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CASE REPORT

Oral Mucosal Melanoma of the Palate in a Patient With a History of Breast Carcinoma: A Case Report

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Abstract

Oral Mucosal Melanoma (OMM) is a rare and aggressive malignancy, often diagnosed at late stages due to its silent progression and carries a poor prognosis. We present a case of a 49- year-old woman with a history of breast cancer who presents with a pigmented lesion on the hard palate, histopathological examination was in favour of a mucosal melanoma. Treatment consisted of surgical excision; the lesion recurred 8 months after the first intervention, with local lymph node invasion; the patient later died of a brain neoplasm of unidentified aetiology.

This case highlights the diagnostic difficulties of the pigmented oral lesion in a patient with history of neoplasm; as well as the aggressiveness and prognosis of OMM.

Keywords: Oral Mucosal Melanoma, Palatal Melanoma, Oral Pigmentation; Prognosis, Recurrence, Surgical Treatment.

1. Introduction

Pigmented lesions of the oral mucosa area heterogeneous group of conditions with abroad range of clinical appearances, fromlight brown to black or blue pigmentation(1). Around 30%-56% of the population have pigmented lesions on theoral mucosa ; they may be physiological or pathological and may result from different aetiologies, the most common being ethnic pigmentation and smoker's melanosis(39.9% and 32.9% respectively)(2,3). Because many of these lesions share similar clinical features, establishing a definitive diagnosis may be challenging.

Among these lesions, oral mucosal melanoma (OMM) is a rare and highly aggressive malignant neoplasm arising from melanocytes within the epithelium. It may develop de novo or arise in an area of pre-existing pigmentation. According to the World Health Organisation (WHO) it represents an entity distinct from cutaneous melanoma, with poorer prognosis (4) Oral mucosal melanoma frequently remains asymptomatic during its early stages, which may delay diagnosis. Consequently, patients often present with advanced disease, rendering the prognosis less favourable.

We report a case of oral mucosal melanoma involving the palate in a 49- year-old woman with a previous history of breast cancer. Diagnosis was challenging because the melanoma developed on pre existing palatal pigmentation in a patient who had recently undergone treatment for another malignancy, and the advanced stage made treatment planning delicate.

2. Case Presentation

A 49-year-old woman, Z.M., was referred to our department on 9 June 2007 for the extraction of tooth 15 associated with painin the region.

Her general medical history was significant for left breast cancer, for which she had undergone mastectomy and lymph node dissection on 27 September 2006. She subsequently received six

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cycles of chemotherapy between 30 September 2006 and 22 January 2007, followed by left supraclavicular radiotherapy from 17 March to 28 March 2007.

For the history of the present illness, the patient reported the presence of a small, asymptomatic pigmented nodule on the palate that had been present for more than six months. During radiotherapy, pain developed in the region of tooth 15, followed by the appearance of a proliferative lesion arising from a pre existing, asymptomatic pigmented area of the palatal mucosa. The lesion interfered with the stability of her upper removable partial denture. Following her initial consultation, the patient had been prescribed amoxicillin and an antiseptic mouthwash (Hextril) with no improvement of the symptoms, at a subsequent consultation, computed tomography (CT) of the facial bones and skull base was requested, and the patient was referred to our department for extraction of tooth 15.

Extraoral examination was unremarkable,with no clinically palpable cervical or facial lymphadenopathy. Intraoral examination revealed tooth 15 was severely decayed, teeth 12, 11, and 23 showed no pathological mobility. A large ulceroproliferative lesion with raised borders was observed in the anterior right portion of the palate. The lesion was pink and overgrowing on a large, flat, irregular and asymmetric brownish-black pigmented area with relatively well-defined margins, extending over the entire right half of the palate. Surrounding gingiva was also covered in scattered brownish spicules. (Figure 1)

The clinical aspect was suggestive of a malignant neoplastic process of the palatal mucosa, the main clinical differential diagnoses included mucosal melanoma and squamous cell carcinoma.

CT examination showed no significant modifications in bone structure. The surrounding soft tissue was of normal thickness compared to contralateral tissue.

