

Extensive Oral Melanoma on the hard palate: case report

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Aim: Oral mucosa melanoma (OMM) is a rare malignant neoplasm with aggressive behavior. This report aims to present a case of a large OMM on the hard palate.

Methods: A 54-year-old Caucasian man attended the Program of Specific Care for Stomatological Diseases of the Federal University of Uberlândia, referred by a general dentist for evaluation of a lesion on the palate. On oral examination, a focal black pigmentation with red areas was observed in the median region of the hard palate. The diagnostic hypothesis was OMM. Upon incisional biopsy, microscopic assessment of the tissue fragment revealed features compatible with OMM. After diagnostic confirmation, the patient was referred to the head and neck surgery service of the local cancer center, where sessions of radiotherapy and brachytherapy were performed.

Results: Although the medical team found an apparent complete radiological response and no cervical lymphadenopathy after treatment, the disease recurred within one year and the patient presented with a poor prognosis.

Conclusion: Systematic clinical examinations of the oral cavity for the detection of asymptomatic and isolated pigmentations are necessary since early diagnosis is essential to increase the chances of curing this aggressive malignancy.

Uniterms: palate, hard; head and neck neoplasms; melanoma; mouth neoplasms.

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INTRODUCTION

Pigmented lesions may affect the oral cavity and are commonly benign. Among the malignancies, oral mucosal melanoma (OMM) presents as a rare and aggressive lesion¹. Although cutaneous melanoma and OMM arise from the atypical proliferation of melanocytes in the epithelial tissue, they are different entities².³. Unlike skin melanoma, there is no relationship between sun exposure and OMM, and its risk factors remain unknown¹. Furthermore, while

cutaneous melanoma is among the ten most common cancer types⁴, OMM accounts for less than 0.5% of all cases².

Primary mucosal melanoma of the head and neck has a higher incidence among white man, with a peak incidence at 50 years of age^{5,6}. Clinically, OMM presents as an asymmetric and irregularly shaped macula or as a nodular ulcerated lesion, and its color may vary between black, brown and purple. The most affected areas are the palate (51.5%) followed by the gingiva (34.2%)^{2,5}. Since most cases are asymptomatic,

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and bleeding and swallowing difficulties emerge in advanced stages, the diagnosis is delayed and results in a poor prognosis and low survival rate².

Additionally, the diagnosis of OMM is challenging due to its multiple histologic features. According to the 5th Edition of the World Health Organization Classification of Head and Neck Tumors, mucosal melanomas may receive several classifications, and the fact 15% to 50% of cases may present as amelanotic tumors hampers the recognition of the disease^{1,2}.

The treatment of OMM may be surgical, radiotherapy, chemotherapy and immunotherapy³. Although there is no well-established consensus on the treatment of OMM, it is believed that complete surgical excision with safety margins is the most effective approach^{2,7}. Surgical treatment is commonly combined with chemo- and radiotherapy and studies have shown that this association confers a lower risk of recurrence³. Beyond that, lymphatic metastasis at the time of diagnosis is a key factor to determine the treatment approach and prognosis⁴. However, studies have shown that the 5-year survival outcome of the disease is poor, ranging from 6.6.% to 26.6%².

Since there is a shortage of concrete information about the etiology of OMM¹ and a lack of consensus on the ideal treatment², more research and reports on the subject are important. Therefore, the present study aims to report a case of an extensive OMM in the palate with late diagnosis.

CASE REPORT

A 54-year-old Caucasian man presented to the Program of Specific Care for Stomatological Diseases (PROCEDE) of the Federal University of Uberlândia, referred by a general dentist for evaluation of a "lesion on the palate". The patient signed a free and informed consent form. On history, the patient reported no symptoms, moderate alcohol consumption and history of smoking for 20 years and being smoke-free for another 20 years. He presented good general health, although his blood pressure was elevated (180/90 mmHg), which was reasonable due to the anxiety caused by the consultation.

