Oral Malignant Melanoma of the Maxilla: A Case Report

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Abstract

A case report of oral malignant melanoma (OMM). An 84-year-old male patient presented with enlarged, swollen anterior left upper gingiva with mild pain lasting eight weeks from the lower occluded teeth. Histopathological examination and immunohistochemical studies confirm OMM.

OBJECTIVES: OMM, a neoplasm of melanocytes, is a rare aggressive tumor of the oral cavity. This paper aims to explain and discuss the clinical features, histopathology and immunohistochemical studies of OMM.

MATERIAL AND METHODS: We report on a case of OMM treated at our institute. An oral examination, differential diagnosis and biopsy were performed for a definitive diagnosis.

RESULTS: Histopathological examination showed sheets of atypical melanocytic tumor cells with abundant cytoplasmic pigmentation. The tumor cells were positive for S-100 protein, HMB-45 and MART 1 or Melan A. A final diagnosis of OMM was made.

CONCLUSION: OMM is a rare tumor of the oral cavity with a poor prognosis; although an aggressive treatment is available to patients. Early diagnosis and aggressive multimodal treatment are important ways for surgeons to achieve a better outcome for patients with OMM.

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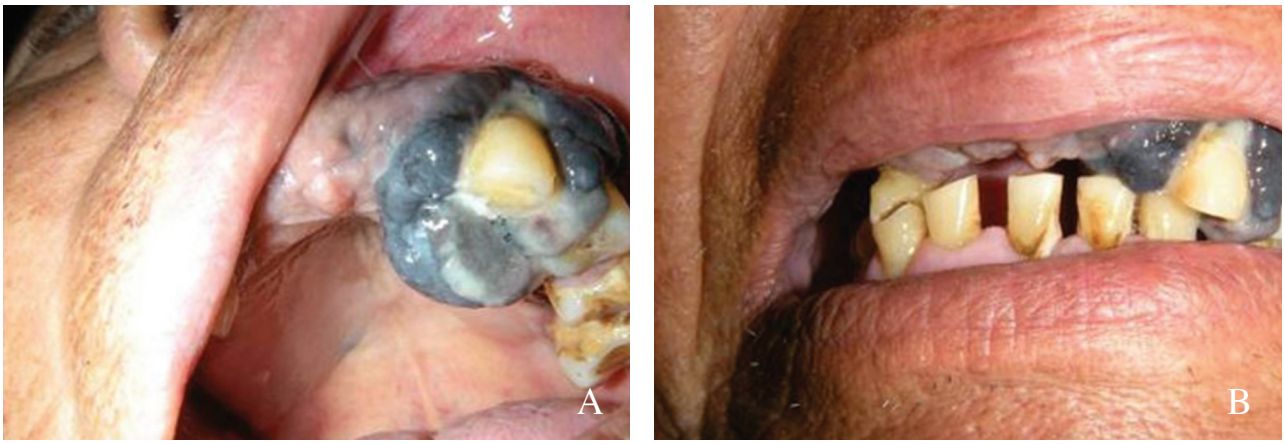
Malignant melanoma is a neoplasm of melanocytes, which originates from neuroectodermal cells.[1,2] Approximately 1% of all melanomas occur in the oral mucosa and of these, 0.5% are responsible for all malignancies arising in the oral cavity.[3,4] OMM and other mucosal malignant melanomas are considered more aggressive than cutaneous malignant melanomas with high rates of recurrence and death.[2,5]

Case Report

An 84-year-old Thai male presented with an enlarged, swollen gingiva on the anterior left maxilla with mild pain lasting eight weeks from the lower occluded teeth. The patient reported that the upper left lateral incisor was fractured due to large dental caries two months earlier, followed by soft tissue arising from the upper left lateral incisor to the upper second premolar tooth. The patient's past medical history was myocardial infarction, hypertension and chronic kidney disease for 10 years. The patient had taken aspirin (81 mg/d), nifedipine (40 mg/d), metoprolol (100 mg/d) and plavix (75 mg/d). His social history included occasional social alcohol use and smoking for many years.