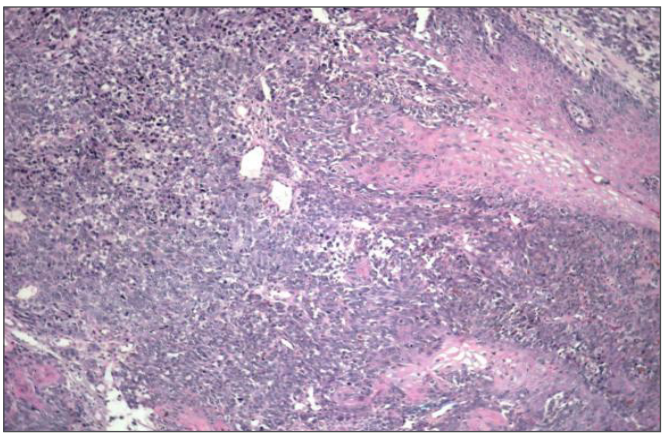


Figure 1. *Intraoral view at the initial presentation.*

An incisional biopsy was performed to establish the diagnosis. Histopathological examination revealed a highly polymorphic population of tumour cells, including spindle-shaped, epithelioid and plasmacytoid cells, as well as round, clear and poorly differentiated cells. Epithelioid tumour cells exhibited hyaline amphophilic cytoplasm and atypical nuclei and were arranged in nests. Spindle cells formed intersecting fascicles. (Figure 2)Immunohistochemical examination is necessary to confirm the diagnosis. Results confirmed the diagnosis of malignant melanoma.

Different hypotheses were considered for the etiological differential diagnosis:

a



b

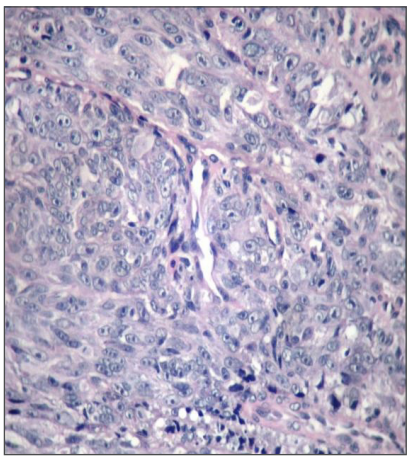


Figure 2. *Histopathological examination showing polymorphic tumour cells: a. view under themicroscope; b Zoomed view of the examined specimen*

- Given the patient's recent history of breast carcinoma, a metastatic lesion to the palatal mucosa was considered. However, the previous breast tumour had been diagnosed histologically as grade 2 invasive ductal carcinoma with two infiltrated lymph nodes, while the histological features of the palatal lesion were consistent with melanoma rather than metastatic breast carcinoma.
- A treatment-related secondary malignancy was also considered because of the recent chemotherapy, the patient had received a TAC protocol (taxotere:145 mg cycloph 750 mg(1500) doxorubicine 60/ m^2(120), however, no established association between this regimen and the development of oral mucosal melanoma could beidentified.
- Malignant transformation of the pre existing pigmented nodule possibly due to repeated trauma from the patient's dentures.

The treatment plan consisted of wide surgical excision of the entire lesion, together with extraction of severely compromised teeth. Following the extensive surgical procedure, the patient underwent prosthetic rehabilitation using a soft-based prosthesis to promote soft tissue healing. (figure 3)

