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CASE REPORT

Desafios no diagnóstico e tratamento do carcinoma ameloblástico: relato de caso

Challenges in the diagnosis and treatment of ameloblastic carcinoma: a case report

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ABSTRACT

Introduction: Ameloblastic carcinoma is a rare malignant odontogenic neoplasm, accounting for less than 2% of all odontogenic tumors. It exhibits aggressive behavior, metastatic potential, and poses significant challenges for early diagnosis, frequently being misdiagnosed as infectious processes. **Case report:** A 56-year-old male patient presented with spontaneous tooth fracture and persistent pain, progressing to submandibular swelling, purulent drainage, and a hardened mass in the mandibular angle. Computed tomography revealed extensive bone destruction and abscess formation involving the parotid, masticatory, and parapharyngeal spaces. Histopathological examination confirmed ameloblastic carcinoma, staged as T4bN1, with invasion of the maxillary sinus, external carotid artery, and cervical lymphadenopathy. Due to tumor unresectability, palliative hypofractionated radiotherapy and multidisciplinary follow-up were instituted. The patient survived for eight months after diagnosis. **Conclusion:** This case highlights the diagnostic challenges related to the insidious progression of ameloblastic carcinoma and its resemblance to infectious conditions, underscoring the importance of early recognition of atypical lesions and timely referral to specialized centers in order to expand therapeutic options and improve prognosis.

Keywords: Ameloblastic carcinoma; Mandible; Odontogenic neoplasms; Head and neck surgery; Otorhinolaryngology.

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RESUMO

Introdução: O carcinoma ameloblástico é uma neoplasia odontogênica maligna rara, responsável por menos de 2% dos tumores odontogênicos. Apresenta comportamento agressivo, potencial metastático e diagnóstico precoce desafiador, frequentemente confundido com processos infecciosos. **Relato de caso:** Paciente masculino, 56 anos, apresentou fratura dentária espontânea e dor persistente, evoluindo com aumento de volume submandibular, drenagem purulenta e massa endurecida em ângulo mandibular. A tomografia computadorizada evidenciou destruição óssea extensa e abscesso em espaços parotídeo, mastigatório e parafaríngeo. O exame histopatológico confirmou carcinoma ameloblástico, estadiado como T4bN1M0, com invasão do seio maxilar, carótida externa e linfonodomegalia cervical. Devido à inoperabilidade, optou-se por radioterapia hipofracionada paliativa e seguimento multidisciplinar. O paciente apresentou sobrevida de 8 meses após diagnóstico. **Conclusão:** O caso ilustra as dificuldades diagnósticas relacionadas à evolução insidiosa e à semelhança com quadros infecciosos, ressaltando a importância do reconhecimento precoce de lesões atípicas e do encaminhamento para centros especializados, a fim de ampliar as opções terapêuticas e melhorar o prognóstico.

Palavras-chave: Carcinoma ameloblástico; Mandíbula; Neoplasias odontogênicas; Cirurgia de cabeça e pescoço; Otorrinolaringologia.

Introduction

Ameloblastic carcinoma is a rare malignant odontogenic neoplasm characterized by the combination of histological features of ameloblastoma with malignant cytological characteristics and aggressive clinical behavior. It accounts for less than 2% of all odontogenic neoplasms and typically arises from a pre-existing ameloblastoma or, less commonly, de novo[1]. Its clinical presentation is insidious, usually manifesting as slowly progressive mandibular swelling, local pain, ulceration, or paresthesia, and it is often diagnosed at advanced stages[2,3].

Definitive diagnosis requires correlation among clinical, radiological, and histopathological findings. Radiographically, the lesion may appear as a uni- or multilocular lytic lesion with ill-defined margins and areas of bone destruction[1,2,4]. Histologically, an ameloblastic pattern associated with cellular atypia, frequent mitotic figures, and tissue invasion are key diagnostic markers. In many cases, immunohistochemistry is required to differentiate it from other malignant lesions of the region[5,6].