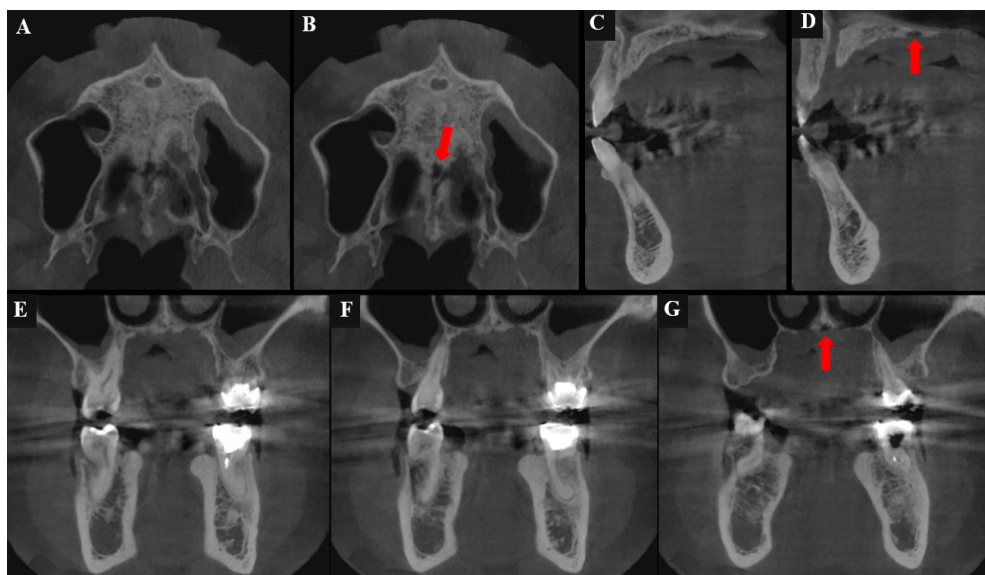
The intraoral exam revealed a black lesion with red areas on the median region of the hard palate, extending from the canine to upper second molars region, measuring approximately 3.5 x 3 cm (Figure 1). Cone beam computed tomography exam showed the erosion of the hard palate on the midline region at the height of the upper molars in axial, coronal and sagittal views (Figure 2), demonstrating bone resorption caused by the lesion. Before the incisional biopsy, 15 mg of midazolam was administered to decrease the patient's blood pressure levels. Tissue samples were collected from three regions: the right and left lateral borders and in the posterior region of the lesion. The postoperative prescription consisted of amoxicillin 500 mg, trometamol ketorolac (Toragesic®) 10 mg and 0.12% chlorhexidine digluconate mouthwash for 7 days.

Figure 1. Initial aspect. The lesion reveals itself as a black macula with red areas in the midline of the hard palate.



Source: Original image.

Figure 2. Cone-beam computed tomography images. A and B. Axial reconstructions with the red arrow showing the erosion of the hard palate in the midline. C and D. Sagittal reconstructions with the red arrow showing the erosion of the hard palate in the midline. E to G. Coronal reconstructions with the red arrow showing the erosion of the hard palate in the midline at the height of the upper molars.

