

Primary malignant melanoma

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ABSTRACT

يُعد الورم الميلاني الذي يظهر في التجويف الفموي نادراً للغاية مما يمثل نسبة 0.2% إلى 8.0% من جميع الأورام الميلانية وعادة ما يظهر في الحنك الصلب واللثة. إن التشخيص والعلاج المبكر مهمان للحد من الإصابة به. تصطبغ خلايا الورم الميلاني مع الأجسام المضادة لكلاً من سرطان الجلد الأسود 45 وبروتين S-100 وبروتين فيميتين وبالتالي يمكن للكيمياء الهوستولوجية المناعية أن تلعب دوراً هاماً في تقييم عمق غزو الورم وموقع الانبثاث. أصيب رجل يبلغ من العمر 76 عاماً بورم ملاني في الفم، في البداية شُخص علي أنه فرط التنسج التفاعلي الناتج عن سوء تناسب الفك السفلي ثم أُزيل الورم جراحياً وكشف فحص الأنسجة عن ورم ملاني عقيدي ولم يكن هناك أي دليل على عودة الورم خلال فترة المتابعة لمدة 4 سنوات.

Malignant melanomas (MM) of the oral cavity are extremely rare, accounting for 0.2% to 8.0% of all malignant melanomas. Malignant melanomas is more frequently seen at the level of the hard palate and gingiva. Early diagnosis and treatment are important for reducing morbidity. Malignant melanoma cells stain positively with antibodies to human melanoma black 45, S-100 protein, and vimentin; therefore, immunohistochemistry can play an important role in evaluating the depth of invasion and the location of metastases. A 76-year-old man developed an oral malignant melanoma, which was originally diagnosed as a bluish reactive denture hyperplasia caused by an ill-fitting lower denture. The tumor was removed surgically, and histopathological examination revealed a nodular-type MM. There was no evidence of recurrence over a 4-year follow-up period.

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Primary malignant melanoma (MM) is a rare tumor. It is originating from the uncontrolled growth of melanocytes found in the basal stratum of the oral mucous membranes.^{1,2} Incidence in the population was 0.073% of all cancers. Approximately 80% of oral melanomas arise in the mucosa of the maxilla, especially occurring on palate and alveolar gingiva. There are various types of lesion, from a typically pigmented macular or proliferative lesion to a non-pigmented. The lesion may also be single, or multiple and primary, or metastatic. Early diagnosis and treatment are important for reducing morbidity and mortality. Malignant melanoma cells stain positively with antibodies to human melanoma black 45 (HMB-45), S-100 protein, and vimentin. Hence, immunohistochemistry has an important role for evaluating the depth of invasion and the location of metastases.³ The objective in presenting this particular case is to describe the clinical features of primary malignant melanoma.

Case Report. A 76-year-old man was presented with a one month history of painless bluish reactive denture hyperplasia in the lower anterior alveolar gingiva. He had a history of primary colon cancer for 6 years. His medical history was significant for hypertension and chronic cardiopulmonary disease. A complete blood cell count, biochemical profile, and urinalysis revealed no significant findings. His chest x-ray was normal. No palpable lymph nodes were found during palpation of the anterior neck. Intraoral clinical examination revealed a non-tender mass on the lower anterior alveolar gingiva, measuring approximately 2 × 1 cm. The mass was dark bluish in color, pedunculated, and had a smooth surface and well-defined margins (Figure 1). There was no other pigmented area in the oral mucosa and no suspicious cutaneous lesions on the patient's body. Radiographic examination revealed an

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ill-defined radiolucent (RL) area in the lower anterior alveolar non-edentulous area (Figure 2). The lesion was considered denture-induced reactive hyperplasia due to chronic trauma due to the patient's ill-fitting denture. The lesion was subjected to an excisional biopsy due to



Figure 1 - Preoperative clinical view of the lesion.



Figure 2 - An orthopantomogram showing an ill-defined radiolucent area in the lower anterior alveolar non-edentulous area.



Figure 3 - Postoperative view of the patient after 3 years.

its well-demarcated margins. The wound was primarily closed with interrupted sutures, and the healing was uneventful (Figure 3). Histopathological examination revealed a nodular-type MM (Figure 4). The tumor was macroscopically polypoid in character with surface ulcerations. The depth of the tumor was 0.5 cm, and the surgical borders were free of tumoral changes. A focal immunohistochemical reaction was observed with HMB-45. The diagnosis for distant metastases (CT scan of chest, brain, and abdomen plus bone scintigraphy) was negative. There was no evidence of recurrence over a 4-year follow-up period (Figure 5). We have read the Helsinki Declaration and have followed the guidelines in this investigation.