Treatment of ameloblastic carcinoma remains challenging, particularly in unresectable cases. Wide surgical resection with tumor-free margins is the treatment of choice when feasible. However, when the tumor invades vital structures or presents at an advanced stage, such as T4b, radiotherapy and palliative care become the main therapeutic strategies[1,2,4,5]. This report aims to describe a case of advanced mandibular ameloblastic carcinoma diagnosed in the context of a long-standing odontogenic infection, emphasizing the associated diagnostic and therapeutic challenges[6,7].

Case Report

A 56-year-old male patient was admitted to the Hospital das Clínicas of UNESP in August 2024, reporting spontaneous tooth fracture approximately 12 months earlier, associated with severe pain that impaired oral hygiene. Approximately 14 days prior to admission, he noted the development of swelling in the left submandibular region, involving cervical levels IIa and IIb, with a saccular shape and cystic consistency, which progressed after five days to spontaneous purulent drainage (Figures 1 and 2).

Concurrently, the patient noticed a hardened mass measuring approximately 5 cm in the left mandibular angle region, associated with local inflammatory signs. He reported that this mass had been present for several months but had not previously sought medical attention.

During hospitalization, empirical treatment with amoxicillin–clavulanate was initiated. Computed tomography (CT) of the face and neck revealed an abscess

involving the left parotid, masticatory, and parapharyngeal spaces, associated with erosion of the ipsilateral mandibular angle and ramus (Figure 3). Surgical drainage was performed, and tissue samples were submitted for histopathological analysis.

Histopathological examination revealed a malignant neoplasm consistent with ameloblastic carcinoma, with perineural and vascular invasion. The microscopic analysis demonstrated atypical morphology, with fragments composed of granulation tissue and features supporting an

Figure 1. Bulging in regions IIa and IIb.

Caption: Visualization of the cervical lesion in frontal view.

Figure 2. Bulging in regions IIa and IIb.

Caption: Visualization of the cervical lesion in lateral view.

ameloblastic pattern, including irregular fragments with areas of keratinization and necrosis (Figure 4), nuclear palisading (Figure 5), layers of cells resembling stellate reticulum, and extensive infiltrative areas composed of atypical squamous cells (Figure 6).

Based on clinical and imaging findings, invasion of the skull base, internal and external carotid arteries, deep masticatory space, and parapharyngeal space was identified, corresponding to T4b staging. Additionally, right-sided cervical lymphadenopathy at level IB measuring 2 cm in its greatest diameter without evidence of extranodal extension was observed, classifying the case as N1. No distant metastases were detected, resulting in an M0 classification.

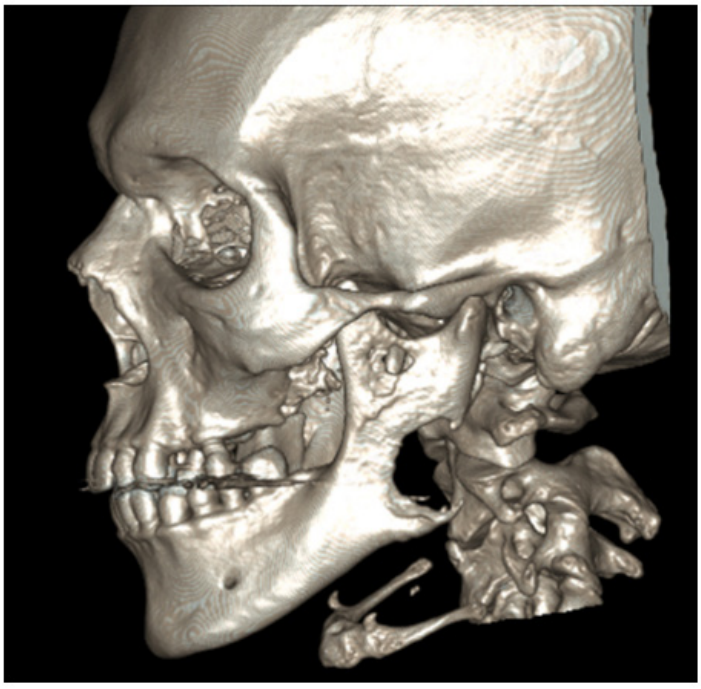

Figure 3. 3D reconstruction image from Computed Tomography.

