Spontaneous regression of oral mucosal malignant melanoma

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Introduction

The oral mucosal malignant melanoma (MM) is a rare neoplasm that develops from melanocytes in the basal layer of the mucosa. The incidence of MM in the oral cavity varies between 0.2 and 8% of all melanomas. Approximately 70% of the mucosal melanomas of the head and neck are located in the paranasal sinuses, while 25% affect the oral mucosa, having a predilection for involving the hard palate (40%) followed by soft palate and gums. Usually, in the physical examination, the MM has been described as an oral mucosa with irregular shape, being non-uniform in color ranging from brown, gray, dark blue and black, and can clinically present as macular, nodular or plaque type, as well as mixed lesion. Suspected lesions should be biopsied, and immunohistochemical analysis is often required for diagnostic confirmation. The spontaneous regression (SR) is related to a partial or complete disappearance of a malignant tumor without treatment, that is, it is ordinarily consist in the capacity of undergoing SR. The majority of SR studies in MM refer to the cutaneous melanoma subtype, and it is believed that partial SR is detected from 10% to 30% of these cases. The incidence of metastatic melanoma with complete SR regarding the primary cutaneous lesion is estimated in 3-15%. However, the spontaneous disappearance of metastases is very rare and usually occurs in cutaneous, subcutaneous or lymph node metastases. Remission in viscera and lungs is extremely rare.
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The SR mechanisms are not fully understood yet, but often follow a mechanical event, such as a biopsy or incomplete excision\(^3\). Other events have been associated, such as local infection, autoimmune diseases, transfusion reaction and abortion\(^3\). Many researches suggest that several different mechanisms can be involved, such as immunological mediation, tumor growth inhibitors and cytokines, inhibition of angiogenesis, seeing that all these mechanisms together push the cell into differentiation or death\(^3\). Evidence of the effectiveness of immunotherapy, the presence of mononuclear cell infiltrates and melanocyte-specific cytotoxic T lymphocyte precursors in peripheral blood are histological issues that demonstrate the importance of the immune system in the SR process\(^4\). An association of depigmentation phenomena, such as nevus halo and vitiligo associated with melanoma SR, has also been reported. This suggests that there are autoimmune factors which can be directed against antigens shared by normal and malignant pigmented cells. It can be noticed that tumor regression is probably mediated by T lymphocytes because high T-helper cell rates are found in the infiltrates, which may reflect a specific immune reaction against tumor cells\(^4\).

Case report

This is a case report of a 52-year-old male, Caucasian, Brazilian, retired, which was referred due to an irregularly shaped, darkly pigmented lesion of the palate (Figure 1A), noted on routine examination by his primary dentist, and an incisional biopsy was made into an area of abnormal tissue (Figure 2), which revealed the MM. The lesion was asymptomatic, and the patient had used dental prothesis for 10 years. The patient's medical history could contain relevant information, such as treatment of infections of syphilis and gonorrhea, dyslipidemia and surgical removal of a benign tumor of the submandibular gland. Regarding the patient's personal life, social history (SocHx), it could be revealed a tobacco use of a 10.2 packs/year and an alcohol intake of 0.5 liter of distilled beverage a day over 22 years. The oral examination revealed a single 3 cm x 2.5 cm blackish and asymmetrical lesion on the hard palate (Figure 1A). No cervical lymphadenopathy was

![Figure 1. A - Dark lesion with irregular borders on hard palate 3.0 x 2.5 cm. B - Hard palate presenting macroscopic regression of the lesion, after six months in the absence of previous therapeutic treatment.](image)
Spontaneous regression of oral mucosal malignant melanoma detected. Additional diagnostic investigations, including abdomen and neck ultrasound (US), Computed Tomography (CT) of the head and neck with contrast, chest X-ray and biochemical exams were normal. An incisional biopsy of the lesion revealed features of melanocytic neoplasia composed of proliferation of atypical melanocytes with large nuclei and evident nucleolus forming nests in the basal region, without signs of tumor invasion in the lamina propria extending onto the upper extracts of the mucosa. A large amount of melanin pigment was also noted (Figure 2). Melanocytes underwent malignant transformations and could invade the mucosal epithelium as well as their limitations above the basal lamina, classifying this melanoma as \textit{in situ}. There was moderate acanthosis in the adjacent epithelium and presence of dermal fibrosis with collagen bundles. The material was submitted to immunohistochemical study, which showed that neoplastic cells were positive for Melan A and negative for AE1/AE3 cytokeratins. Neoplastic cells were also positive for S100 protein screening and for HMB45 screening. The patient refused an immediate surgery and came back for an outpatient consult review after nine months. Surprisingly, the lesion showed an almost complete SR with a residual of 6mm dark spot surrounded by an unpigmented mucosa (Figure 1B). Thus, The patient accepted the surgical treatment, that was performed with a wide local excision, including this residual small pigmented spot and the original boundaries of the primary tumor, including a 5mm surgical margins. The surgical defect was reconstructed using a skin graft. Pathological analysis of the lesion showed there was no residual of the melanocytic neoplasia. However, there was a peripheral thinning area corresponding to the previous incisional biopsy and an intense fibrosis under this area due to deposition of collagen fibers.
A slight mucosal thickening and mild inflammatory reaction were observed in the adjacent areas (Figure 3). The patient remains under follow up and it is probably not at risk of contracting the disease again, even six years after the diagnosis.

**Discussion**

The etiology regarding oral mucosal MM is still uncertain, with divergent opinions in the literature. Some authors suggest smoking, mechanical irritation due to oral prostheses, and alcohol abuse as risk factors. In this case report, the initial diagnosis of oral mucosal MM was defined by the histopathological slides and the immunohistochemical study showed positive for Melan-A, S100, HMB45 and negative for cytokeratins, confirming this way, the diagnosis of oral mucosal MM. The analysis of the excised specimen nine months after the initial biopsy revealed no residual neoplasia, and the patient was not submitted to any curative or alternative treatment in the period between the two biopsies. The speculated SR mechanisms may derive from multiple factors, such as hormonal influence, immunological reactions, inhibition of angiogenesis, differentiation of tumor cells, necrosis, among others. McKay et al. suggested that Natural Killers (NK) are the first cells to play a role in cutaneous MM regression by stimulating T-helper lymphocytes that recruit specific cytotoxic T lymphocytes. In this case, the initial incisional biopsy showed inflammatory signal and scar formation, surrounding the malignant melanoma cells, which could represent a desmoplastic reaction of the disease or already indicate the beginning of the regression process, that is, before the initial biopsy. There were some reports in the literature of SR.
regarding primary cutaneous MM, but only one case among them was similar to our results. Rajan and Samant⁵ published a case of SR concerning the palate mucosal of MM, with absence of the tumor after the incisional biopsy, without documentation of the clinical regression showed in our case report.

References