Discussion. Pigmented lesions of melanocytic origin rarely occur in the oral cavity. Oral melanomas are estimated to represent 1% to 2% of all oral

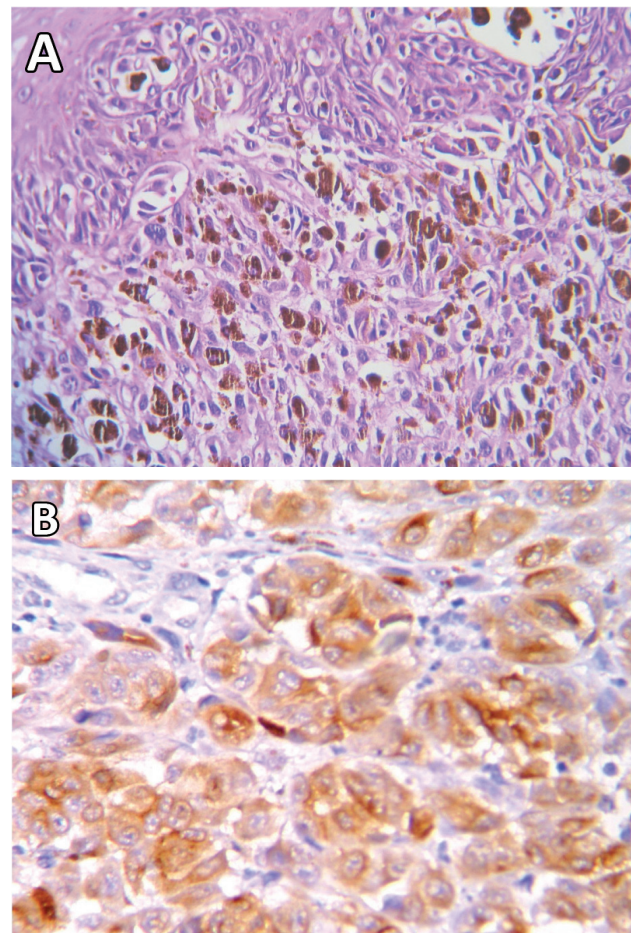


Figure 4 - Histopathological examination showing: A) Invasive tumour cells with heavy melanin pigmentation (hematoxylin & eosin, $\times 200$), and B) Immunohistochemical common reaction with HMB-45 (high power field $\times 400$).

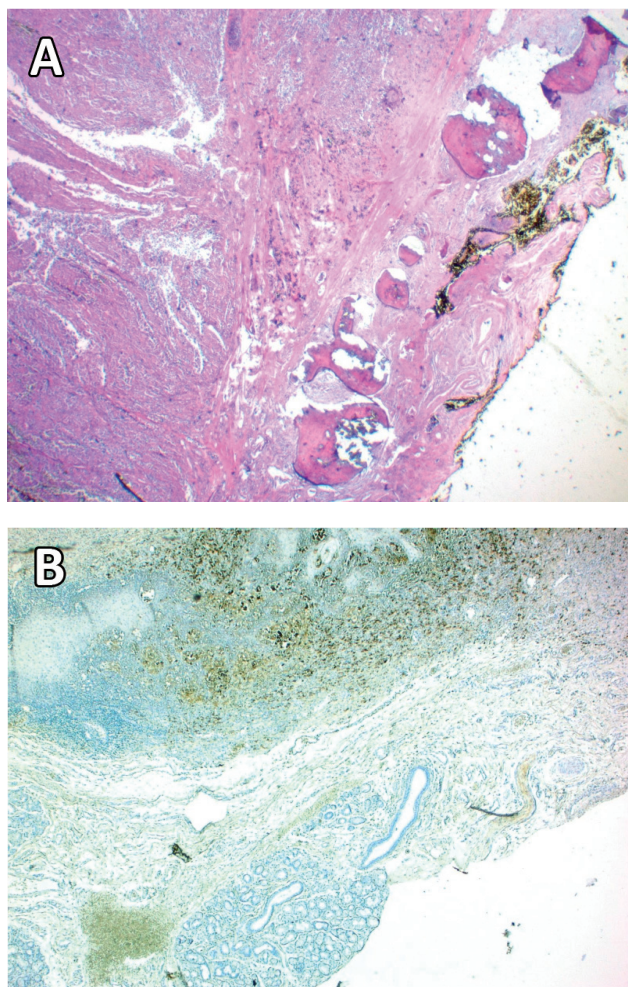


Figure 5 - Histopathological examination showing: A) The bottom margin (labelled in black) was intact and reactive bone trabeculae were observed (hematoxylin and eosin, $\times 20$), and B) In another section, HMB-45 immunohistochemistry demonstrated that the lesion shows no continuity at the bottom of the margins (Biotin-Streptavidin peroxidase, high power field, $\times 20$).