Caption: Erosion of the mandibular angle and ramus.

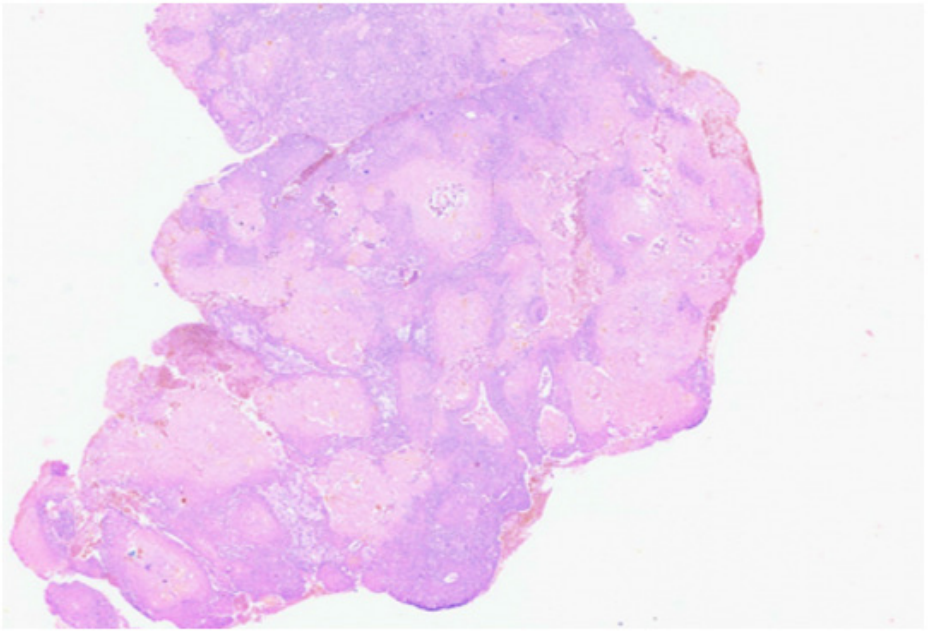

Figure 4. Histopathological slide.

Caption: Areas of keratinization and necrosis.

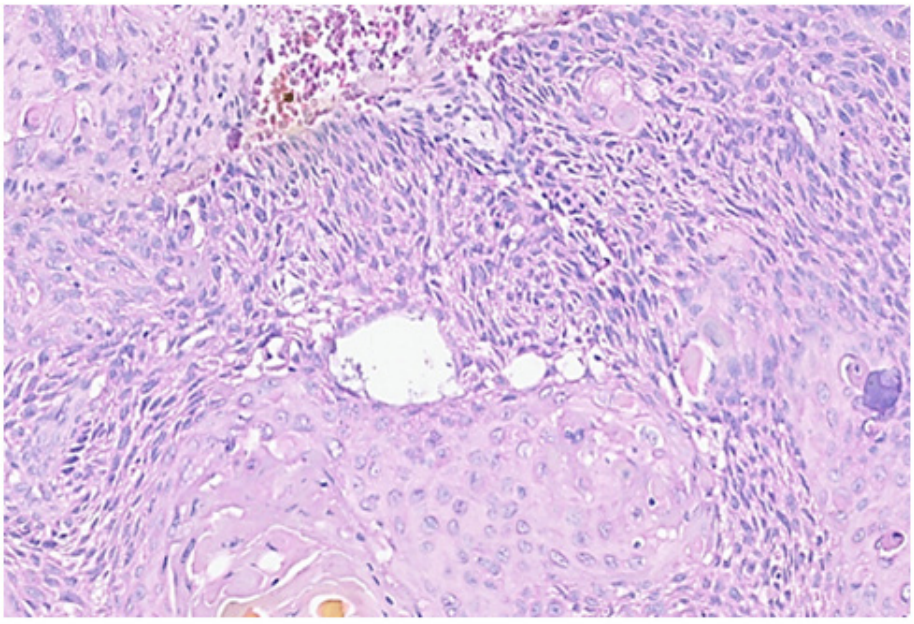

Figure 5. Histopathological slide.

