservative procedures, but they imply a greater functional and aesthetic impact on the patient (Gasparro et al., 2024).

Despite the wide use of surgical intervention, there is still no consensus regarding the most appropriate therapeutic approach for the treatment of ameloblastoma. Different systematic reviews have discussed this controversy, evaluating outcomes such as tumor recurrence, impact on quality of life, and aesthetic and functional impairment (Gasparro et al, 2024).

In the field of molecular biology, specific mutations have been identified as drivers of tumor development. The BRAF V600E mutation is the most frequent, occurring in about 63% of cases, predominantly in the mandible (Quisiguiña-Salem et al., 2024; Fuchigami et al., 2021). The mutation in the SMO gene, on the other hand, seems to be more associated with lesions in the maxilla (Fuchigami et al., 2021). Understanding these signaling pathways has paved the way for molecular targeted therapies, such as the use of BRAF inhibitors (Vemurafenib and Dabrafenib), which have been shown to reduce tumor volume in cases of recurrence (Fuchigami et al., 2021; Quisiguiña-Salem et al., 2024).

The incorporation of combined therapeutic strategies has been progressively discussed as a promising alternative in the management of ameloblastoma, especially in extensive, recurrent, or localized cases in anatomically complex regions. Recent evidence suggests that the use of neoadjuvant targeted therapies, such as BRAF inhibitors in tumors carrying the V600E mutation, can promote a significant reduction in the volume of the lesion, allowing less mutilating surgical approaches and greater preservation of adjacent structures, without compromising oncological control. In this context, surgery is no longer an isolated intervention and becomes part of a staggered therapeutic protocol, in which the decision between marginal, segmental, or conservative resection is guided not only by clinical-radiographic criteria, but also by molecular and histopathological findings. At the same time, the planning of immediate reconstruction, by means of autogenous bone grafts, microvascularized flaps, or personalized prosthetic

devices, has demonstrated a positive impact on the early restoration of masticatory function, facial symmetry, and quality of life. Thus, the contemporary therapeutic paradigm of ameloblastoma moves towards an integrative model, in which tumor control, functional rehabilitation, and morbidity reduction are addressed simultaneously and in a personalized manner, reinforcing the importance of evidence-based protocols and specialized multidisciplinary action.

Histopathologically, unicystic ameloblastoma is subclassified into three distinct variants, based on the proliferation pattern and extension of the odontogenic tumor epithelium: luminal, intraluminal, and mural. In addition, the distinction is decisive for therapeutic planning, since it dictates the biological behavior of the lesion, the luminal and intraluminal variants, as they are confined to the epithelial lining without invasion of the fibrous capsule, are subject to conservative approaches (Ouertani et al., 2024). On the other hand, the mural variant is characterized by the infiltration of epithelial islands into the fibrous wall of the cyst, mimicking the aggressive behavior of solid or multicystic ameloblastoma, therefore, for this subtype, a radical therapy is recommended, involving marginal or segmental bone resection, followed by reconstruction procedures for morphofunctional rehabilitation of the patient (Ouertani et al., 2024).

Rehabilitation in pediatric patients requires protocols that consider continuous facial growth. Techniques such as marsupialization combined with orthodontic treatment have allowed the preservation and eruption of impacted teeth in the tumor, avoiding early mutilations (Guo et al., 2022). In selected cases of unicystic ameloblastoma, tooth replantation after conservative enucleation showed clinical success and healthy root development in long-term follow-up (Ouertani et al., 2024).

For cases with intracranial involvement, radical surgery with margins of 1.0 to 3.0 cm is recommended to ensure survival, given that recurrence in these areas can be fatal (Armocida et al., 2022). On the other hand, for intraosseous lesions that do not involve soft tissues, the conservative approach may be recommended as a first-line to optimize quality of life, as long as it is accompanied by a strict and frequent follow-up protocol (Gasparro et al., 2024). Recurrence control requires radiographic monitoring for long periods, and follow-up for up to 25 years is suggested (Quisiguiña-Salem et al., 2024).