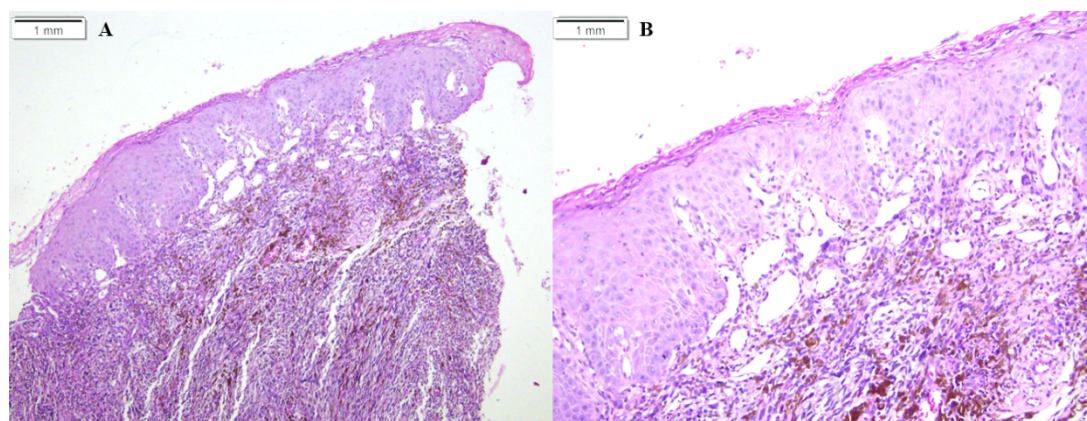


Source: Original image.

The patient returned after 1 week to remove sutures and receive the histopathological report. Microscopic examination revealed a mucosa covered by stratified epithelial tissue, partially ulcerated, and the presence of malignant neoplasm deeply invading the underlying connective tissue consisting of cells with a shape ranging from spindle, ovoid to epithelioid, sometimes diffusely dispersed, sometimes forming small nests. Individually, these cells exhibited an intense polymorphism, nuclear hyperchromatism, with some cells resembling a vesicular nucleus, anisocytosis, anisokaryosis and nucleoli evident in most of them, and cytoplasm ranging from vesicular to eosinophilic, with many of them containing melanin pigments. Small necrotic areas were observed in the interior

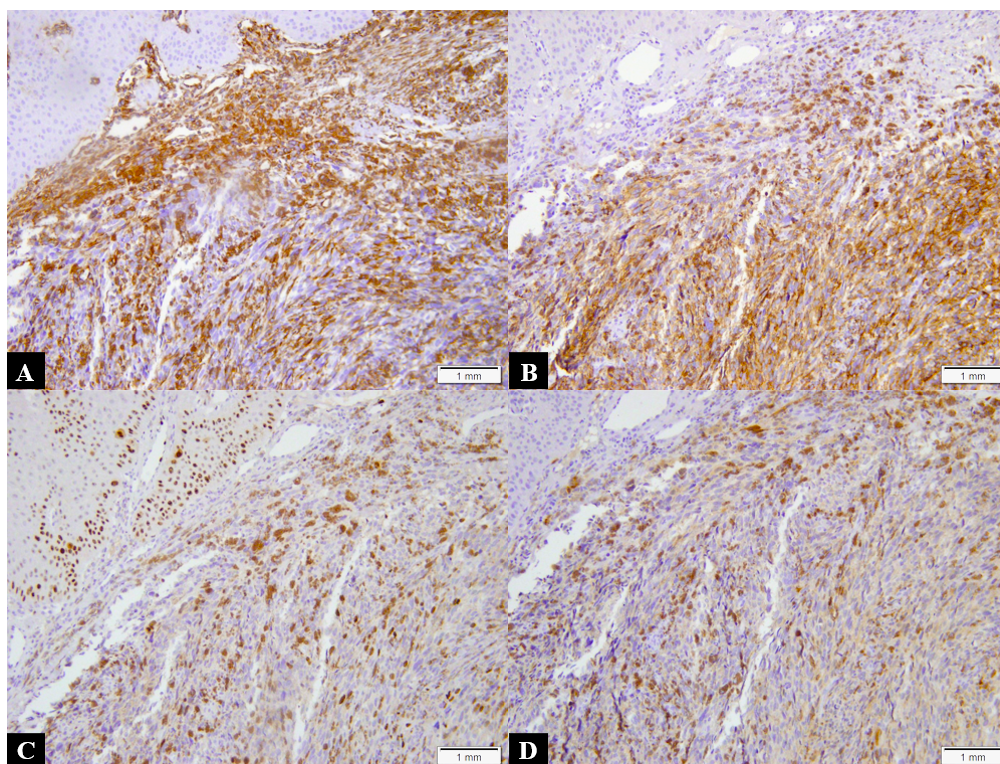
of the tumor as well as leukocyte infiltration, which was preferably located on the periphery. Figures of typical and atypical mitoses were frequently observed. Of note, it was possible to notice tumor cells permeating blood vessel walls; however, tumor emboli were not observed. In the fragments obtained from the margins of the lesion, there was a proliferation of melanocytes at the epithelial-conjunctive junction, with some of them located in the upper layers of the epithelial tissue (Figure 3). Immunohistochemical analysis detected positive staining for vimentin, S-100, HMB45 and Ki67 (30% of neoplastic cells), while epithelial, lymphoid and smooth muscle markers were negative (Figure 4). A conclusive diagnosis of primary OMM was established in May 2019.