Caption: Palisade-like distribution of nuclei.

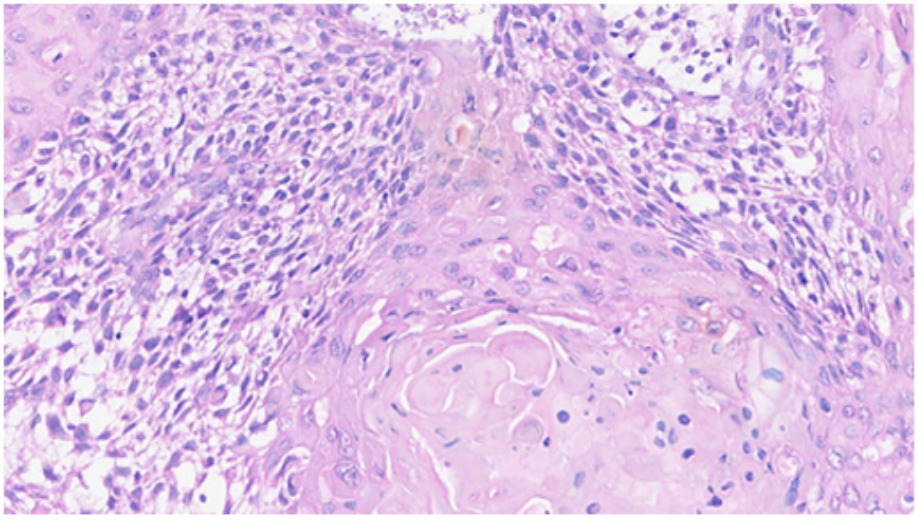

Figure 6. Histopathological slide.

Caption: Stellate reticulum and areas with atypical squamous cells.

Given the advanced stage and unresectability of the lesion, palliative hypofractionated radiotherapy was chosen. The patient remained under outpatient follow-up by medical oncology, radiotherapy, head and neck surgery, and palliative care teams for eight months after diagnosis, when he died.

Three months after completion of palliative radiotherapy, follow-up CT demonstrated lesion progression, characterized by an expansive and infiltrative mass with heterogeneous enhancement and a central cystic/liquefied area involving the muscles of the left masticatory space (masseter, pterygoid, and temporalis muscles) (Figures 7 and 8).

Additional findings included erosion of the left mandibular ramus, angle, posterior body, neck, and condyle, involvement of the left mandibular nerve canal, and circumferential encasement of branches of the left external carotid artery. The lesion extended anteriorly into the left maxillary sinus, with erosion of its posterior walls (lateral and medial), the left pterygoid process and its laminae, alveolar bone of the left maxillary dental arch, and

the posterior margin of the ipsilateral hard palate, as well as involvement of the palatal and buccal gingiva.

There was infiltration of adjacent buccal and parapharyngeal fat planes, involving both supra- and infrazygomatic portions of the buccal and masticatory spaces. The lesion caused obliteration and bone erosion of the pterygopalatine fossa, pterygomaxillary fissure, and inferior orbital fissure. Laterally, the left parotid gland was involved; medially, the left tonsillar fossa, soft palate, parapharyngeal space, and left glossotonsillar sulcus were affected.

Obliteration of the left nasal cavity was observed, with focal bone erosion of the anterior, medial, inferior, and posterior walls of the left sphenoid sinus, involvement of the clivus, and extension to the posterior cranial fossa

Image 7. Radiological evolution.

Caption: Expansive and infiltrative lesion.

Image 8. Radiological evolution.

Caption: Expansive and infiltrative lesion.

(extra-axial). The cavernous sinus was involved, with erosion of the petrous portion of the left temporal bone and circumferential involvement of the right carotid artery (petrous segment/carotid canal), with extension to the middle cranial fossa. Erosion of the left sphenoid trigone and involvement of the left orbital apex were also noted. The lesion measured approximately 14.0 × 10.0 × 10.0 cm.