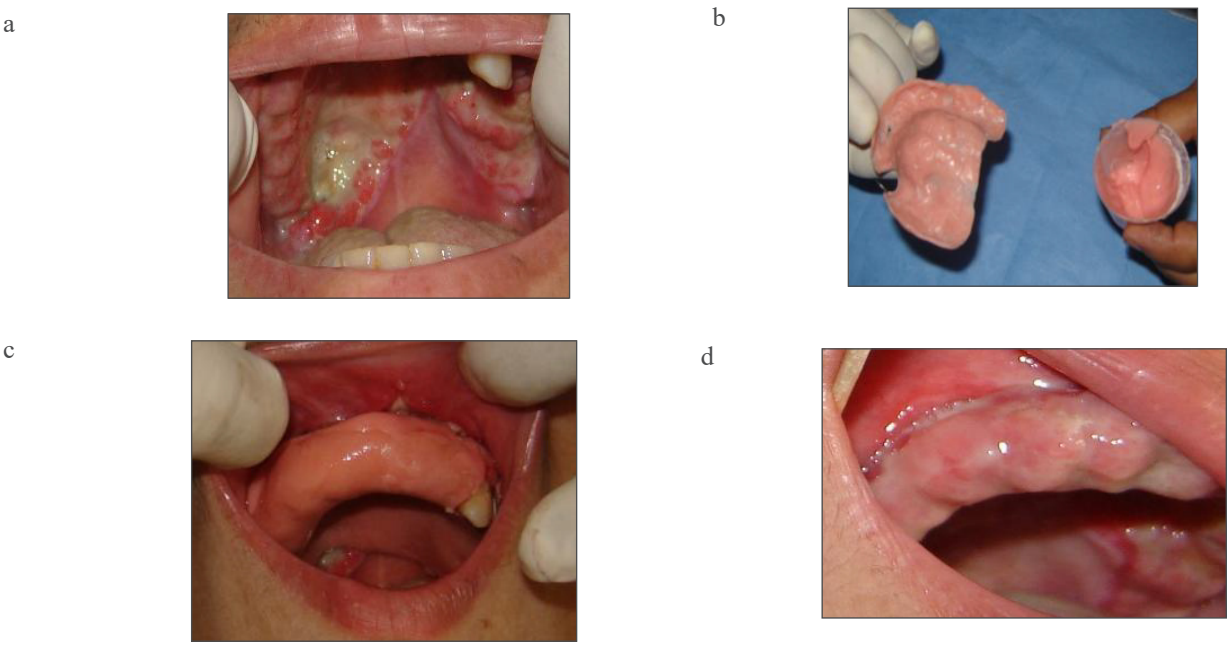


Figure 3. *Prosthetic rehabilitation: a. Intra-oral view after the surgery; b. Soft based resin palatal plate;c. the prosthesis inserted intraorally; d. soft tissuehealing*

On 22 April 2008, approximately eight months after the initial surgery, the patient returned with left cervical lymphadenopathy and three irregular ulcerated lesions involving the right and left sides of the palate and the gingiva adjacentto tooth 23. The lesion on the left side of the palate had raised borders and was located on erythematous, clinically inflamed mucosa. The clinical findings were indicative of a local recurrence with cervical lymph node metastasis. (Figure 4)

A preoperative assessment and CT scan of the facial bones were performed. The patient subsequently underwent further surgical treatment at the Centre Pierre et Marie Curie (CPMC), including cervical lymph node dissection.

The patient died in February 2009 following the development of cerebral metastasis.The origin of the cerebral metastasis could not be established because histological examination of the intracranial lesion was not performed. Therefore, an association with either the previous breast carcinoma or the oral mucosal melanoma could not be definitively established.

3. Discussion

Oral mucosal melanoma is an extremely rare and aggressive malignant neoplasm originating from melanocytes of the oral mucosa. It is more aggressive and of poorer prognosis than cutaneous melanoma.

OMM is not associated with ultraviolet exposure unlike cutaneous melanoma. Its aetiology remains unidentified although some authors suggest formaldehyde, tobacco, or chronic irritation; no consistently established predisposing factor has been identified.(5)

Oral mucosal melanomas account for 0.2−8 % of all melanomas, with a slightly higher male predominance; It most frequently occurs in older adults, between the fifth to seventh decades of life (median age between 52 and 67). Similar to our case, the palate is the most commonly affected site accounting for ~47.5 % ofcases. (6–8)

Clinically, OMM may present as a brown, blue-black or variably pigmented macule, plaque or nodule. Lesions may be polychromatic and may display asymmetry, irregular borders, elevation, ulceration or bleeding; approximately 30%–37% of cases arise in pre-existing oral pigmentation. 10-30% are amelanotic and therefore lack the pigmentation that usually raises clinical suspicion.

Early lesions are most frequently asymptomatic and progress slowly overseveral months or years, of note 20% of patients report pain, our patient had pain in the region of the lesion, with the presence of the severely decayed tooth. Advanced lesions may be associated with tooth mobility, underlying bone destruction, and regional lymphadenopathy. (9)

The clinical appearance of OMM may overlap with other pigmented oral lesions. Features that should increase clinical suspicion include asymmetry, irregular borders or colour, ulceration and bleeding (10). The AEIOU criteria have been proposed as a clinical aid for identifying potentially malignant mucosal melanocytic lesions (11):