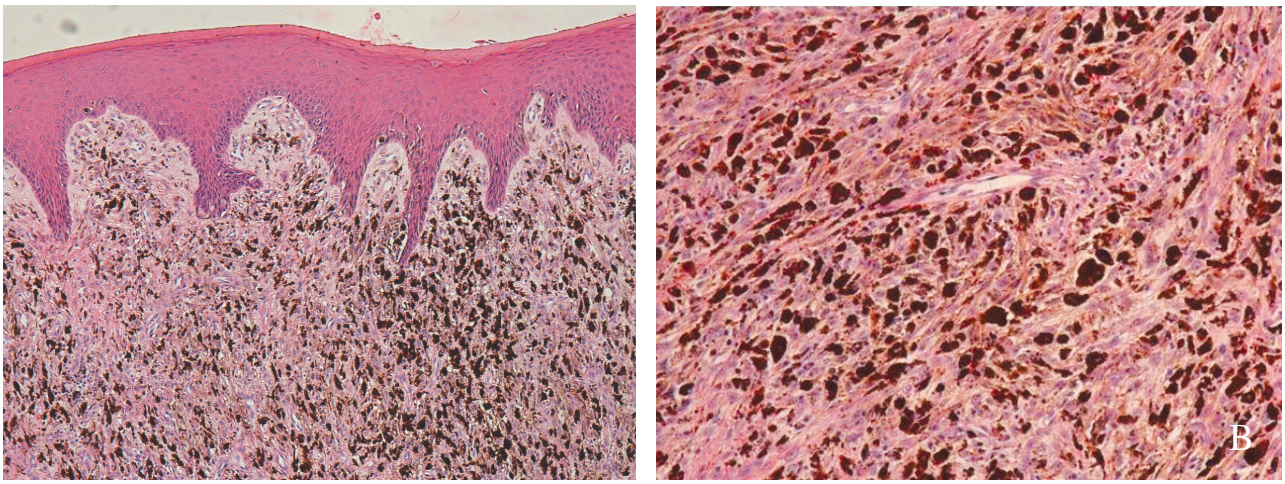
The extraoral examination was within the normal range. No cervical lymphadenopathy was apparent on physical examination. Intraoral examination revealed a lobulated mass from the retained root of the upper left lateral incisor to the upper second premolar tooth with variably gray to black pigments. Scattered black macules and patches were also observed on edentulous area of the upper anterior teeth and mid palate (Figure 1A). Ulcers replaced by pseudomembrane due to the lower occluded teeth were also noted (Figure 1B). The differential diagnosis included malignant tumor, suggestive of melanoma, Kaposi's sarcoma, or leukemia/lymphoma.



(A) A lobulated mass with variably gray to black pigments with scattered black macules and patches on the edentulous area of upper anterior teeth and mid palate.

(B) Ulcers replaced by pseudomembrane due to lower occluded teeth.

Figure 1: Intraoral examination



(A) An oral mucosa and the underlying fibrous connective tissue was infiltrated by sheets of atypical melanocytic cells. (H&E, x100)

(B) The malignant melanocytic cells showing pleomorphism, large hyperchromatic nuclei with abundant cytoplasmic melanin pigments. (H&E, x400)

Figure 2: Histopathology

An extraction of the retained root of the upper left lateral incisor, canine and an incisional biopsy under local anesthesia were performed.

Microscopically, the section revealed sheets of atypical melanocytic cells showing pleomorphism, large hyperchromatic nuclei with abundant cytoplasmic melanin pigments within the connective tissue covered by a normal oral epithelium (Figure 2). Immunohistochemically, the tumor cells were positive for S-100 protein, HMB-45 and MART 1 or Melan A (Figure 3). The diagnosis of OMM was finally made. After diagnosis, the patient was referred to the regional cancer center for further workup and definitive treatment. However, patient denied all treatments and chose supportive treatment.

Two months later, the patient returned complaining of a swollen and painful palate. The lesion extended to the left molar area with more remarkable hyperpigmentation than that seen at the first visit (Figure 4). Lymphadenopathy of the left submandibular gland was found. However, the patient continued to deny all treatments and home hospice care.