Discussion

Ameloblastic carcinoma is a rare malignant odontogenic neoplasm, representing less than 2% of all odontogenic tumors according to the World Health Organization (WHO, 2022). Unlike benign ameloblastoma, this variant exhibits aggressive behavior, infiltrative growth, metastatic potential, and high recurrence rates[1,2,3,5]. Most cases occur between the fourth and seventh decades of life, with a slight male predominance. Although no consolidated data exist regarding its incidence in Brazil, it remains an underreported entity, with few cases described in referral centers, including the present report[10,11,13,14].

Ameloblastic carcinoma must be distinguished from metastatic ameloblastoma, as both share an odontogenic origin but differ substantially in biological behavior and diagnostic criteria. In ameloblastic carcinoma, malignant cytological atypia is evident in the odontogenic epithelium, including nuclear pleomorphism, atypical mitoses, necrosis, and an infiltrative growth pattern, regardless of the presence of metastases. In contrast, metastatic ameloblastoma retains histologically benign features identical to conventional ameloblastoma in both the primary and metastatic sites, with diagnosis based solely on metastatic clinical behavior, most commonly pulmonary. Thus, histological malignancy of the epithelium constitutes the key differentiating feature[10,20].

Similarly, ameloblastic carcinoma must be differentiated from primary intraosseous carcinoma (PIOC), which represents a squamous cell carcinoma arising within the jawbones without contact with the oral mucosa. Histologically, PIOC demonstrates features typical of squamous cell carcinoma, such as keratin pearl formation and intercellular bridges, without evidence of odontogenic differentiation. In contrast, ameloblastic carcinoma preserves, albeit atypically, characteristic odontogenic architecture, including peripheral palisading, reverse nuclear polarity, and stellate reticulum-like areas. The WHO 2022 classification emphasizes this distinction by defining ameloblastic carcinoma as a malignant odontogenic epithelial neoplasm distinct from intraosseous carcinomas derived from squamous epithelium, reflecting differences in histogenesis, biological behavior, and therapeutic management[10,20].

The differentiation between ameloblastic carcinoma and odontogenic sarcomas was also discussed with the pathology team, as this distinction is critical, particularly in aggressive and poorly differentiated cases. This differentiation relies on three main pillars: epithelial origin and pattern, presence or absence of ameloblastic differentiation, and localization of malignant cytological features within either the epithelium or the stroma[10,21].

In ameloblastic carcinoma, the neoplasm is epithelial in nature, as demonstrated in the present case, whereas odontogenic sarcomas show benign or absent odontogenic epithelium. Characteristic histological features of ameloblastic carcinoma include stellate reticulum, increased nuclear-to-cytoplasmic ratio, atypical mitoses, necrotic areas, and perineural and vascular invasion, all observed in this case. Conversely, odontogenic sarcomas exhibit spindle-shaped cells, marked pleomorphism, fascicular growth patterns, and production of dysplastic dentin, with benign, sparse, or absent odontogenic epithelium lacking atypia, mitoses, or invasion. Therefore, malignancy resides in the stroma rather than the epithelium, which is incompatible with the present findings[10,21].

Due to the rarity of ameloblastic carcinoma, no specific TNM staging system exists for this neoplasm. Clinical staging is therefore performed using TNM principles applied to malignant tumors of the oral cavity and jawbones, considering the extent of the primary tumor, regional lymph node involvement, and presence of distant metastases[10,21].

Radiographically, ameloblastic carcinoma may resemble classic ameloblastoma, presenting as a uni- or multilocular osteolytic lesion. However, features such as irregular margins, extensive cortical destruction, invasion of adjacent soft tissues, and involvement of neurovascular structures are suggestive of malignancy. In the present case, CT demonstrated an abscess involving the parotid, masticatory, and parapharyngeal spaces, as well as mandibular bone destruction, consistent with advanced invasive disease. The prolonged interval between initial symptoms (spontaneous tooth fracture and persistent pain) and medical consultation contributed to diagnosis at a T4b stage with nodal involvement[1-6,12,15].