The rehabilitation process after ameloblastoma treatment comprises multiple stages, starting in the immediate postoperative period and extending over weeks or months, depending on the complexity of the surgical procedure performed. The initial

phase involves tissue recovery and functional control, while the subsequent stages aim at the progressive restoration of mobility and strength of maxillomandibular structures, often with the aid of physical therapy and complementary therapies, when indicated.

In situations in which surgical treatment involves extensive resections, significant changes in masticatory function, speech articulation, and facial harmony may occur. In the absence of adequate rehabilitation planning, these changes tend to significantly compromise the patient's quality of life, as highlighted by Gasparro et al. (2024). Thus, it is essential that rehabilitation be carefully planned, considering the extent of the injury, the surgical technique employed and the individual particularities of the patient, in order to reduce the functional and aesthetic limitations resulting from the treatment.

With the adoption of appropriate rehabilitation protocols and continuous follow-up, many patients have a satisfactory recovery, with reestablishment of oral functions and improvement of the aesthetic aspect, enabling the return to daily activities and active social life. This aspect is especially relevant in view of the impact that surgical interventions can have on the stomatognathic system.

In cases addressed by conservative techniques, such as decompression, marsupialization, and enucleation, greater preservation of bone and dental structures is observed, which favors a more predictable and less invasive functional rehabilitation. These approaches contribute to the maintenance of anatomical integrity and facilitate the progressive recovery of oral functions.

Thus, post-treatment ameloblastoma rehabilitation protocols should be understood as a continuous process and integrated with global therapeutic planning. The coordinated action of a multidisciplinary team, involving surgeons, orthodontists, prosthodontists, and other health professionals, is essential to ensure morphofunctional recovery, long-term stability of results, and consistent improvement in patients' quality of life (Gasparro et al., 2024).

4 CONCLUSION

Contemporary management of ameloblastoma requires an individualized approach that balances oncological management and functional rehabilitation. The therapeutic choice should be based on the histological subtype and the extent of the lesion, opting for radical resections to minimize recurrences or conservative techniques in selected cases, always accompanied by prolonged imaging surveillance (Gasparro et

al., 2024; XU et al., 2024). The integration of molecular biomarkers opens up prospects for adjuvant targeted therapies (Quisiguiña-Salem et al., 2024). Multidisciplinary rehabilitation, planned from the outset, is crucial to restore function and quality of life (Gasparro et al., 2024). Therefore, optimal treatment overcomes the radical/conservative dichotomy, requiring patient-centered care, guided by integrated data, and performed by an interdisciplinary team. In more severe situations, such as intracranial extension, radical surgery remains the necessary standard (Armocida et al., 2025).

Ameloblastoma represents a benign odontogenic neoplasm with high biological and clinical impact, whose local aggressiveness, histopathological variability, and high potential for recurrence support the complexity of its therapeutic management. The analysis of contemporary evidence demonstrates that there is no single protocol capable of universally meeting the needs of patients, since the balance between oncological control, functional preservation and quality of life requires an individualized and multidimensional approach.

Radical resections offer greater safety in tumor control and reduction of recurrence, especially in multicystic subtypes, mural variants, and presentations with extension to critical structures. However, such conducts can result in significant aesthetic and functional morbidity, reinforcing the need for immediate rehabilitation planning and morphofunctional reconstruction. On the other hand, conservative interventions have been shown to be feasible in selected cases, especially in unicystic ameloblastoma and in young patients, as long as they are associated with strict and prolonged follow-up protocols.

The rehabilitation process is an essential pillar of the treatment, and should be started early and conducted by a multidisciplinary team, with the objective of restoring the patient's masticatory function, facial aesthetics and psychosocial insertion. Longitudinal surveillance is inseparable from therapeutic success, considering that the risk of recurrence can persist for decades, justifying systematic clinical-radiographic follow-up.

It is concluded that the therapeutic approach to ameloblastoma should transcend the binary between radicality and conservation, adopting an integrative model that combines diagnostic accuracy, biological control, functional rehabilitation and long-term monitoring. The consolidation of this paradigm depends on the incorporation of biomarkers, the refinement of risk stratification criteria, and the strengthening of

interdisciplinary action, with a view to more predictable results, lower morbidity, and better quality of life for the patient.

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