

## Up-to Date Review And Case Report

# Oral manifestations of a sinus melanoma: case report and literature review

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**Abstract – Introduction:** Mucosal melanoma (MM) is a rare malignancy of the head and neck. Sinonasal melanomas are the most frequent, followed by oral melanomas. **Observation:** A 67-year-old patient with a known left sinus melanoma initially treated with immunotherapy was referred for consultation concerning mobile teeth. A pigmented lesion infiltrating the left maxillary arch in the molar area was detected. The malignancy had invaded the oral mucosa. Despite many proposed treatments (immunotherapy, chemotherapy, and radiotherapy), the patient showed metastatic progression, which resulted in death. **Discussion:** Sinus MMs are malignancies with poor prognosis because these are often diagnosed in the late stages of disease progression. As these tumors are rare, there is no treatment consensus and surgery remains the best option. Diagnosis of pigmented lesions of the oral mucosa is sometimes complicated because of various implied etiologies. **Conclusion:** This case report shows that sinus MMs can induce pigmentation in the oral mucosa. These are rare malignancies with poor prognosis, for which no treatment consensus exists to date.

## Introduction

Mucosal melanoma (MM) is a rare malignancy, with an estimated incidence of 0.7 new cases per 100,000 individuals per year. MMs account for 0.2%–10% of all melanomas detected in the head and neck. MM is one of the most aggressive tumors of the head and neck, with a very high risk of local or distant recurrence [1].

Sinonasal melanomas are the most common form of MM (66%) followed by oral MM (25%), and they represent 4% of all sinonasal tumors [2]. Their peak incidence occurs around the age of 60.

## Observation

A 67-year-old patient consulted in June 2016 for left cervical lymphadenopathy. Examination revealed a tumor of the left maxillary sinus. Tumor biopsies revealed melanocytic tumor proliferation, suggesting melanoma or a melanocytic nevus. Melanoma was diagnosed based on the infiltrative nature of the tumor.

The patient's family history included a cutaneous melanoma of the knee that affected her sister. In 2002, the patient benefited from the placement of an individualized stent for coronary artery disease and was treated with acetylsalicylic acid, acebutolol, and pantoprazole. She also presented phototype I according to the Fitzpatrick's classification.

Intraoral clinical examination revealed a melanotic tumor mass approximately 4-cm long, which had started to infiltrate the gingiva of the maxilla. The teeth in the area were loose. Tooth extracting was proposed (Fig. 1).

Extension examination revealed osteolysis of the adjacent bone structures and invasion of the nasal fossae and pterygoid muscles (Fig. 2). Jugular and carotid satellite lymphadenopathies under the chin as well as secondary bone and liver lesions were detected.

Genome analysis was performed, and no BRAF, CKIT, or NRAS mutations were detected. The patient's medical records were reviewed at a Multidisciplinary Consultation Meeting (MCP). Because of the local extension, inoperable nature, and distant metastases of the tumor, treatment with immunotherapy (pembrolizumab) was initiated in late September 2016. Irradiation of the primary lesion was proposed to improve local control and to limit local progressive risks (pain or eating disorders). The treatment was delivered as 60 Gy in 30 sessions

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**Fig. 1.** Intraoral photograph showing melanocyte infiltration in the gingival mucosa and the tissue loss around the second maxillary left molar.



**Fig. 3.** Intraoral photograph 3 weeks before initiating the radiotherapy, a diminution of the tumor volume can be noticed.



**Fig. 2.** Sagittal split showing the tumor, the osteolysis, and the relationship with the upper maxillary left molar.

over 6 weeks, allowing a clinical response estimated at 50% at 3 weeks after the end of the irradiation (Fig. 3). No unusual toxicity was noted because of the combination of pembrolizumab and radiotherapy.

The patient subsequently developed lymph node and lung metastases and received a second line of ipilimumab immunotherapy. Chemotherapy with docetaxel and then fotemustine was initiated for subcutaneous and bone metastases. Despite these treatments, the patient died from metastatic progression.

### Comments

The sinonasal MM has a poor prognosis, because of its late management, which at the time of the diagnosis is usually accompanied by adenopathies. According to Ascierto *et al.*, the 5-year survival rate for individuals over 65 years of age is 19% [3]. This rate is low because patients present late, with nonspecific clinical signs of the disease such as unilateral, permanent, or progressive nasal obstruction and epistaxis in the initial stages. Subsequently, the appearance of pain, tearing, rhinorrhea, and, in the most advanced stages, a junctional swelling, nasal deformity, and exophthalmia can be noted [3,4].

To date, there is no clear consensus regarding MM treatment. The treatment of choice for these tumors remains surgical excision leaving healthy margins [5]. However, the frequency of recurrence is very important in this type of

pathology [3,6–9]. Complete surgical resection (R0) is difficult to perform due to the anatomical proximity of certain significant or vital structures.