Figure 3. Microscopic view of the tissue fragment obtained from the incisional biopsy stained with hematoxylin and eosin. A. 10x increase showing the fragment. B. 20x increase highlighting the dermis and epidermis transition in which there is a proliferation of melanocytes at the epithelial-conjunctive junction.



Source: Original image.

Figure 4. Immunohistochemistry (IHC) images at $\times 200$ magnification for vimentin (A), HMB-45 (B), KI-67 (C) and S-100 (D).



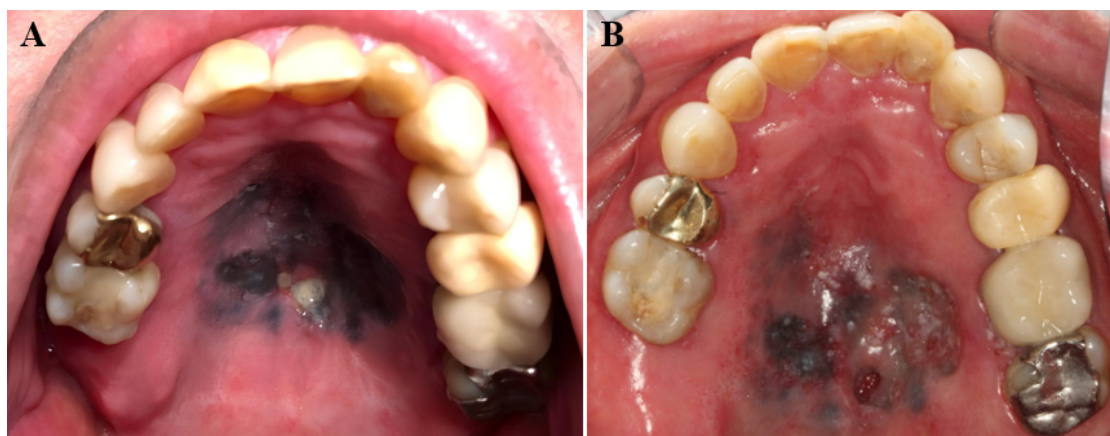
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Upon diagnosis, the patient was referred to the local cancer center for consultation with the head and neck surgery area. Initially, a positron emission tomography-computed tomography (PET-CT) scan was performed to investigate the extent of the cancer. The images were acquired with a multislice computed tomography device after an intravenous injection of 8.98 mCi of fluorodeoxyglucose-18F. There was uptake of the radiopharmaceutical in a mild thickening of the soft tissues adjacent to the hard palate associated with an apparent irregularity in the palatal bone cortex, suggesting erosion in the bone adjacent to the lesion. Thus, the presence of a neoplastic process was identified only in the palatal region, without other areas of increased uptake.