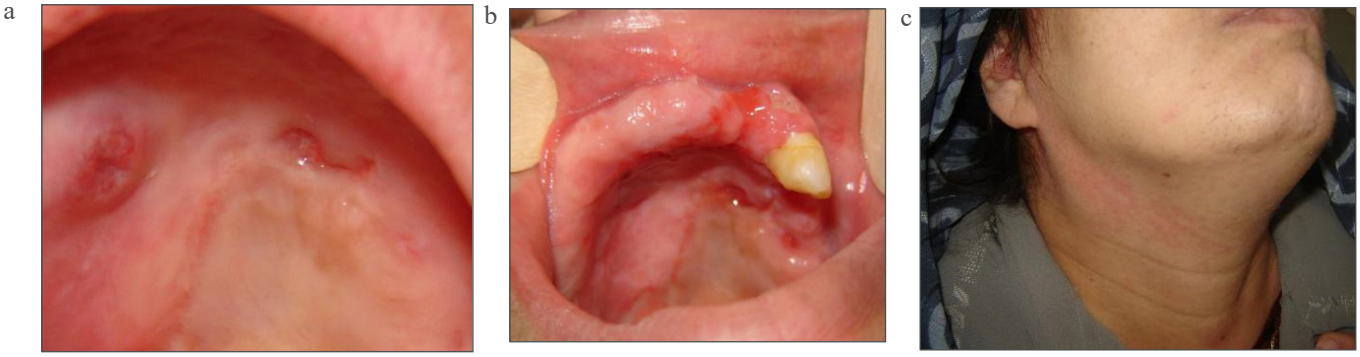


Figure 4. *Recurrence: a. and b. intraoral view; c. cervical lymph node*

- **A – Age:** older than 50 years ·
- **E – Ethnicity:** higher incidence in Asian, His panic and African populations
- **I – Irregularity:** irregular borders and/or colour
- **O – location:** the palate
- **U – Ulceration**

All these criteria were present in our patient.

Given the rapid progression and aggressive behaviour of OMM and its potential for early dissemination, any clinically suspicious persistent, pigmented lesion should undergo biopsy. Biopsy is essential to confirm the diagnosis before initiating aggressive therapies such as radical surgery, it is not associated with disease spread or worse prognosis(12– 16). For the diagnosis, the National Comprehensive Cancer Network recommends histopathological examination with immunohistochemistry, including S100, HMB-45 and Melan-A(17),WHO further adds SOX10, MITF and tyrosinase. (4)

Once the diagnosis of oral mucosal melanoma has been established, appropriate imaging and assessment for regional and distant disease are required.

Surgical excision with margins remains the principal treatment for oral mucosal melanoma. However, achieving wide surgical margins may be technically difficult due to the anatomical complexity and the proximity of critical structures, for palatal tumours, surgical management consists in a maxillectomy; in our patient, surgical treatment was not radical, which may have contributed to the rapid recurrence of the disease.

Radio therapy may be considered for local control, but may not affect overall survival and prevention of distant metastasis.

Management of the cervical lymph nodes isanother area of clinical debate. Neck dissection is generally considered whenregional metastatic disease has been confirmed, whereas elective or prophylactic neck dissection remains controversial inclinically node-negative patients. Other metastases are treated surgically if the number of lesions permits.(18)

Adjuvant therapies have also evolved, chemotherapy and immunotherapy have been suggested; interferon, ipilimumab (anti-CTLA-4), nivolumab (PD-1 inhibitor) and C-Kit inhibitors are some of the therapies currently being studied. (17,9)

The most common sites for metastasis of mucosal melanomas are: lymph nodes, lungs and liver (20) . Cerebral metastaseshave an incidence of ~9%, compared tobreast cancer in which cerebral metastasishave an incidence of 15-32% (21–23) , thiscould indicate that in the present case, the patient developed cerebral metastasis from her breast cancer; however, because the cerebral lesion was not histologically examined, its relationship to the oral melanoma or the patient's previous breast carcinoma cannot be established with certainty.

OMM has a poor prognosis, the reported five-year survival rates of mucosal melanomas do not exceed 35%; with poorer prognosis in amelanotic lesions, with a five-year survival rate as low as 6.2%.(6,24,25)

Factors affecting outcome: include patient age, tumour location, invasion of the underlying bone, regional lymph node involvement, and completeness of surgical resection. Tumours involving the palate and posterior maxillary gingiva have been reported to have a more favourable prognosis. (26–28)

The poorer prognosis of OMM may be due to late diagnosis, high propensity for local recurrence, regional lymph node involvement and distant metastasis.

Follow up and long-term surveillance is therefore essential after treatment of OMM.

4. Conclusion

Oral mucosal melanoma is a rare but highly aggressive malignancy that may initially present as an apparently innocuous area of oral pigmentation.

The present case illustrates the importance of carefully evaluating persistent or changing oral pigmentation. Prompt biopsy and appropriate histopathological and immunohistochemical assessment are essential for establishing the diagnosis.

Early recognition and diagnosis may allow treatment before extension, possibly enhancing patient survival.

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