The malignant transformation of ameloblastoma or the de novo development of ameloblastic carcinoma remains controversial. Recent studies suggest that genetic alterations involving BRAF V600E, p53, and SMO may be associated with tumorigenesis and progression, potentially opening avenues for targeted therapies[2,7,8]. Nevertheless, treatment remains primarily surgical when feasible. In unresectable cases such as the present one, radiotherapy represents a palliative alternative with limited efficacy. No standardized chemotherapy protocols exist, and its use is generally restricted to clinical trials or refractory metastatic cases[9,10].

Skull base involvement by ameloblastic carcinoma is rare but clinically decisive. Long-term reviews report distant metastases in approximately 26% of mandibular cases and 23% of maxillary cases, while tumors originating at the skull base may reach rates of up to 33%, with one-third exhibiting intracranial metastases, reflecting a more aggressive behavior and worse prognosis[15].

Individual case reports describe dural invasion, middle cranial fossa involvement, extension from the maxillary sinus, and even hematogenous metastasis to the pituitary gland, all associated with high morbidity[2,5,13,14]. Invasion of the cavernous sinus and intracranial segment of the internal carotid artery, although exceptional, characterizes

T4b disease and generally contraindicates radical oncologic resection, being reported in 2–7% of locally advanced head and neck tumors[10-12].

In such scenarios, overall survival decreases substantially. While metastatic ameloblastoma may be associated with prolonged survival (≈17 years), ameloblastic carcinoma demonstrates a far more aggressive course. Clinical studies and systematic reviews report a 5-year mortality rate of approximately 30%, corresponding to a 5-year survival of 65–70%[16-19]. This rate may be even lower in cases with skull base invasion, which are associated with frequent local recurrence, difficulty achieving complete resection, and poorer prognosis. From a therapeutic standpoint, wide surgical resection with free margins is ideal but becomes unfeasible with cavernous or carotid involvement; in such cases, radiotherapy (conventional or stereotactic) and multidisciplinary palliative strategies represent the main alternatives, with some reports suggesting benefit from endoscopic techniques or particle therapy in specialized centers[8,9,15,16,18].

The apparent underreporting of ameloblastic carcinoma in Brazil may be partially explained by the inherent diagnostic difficulty of this rare neoplasm, as its histopathological features may overlap with those of other aggressive odontogenic lesions, requiring clinicoradiological correlation and, often, immunohistochemical analysis for definitive diagnosis[10,19,22].

Additionally, referral bias, concentration of cases in tertiary centers, and regional disparities in access to specialized otorhinolaryngology and head and neck surgery services may contribute to its underrepresentation in the national literature. The WHO itself highlights the rarity of ameloblastic carcinoma and the complexity of its distinction from other malignant odontogenic neoplasms, which may impact accurate reporting. Classical studies also emphasize diagnostic variability and the potential underestimation of its incidence in institutional and population-based series[10,19,22].

This case illustrates the challenges in early diagnosis of malignant odontogenic tumors, particularly in contexts of delayed healthcare-seeking behavior. The insidious progression, resemblance to infectious or benign conditions, and lack of specific protocols for advanced cases reinforce the need for heightened clinical vigilance and further research into alternative therapeutic strategies. Early recognition of atypical oral lesions and timely referral to specialized centers are essential to improve prognosis.

Conclusion

Ameloblastic carcinoma is an extremely rare neoplasm with aggressive behavior and challenging management, and early diagnosis remains a major clinical challenge. The present case demonstrates how silent progression and resemblance to infectious processes may delay diagnostic suspicion, resulting in advanced-stage presentation with limited therapeutic options. This underscores the importance of recognizing atypical features in persistent odontogenic conditions, early referral to specialized centers, and the need for further studies to support effective therapeutic strategies, particularly for unresectable cases.

Author's contributions

We describe contributions to the papers using the taxanomy (CRediT) provided above:

Conceptualization, Investigation, Methodology, Visualization and Writing – Review Editing: RA Freitas; SAT Weber. *Project Administration, Supervision and Writing – Original Draft*: RA Freitas; KMP Souza; IJA de Oliveira. *Validation, Software, Data Curation and Formal Analysis*: GP da Silva; SAT Weber.

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