The medical team contraindicated the surgical approach and decided to treat the patient with a combination of radio- and brachytherapy sessions. The patient underwent a pre-radiotherapy dental consultation in which the need for endodontic treatment of maxillary

left central incisor was indicated and carried out in two weeks. Then, the patient's treatment started and consisted of approximately 60 Gy divided into 27 sessions of radiotherapy and 30 Gray divided into 4 sessions of brachytherapy. At the end of the sessions, the medical team found an apparent complete radiological response and no cervical lymphadenopathy.

By the end of radio- and brachytherapy, the patient was reevaluated by the dental team in PROCEDE, who visualized a decrease in the size of the lesion and a necrotic area of approximately 3 mm in the most posterior portion of the lesion, close to the midline (Figure 5A). After careful inspection, bone exposure was observed in this region and diagnosed as osteoradionecrosis. For treatment, he was prescribed chlorhexidine mouthwash three times a day and topical irrigation with propolis once a week. At follow up, the patient reported improvement in the discomfort caused by osteoradionecrosis and a better clinical aspect could be observed (Figure 5B).

Figure 5. Initial (A) and final (B) aspect of the palate treated for osteoradionecrosis.

Source: Original image.

In May 2021, the lesion recurred and metastasis to the lymph nodes was confirmed. A new biopsy of the palate was conducted and neck dissection performed. Shortly after, metastasis to the pancreas, peritoneum and lungs was identified. The patient underwent biliary surgery and was set on exclusive palliative support in October 2022. In March 2023, the patient was admitted to the hospital with symptoms as abdominal pain, jaundice and fever, indicating sepsis caused by the tumor on the biliary tract. The systemic infection led to the patient death in April 2023.

DISCUSSION

OMM is an aggressive and rare malignant neoplasm, corresponding 0.5% of all melanomas². The profile of the present case agrees with most of the reports in the literature. For sex and age, it corroborates recent studies that reveal higher prevalence among men in the fifth decade of life^{2,5,6}, and the location of the lesion confirmed the palate as the most affected area². Regarding the race, it is in accordance with studies that report a higher prevalence in Caucasian patients^{5,8}. However, a previous study reported that Japanese individuals are more predisposed to OMM⁹. As the data are contradictory, future epidemiological and genetic studies are needed to strengthen possible ethnic predisposition.

It is known that cutaneous and mucosal melanomas arise from the neoplastic transformation of melanocytes in the basal layer of the epithelium^{2,3}. While skin melanoma is related to sun exposure, the risk factors underlying OMM are still unknown¹. Some studies have shown possible participation of agents such as microtrauma and smoking on the

lesion etiology^{10,11}. Although the patient reported being a smoker for twenty years, there is not enough evidence in the literature to support the association between tobacco and the tumor. Additionally, the habit had been suspended for more than twenty years before the diagnosis, which makes this relationship even more improbable.

Histopathological analysis of tissues obtained by incisional biopsy was sufficient to establish, unequivocally, the diagnosis of mucosal melanoma. Usually, melanocytic forms of melanoma can be safely diagnosed by conventional histopathology, with no need for immunohistochemistry¹². However, even so, this test was performed and showed positive results for vimentin, S100 protein, human melanoma and ki67. The immunohistochemical panel confirmed the diagnosis of OMM.

Once the diagnosis is established, therapeutic alternatives to OMM include surgery, radiotherapy, chemotherapy and immunotherapy, alone or in combination^{3,12}. Although there is no universal protocol, surgery is considered the main form of treatment^{2,7}. Studies show that the combination of surgical approach and radiotherapy decreases the chance of recurrence, and that radiotherapy alone leads to an inferior 5-year survival than surgery alone³. Due to the extent and site of the injury reported, surgery was contraindicated by the medical team because it would cause great tissue loss with impairment of speech, mastication, and swallowing¹³. Despite the compromise of aesthetic and functional aspects, maxillectomy could be accompanied by rehabilitation with prosthetic obturators, which is valuable for irradiated patients and has already shown to improve oral health-related quality of life^{13,41}.