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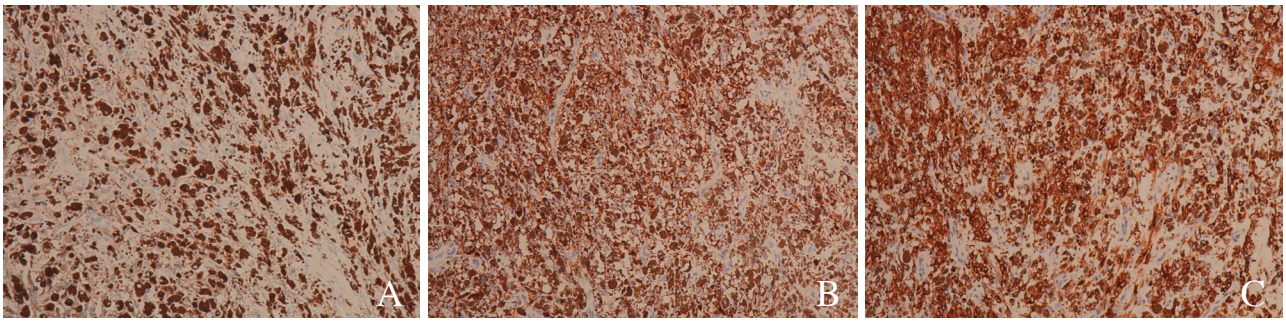

(A) The tumor cells were positive for S-100 protein. (S-100 protein staining, x200)

(B) The tumor cells were positive for HMB-45. (HMB-45 staining, x200)

(C) The tumor cells were positive for MART 1 or Melan A. (MART 1 staining, x200)

Figure 3: Immunohistochemistry study

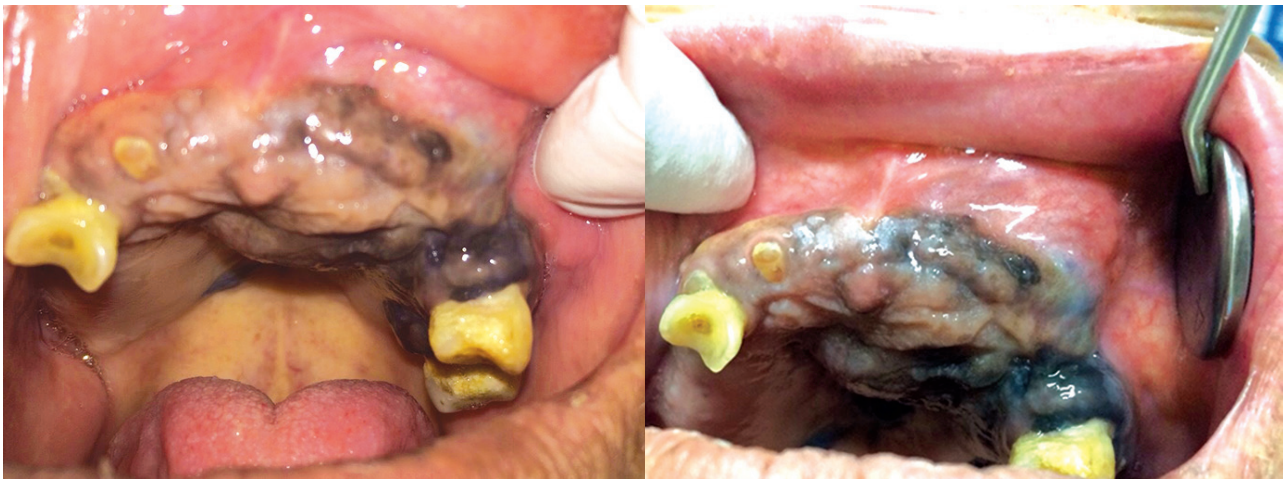

Figure 4: Two months follow-up. Swollen palate and lesion extending to the left molar area with an increased hyperpigmentation.

Discussion

OMM is a rare neoplasm with the palate and maxillary gingiva as the most common sites, where 80% of all oral melanomas are reported.[3,6] Most cases of oral melanoma occur between the ages of forth and seven decades and some reports have demonstrated a male preponderance.[7] The exact etiology of OMM is unknown; however, tobacco use, chronic irritation from ill-fitting dentures, ingested and inhaled environmental carcinogens at a high internal body temperature, have been proposed to play some role, but this has not been confirmed.[4,8,9] Although exposure to ultraviolet radiation is a key risk factor for cutaneous melanoma, it has not been associated with the development of mucosal melanoma. When compared to cutaneous melanomas, mucosal melanomas often have different genetic aberrations. BRAF mutations are rare in mucosal melanomas, while activating mutations of C-KIT, a cell surface receptor tyrosine kinase, are identified more frequently.[10] In addition, p53 protein alterations have been observed in about two-thirds of OMM.[11] Most cases of oral OMM occur from apparently normal mucosa, but it has been shown that about 30% of cases are preceded by oral pigmentations for several months or even years.[8,12] Swelling has been reported to be the most common initial symptom and sign of OMM, which is usually accompanied by pigmentation.[7,13] In amelanotic melanomas, pigmentation is generally absent.[14]

In the present case, the patient was an 84-year-old male with a rapidly pigmented enlarging mass. The age, gender, the rapid onset and the site of lesion led the clinician to suspect a malignant tumor of non-odontogenic origin, more specifically a malignant melanoma. In this case, oral malignant melanoma arises de novo.