malignancies and account approximately 0.2% to 8.0% of all melanomas.² In the differential diagnosis of oral melanotic macules, various benign lesions (amalgam tattoo, oral melanotic macule, nevi, melanoacantoma³) to life-threatening malignant entities, such as poorly differentiated carcinoma and large cell anaplastic lymphoma, must be taken into account. An attentive clinical and pathological examination must be made to prevent progression to oral malignant melanoma (OMM).^{4,5} Malignant melanomas is a rare and aggressive tumor of melanocytic origin. It has a much poorer prognosis than its counterpart on the skin. Malignant melanoma affects the mucous membranes of the nose, paranasal sinuses, and pharynx.^{5,6} The etiology of

OMM is unknown. Sunlight, smoking, and chewing tobacco are an etiological factors. However, there is no proof for these theories.⁵ Chronic irritation from ill-fitting dentures and inhaled environmental carcinogens have also been suggested.⁴ Symptoms of oral melanomas arise de novo, and bleeding and pain, swelling, and pigmentation are often the initial signs. Oral malignant melanoma uniformly brown or black or have variable pigmentations, such as grey, red, purple, and white.³ The most commonly involved intraoral sites are the palate and maxillary alveolar gingiva.⁴ Oral malignant melanoma usually occurs in the fourth to sixth decades of life. A distinct predilection was noted for mucosal melanoma, with men being affected 3.5 times more frequently than women.³ In this case, the patient had a one month history of an exophytic hyperplastic mass of dark bluish color, which had been attributed to irritation due to ill-fitting denture; the lesion was dark bluish in color, pedunculated, and had a smooth surface and well-defined margins. Mucosal melanomas may be primary or metastatic. Green et al⁷ reported the diagnosis of primary OMM following the exposure of a clinical and microscopic tumor in the oral cavity, the presence of junctional activity in the oral mucosa, and no other primary site were seen. For the diagnosis of OMM, the ABCDE checklist (asymmetry, border irregularities, colour variations, diameter of >6 mm, and elevation and a raised surface) for the identification of cutaneous melanomas can also be used for oral melanomas.^{3,4} As for checklist, this case was a symmetrical; $2.0 \times 1.0 \times 0.8$ cm in dimension; and had regular borders, a dark bluish color, and an elevated surface. Biopsy and radiological examinations (CT, MRI) were used to evaluate primary tumors, invasions, and distant metastases. Marx and Stem⁸ recommended a chest radiograph every 6 months postoperatively to identify metastases as the lungs and liver are commonly affected sites with OMM metastases. In our patient. We used CT scans of the chest, brain, and abdomen plus bone scintigraphy to assess distant metastases. During the study, our patient was still alive with no recurrence or metastasis and under close follow-up.

Surgery is the most effective treatment for MM. However, wide resection with a surgical margin of 20 to 50 mm is not always possible for an OMM.⁹ The proximity of vital structures sometimes difficult or impossible. The tumor mass depth in this case was 0.5 cm, and the surgical margins were free of tumor cells. In the literature⁴ suggested a protocol for the management of OMM: 1) Excision of primary lesions using an intraoral approach and involving at least 1.5 cm healthy tissue; 2) Excision of any lymph node metastasis; and

3) Consider chemotherapy. Tanaka et al¹⁰ reported that OMM was controlled with surgery, then chemotherapy, and radiotherapy. We reported that the primary lesion was controlled with surgery (92.3%). In the non-surgery group treated with radiotherapy, 53% of cases were controlled.¹⁰ Thus, chemotherapy and radiotherapy play only adjuvant roles in the treatment of OMM. We excised the lesion due to its well-demarcated margins. In many cases, melanoma cells have involved melanin granules; however, they did not produce melanin. Lack of melanin production may cause diagnostic problems at the light microscopic level because melanoma may be detected like an undifferentiated tumors. We found that S-100 protein, MART-1, and HMB-45 reactivity of the lesional cells are useful in distinguishing such melanomas from other malignancies in immunohistochemical studies.⁵ Histopathological examination in this case showed typical characteristics of an OMM (invasive tumor cells with heavy melanin pigmentation (Figure 4). Immunohistochemistry was effective for a definitive diagnosis. In this case, a focal immunohistochemical reaction was observed with HMB-45 (Figure 4). The prognosis of OMM, although poor, is highly variable. The 5-year survival rate ranges from 5.2% to 20%. However, favorable results were reported, and it was suggested that the disease is potentially curable if diagnosed and treated at an early stage.⁹

In conclusions, OMM is a rare malign tumor of the oral cavity that has a very poor prognosis. Early diagnosis and treatment are essential for a less poor prognosis. All pigmented lesion in the oral cavity should be examined closely. Biopsy of any growing pigmented lesion are vital for detecting MM in oral cavity. Immunohistochemistry

and other advanced diagnostic methods should be use to evaluate the depth of invasion and the definition of metastases.

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Case Reports

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