Even there was invasion of adjacent bone in the case described, there was no evidence of regional and distant metastasis at first assessment. Nonetheless, due to the aggressiveness of OMM, the American Joint Cancer Committee (AJCC) classified all primary tumors having only a T3 or T4 primary designation¹. Regarding the prognosis, studies show poor 5-year survival², which corroborates the outcome of the present case. It is noteworthy that the non-surgical approach adopted by the medical team may have influenced the poor prognosis seen here.

At end of the radio- and brachytherapy sessions, there was an improvement in the clinical feature of the lesion, but osteoradionecrosis arose as an adverse effect of treatment. This complication is common in patients undergoing radiotherapy in head and neck regions and may be present in 33% of patients¹⁵. The osteoradionecrosis was treated and monitored by the dental team, and improvement in the discomfort reported by the patient and improvement of the clinical feature could be observed after treatment with chlorhexidine mouthwash and topical irrigation with propolis.

The moment of diagnosis directly influences the patient's future condition. It is known that neoplasms recognized in early stages have better prognosis than more advanced cases². The present report demonstrates the aggressive character of OMM despite the absence of metastasis in the initial evaluation. Therefore, the recognition of these lesions at incipient levels becomes essential for survival and biopsies in pigmented lesions with no cause or effect are mandatory to rule out OMM.

CONCLUSION

The present report demonstrates a case of an extensive OMM with late diagnosis. This kind of lesion is rare in the oral cavity and presents an extremely aggressive behavior. For this reason, dentists must be careful in routine examinations, especially when there are focal pigmented lesions. Biopsies are mandatory in incipient lesions to rule out the possibility of malignancy. The moment of diagnosis of OMM directly influences the effectiveness of the treatment and the patient's survival.

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CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Camila Silvério Carvalho Vieira: Writing – review & editing. **Luciano Leite de Castro:** Writing – original draft preparation. **Pedro Urquiza Jayme Silva:** Writing – original draft preparation. **Thallys Rodrigues Félix:** Investigation, Case conduction. **Luiz Fernando Barbosa Paulo:** Investigation, Formal analysis. **Ana Fernanda Ribeiro Rangel:** Investigation, Formal analysis. **Gabriella Lopes de Rezende Barbosa:** Investigation, Formal analysis, Writing – original draft preparation, Funding acquisition and Supervision.

DECLARATION OF CONFLICT OF INTEREST

None.

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Melanoma Oral extenso em palato duro: relato de caso

Objetivo: o melanoma da mucosa oral (MMO) é uma neoplasia maligna rara, de comportamento agressivo. O objetivo deste relato é apresentar um caso de MMO volumoso em palato duro.

Métodos: homem branco, de 54 anos, compareceu ao Programa de Atenção Específica em Doenças Estomatológicas da Universidade Federal de Uberlândia, encaminhado por um dentista generalista para avaliação de uma lesão em palato. Ao exame bucal, observou-se pigmentação negra focal com áreas avermelhadas na região mediana do palato duro. A hipótese diagnóstica foi de MMO. Após biópsia incisional, a avaliação microscópica do fragmento tecidual revelou características compatíveis com MMO. Após a confirmação diagnóstica, o paciente foi encaminhado ao serviço de cirurgia de cabeça e pescoço do centro oncológico local, onde foram realizadas sessões de radioterapia e braquiterapia.

Resultados: embora a equipe médica tenha encontrado resposta radiológica aparentemente completa e ausência de linfadenopatia cervical após o tratamento, a doença recidivou em um ano e o paciente apresentou prognóstico não favorável.

Conclusão: exames clínicos sistemáticos da cavidade oral para a detecção de pigmentações assintomáticas e isoladas são necessários, visto que o diagnóstico precoce é essencial para aumentar as chances de cura dessa neoplasia maligna agressiva.

Descritores: palato duro; neoplasias de cabeça e pescoço; melanoma; neoplasias bucais.