Histopathology of oral malignant melanoma is similar to cutaneous melanoma, with an initial phase characterized by 'radial growth phase' followed by invasion of the underlying tissues as a so-called 'vertical growth phase'. Concerning the typical cutaneous melanoma categories, OMM does not fit exactly into any of those categories including superficial spreading melanoma, nodular melanoma (NM), lentigo maligna melonoma and acral

lentiginous melanoma (ALM). There is, however, some similarity to ALM and NM.[3,13] ALM is the most common form of oral melanoma whereas NM is typically found in oral amelanotic melanoma.[14,15] The malignant tumor cells of oral malignant melanoma show a wide variety of shapes, including spindle cells, plasmacytoid cells, clear cells, small round blue cells and epithelioid cells, arranging into sheets, organoid/alveolar or desmoplastic formation.[13,16] Usually, the malignant melanocytes can be diagnosed with confidence on hematoxylin and eosin (H&E) stained sections, which show intracytoplasmic melanin pigments. Various markers commonly used to confirm malignant melanomas are S-100 protein, HMB-45, and MART 1 or Melan A.[7] These markers are used for the identification of melanocytic tumor cells, especially in amelanotic melanoma and micrometastases in lymph nodes.[7,17] Other types of staining are Fontana Masson, tyrosinase, microphthalmia-associated transcription factor (MITF).[3,8,18]

The general histopathologic appearance of this case demonstrated epitheloid cells and a few spindle-shaped tumor cells with abundant cytoplasmic melanin granules. Furthermore positive staining for S-100 protein, HMB-45 and MART 1 or Melan A strongly confirmed the diagnosis of melanoma. The major pathological type of the lesions on maxilla was NM.

When dealing with any oral lesions histopathologically diagnosed with melanoma, it is crucial to perform an extensive investigation to evaluate the infiltration of the tumor and possible distant metastasis. OMM has been known for its metastatic preference to the lung, liver, brain and bone.[13,19] A variety of radiological examination such as computed tomography, magnetic resonance imaging or positron emission tomography have been proved to be useful for evaluation of primary tumor as well as regional or distant metastases.[7]

Treatment of OMM is currently controversial and there is no consensus regarding the best therapeutic approach.[7] However, surgery remains the major treatment modality, with additional radiotherapy and/or chemotherapy in order to prevent recurrence and metastasis. Although patients have been provided with the aggressive resection and multimodal treatments, prognosis of OMM is still very poor.[7]

The 5-year survival rate for patients with OMM remains poor and it has been reported to be 5-20% after diagnosis.[20] The poor outcome of these patients may be partly a result from a delay in diagnosis.[14] As the mucosal surfaces of the oral cavity are not regularly self-examined and these surfaces are not noticeable to others, the lesion may remain asymptomatic, and continue to grow overlooked for some time. Ultimately, most tumors have invaded into the deeper important facial structures and can reach a fatal thickness due to unconstrained growth.[21]

In this case, the patient denied all investigations, treatments and home hospice care; therefore the staging could not be evaluated. Finally, clinicians should be aware that an early diagnosis and treatment may result in increased survival rates for these patients. To accomplish this, the oral cavity should be carefully and routinely investigated, and all pigmented lesions with no apparent association with known physical or chemical factors should be biopsied.

Conclusion

OMM is a rare tumor of the oral cavity, with very poor prognostic outcome. Local, regional, and distant metastases arise despite aggressive multimodal treatment. Because late diagnosis with advanced disease at the time of diagnosis is the only confident predictor of outcome, careful clinical and pathologic work-up of any suspected melanotic lesions should be carried out to diagnose oral malignant melanoma in its early stage. Definitive diagnosis of this fatal disease requires histopathological and immunohistochemical investigations.

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