The use of radiotherapy in MM treatment remains controversial: It is used as an adjuvant treatment, and in case of surgical contraindication, as analgesic or palliative treatment. Indeed, these tumors are categorized as not radiosensitive. In the literature, improvements in local and regional control, with no effect on overall survival after 5 years, has frequently been reported [3,5,9].

Recently, the use of targeted therapies (tyrosine kinase receptor inhibitors) and advances in immunotherapy (PD1/PDL1 nivolumab or pembrolizumab) have led increased patient survival, particularly in cases of unresectable or metastatic tumors [3,10,11].

The diagnosis of pigmented lesions of the oral mucosa can be complex. In the present case, an extensive, diffuse, dark blue, slate lesion of the oral cavity was present. This type of lesion must be systematically biopsied (except in the case of suspicion of vascular lesion, which requires arteriographic or Doppler evaluation).

In some cases, MM may be in an achromic form. The diagnosis is often poorer because of the aggressive nature of the tumor and its more difficult diagnosis [3]. Several differential diagnoses of various etiological origins can be evoked when dealing with pigmented lesions of the oral mucosa.

Systemic disease-related colorations include Laugier–Hunziker syndrome, hemochromatosis, endocrine disorders, such as acromegaly and McCune–Albright syndrome, Cushing’s disease or syndrome, hyperthyroidism, neurofibromatosis, and beta thalassemia [12,13]. Carney complex is characterized by pigmented macules on the lips in 50% of the cases. This is a potentially severe disease due to the presence of cardiac myxomas. Mucosal signs can sometimes be the first sign of this disease [12]. Peutz–Jeghers syndrome results in cutaneous and mucosal hyperpigmentation, with perioral pigmented macules on the oral mucosa as well as intestinal and gastric hamartomatous polyposis. These polyps are associated with a risk of malignant degeneration in 2%–3% of the cases. There is also an increased risk of breast, ovarian, and testicular tumors [12]. Finally, Addison’s disease or primary adrenal insufficiency may cause a diffuse grayish discoloration of the mucous membranes [12].

Colorations may be related to a chronic inflammatory condition, such as lichen planus or sarcoidosis. Mucosal colorations may also have an extrinsic origin, as in the case of heavy metal poisoning (lead, mercury, or silver) and ethnic coloring (tattoos or amalgam tattoos), or an iatrogenic origin.

Some colorations can be of neoplastic origin. Oral melanoma is the most frequently found malignant tumor, accounting for ~1% of all melanomas and 0.5% of all malignant tumors in the oral cavity [14]. Oral melanomas can be brown, black, gray, purplish, or depigmented [15]. In fact, in 35% of the cases, oral melanomas are achromic, making diagnosis more difficult [13]. The overlying mucosa may be smooth, intact in appearance, or ulcerated. The presence of locoregional

**Table I.** Causes of pigmented lesions of the oral mucosa according to their origin.

Coloration	Etiology
Physiological coloration	Melanic ranges in melanodermic patients
Coloration related to a systemic disease	Laugier–Hunziker syndrome Hemochromatosis Acromegaly, McCune–Albright syndrome, Cushing’s disease, or hyperthyroidism Beta Thalassemia Carney’s syndrome Peutz Jeghers syndrome Addison’s disease
Coloration related to a chronic inflammatory condition	Oral lichen planus Sarcoidosis
Coloration caused by a tumor	Kaposi sarcoma Nevus/mole Melanosis Malignant melanoma
Exogenous coloring	Foreign body (graphite or tar) Ethnic tattoos Consumption of certain foods: Betel nut ( <i>Areca</i> ) Exposure to heavy metals: Bismuth, lead, silver, or mercury Melanosis caused by smoking Amalgam tattoos
Coloration of traumatic origin	Melanoacanthoma Petechiae, purpura, bruise, or hematoma
Coloration of iatrogenic origin	Minocycline Synthetic antimalarials Amiodarone Clofazamine Zidovudine Ketoconazole Chemotherapy treatment: Busulfan and doxorubicin Phenothiazines
Vascular/hematological coloration	Varicose veins Telangiectasia Benign lymphangioma Hemangiomas Vascular malformation

lymphadenopathy is possible and is a clear sign of a worse prognosis [15]. Benign nevi may look similar to oral melanomas.

Kaposi's sarcoma is frequently found on the palate of HIV Patients on SIDA stage. Finally, some coloration may have a vascular origin, such as hemangiomas that are common in the oral cavity. Table I presents a non-exhaustive list of the main causes of mucosal colorations sorted by their possible origins [12,13,16].

## Conclusion

Pigmented lesions of the oral mucosa can be of various origins. Practitioners should always consider the possibility of a malignant melanoma when dealing with a suspicious, rapidly evolving lesion. Here, we have detailed the case of an oral manifestation of sinus melanoma in the form of a pigmented mucosal lesion. It is pathology with a poor prognosis and difficult treatment, and there is no treatment consensus. Surgery remains the best option to date, despite a high frequency of local or regional recurrence.

**Conflicts of interests:** The authors declare that they have no conflicts of interest in relation to this article.

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