

Malignant Melanoma of the Oral Cavity: A Review

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Abstract: Primary malignant melanoma is a rare and aggressive neoplasm that originates from the proliferation of melanocytes. Most of the mucosal melanomas are usually asymptomatic in early stages, and presents as pigmented patch or a mass delaying the diagnosis until symptoms of swelling, ulceration, bleeding, or loosening of teeth are noted. The prognosis is extremely poor, especially in advanced stages. Therefore, any pigmented lesion of undetermined origin should always be biopsied.

Keywords: Malignant melanoma, oral mucosa, pigmented lesion

1. Introduction

Primary malignant melanoma of the mouth is an extremely rare tumor arising from the uncontrolled growth of melanocytes found in the basal layer of the oral mucous membrane. Its actual incidence in the population at present is unknown, but is estimated to vary widely between 0.2% and 8% of all melanomas and 1.3% of all cancers. It has a higher prevalence in blacks, Japanese, and Indians of Asia due to more frequent finding of melanin pigmentation in oral mucosa of these races(1). Nearly 80% of oral malignant melanomas arise in the mucosa of the upper jaws in elderly patients, with the majority occurring on keratinizing mucosa of the palate and alveolar gingiva. Other sites include mandibular gingiva, buccal mucosa, tongue, and floor of the mouth. It is asymptomatic and detected only when there is ulceration or hemorrhage of the overlying epithelium. The delayed detection may be the cause for the poor prognosis with a 5-year survival being between 10% and 25%[1,2].

2. Clinical Features

Most cases occur between the fourth and the seventh decade of life, with an average of 55-57 years old (3), not very frequently below 30 years old (4). Apparently the malignant melanoma of the oral cavity has a predilection for the male gender (5), in a male-female ratio of 2:1. The areas in which they appear in order of frequency are: the hard palate (where 40% of the cases have been reported), followed by upper gingival mucosa, lower gingival mucosa, buccal mucosa, tongue and floor of mouth. The clinical characteristics are variable, such as macular lesions, plate (with horizontal growth, which often correspond to melanomas in situ in the histopathologic examination) and nodular (with clinical ulceration, usually of an invasive type or combined at a microscopic level); their colors vary from dark blue to black and their edges are regular or irregular. The symptoms of the oral mucosal melanoma include: bleeding (referred to in the diagnosis as the most frequent sign), pain (it often appears late) and presence of melanotic pigmentation (in one third of the patients before the diagnosis) (6). The ABCDE criteria used in the clinical diagnosis of cutaneous melanoma may also be used for OMM. These are: Asymmetry in the shape of the lesion, border irregularities, color variation, diameter >6 mm and evolving changes in the lesion over time are characteristic criteria.



Figure 1: Intraoral photograph showing bluish-black pigmentation on the labial attached gingiva extending from the right maxillary canine region to the central incisor, crossing the midline and extending to the left lateral incisor



Figure 2: Intraoral photograph showing a black proliferative growth on the palatal aspect of anterior teeth

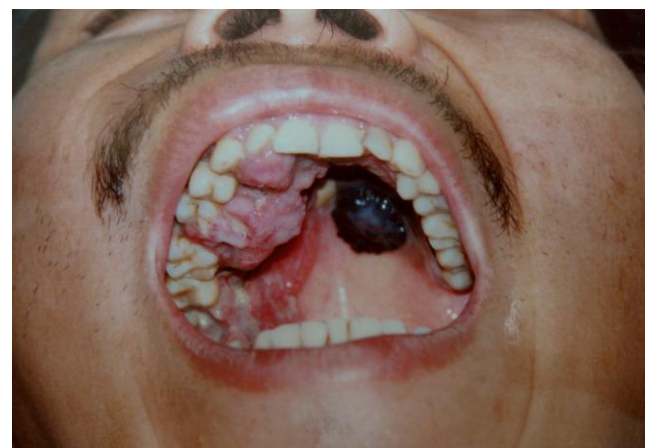


Figure 3: Patient with oral melanoma on hard palate

Etiology

Its etiology is unknown, although sometimes it is placed on pre-existing long-term melanosis involving 33 to 55% of the mucosal melanomas of the head and neck, other possible etiological factors for this neoplasia are: mechanical trauma such as denture irritation, use of tobacco, exposure to formaldehyde and alcohol.

Histopathology

Histologically it is characterized by the proliferation of atypical melanocytes with a wide variety of shapes, including the one of the spindle, of plasmacytoid cells, clear cells and some epithelioid cells, located along the junction between the epithelial and the connective tissue, as well as invading the connective tissue (7). It also describes histological stages of the oral malignant melanoma in 3

phases: Stage I primary site, Stage II with lymph node metastasis and Stage III with distant metastasis. The immunohistochemistry has referred positivity in a varying level for the antigens related to the melanoma: NKI/C-3, S-100 protein, gp100 (HMB-45), Mart-1 (Melan-A), vimentin, tyrosinase and microphthalmia transcription factor (MiTF) that are useful in the diagnosis. The vimentin is the most consistent, but the less useful for the diagnosis; the S-100 protein positivity is nonspecific, but due to the fact that it is negative in most of the tumors that are considered in the differential diagnosis, this stain is very important; the HMB-45 is a much more specific marker than protein S-100; the Melan-A is positive in approximately 80% of melanomas and MiTF positivity is above the 90%. The oral melanoma has a metastatic predilection for lymphonodes, lungs, liver, brain and bones.

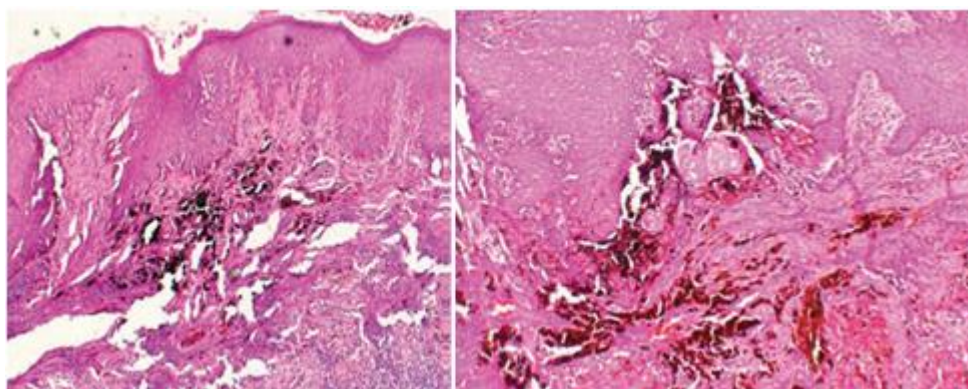


Figure 4: Photomicrographs showing infiltration of malignant melanocytes into the connective tissue (hematoxylin and eosin stain). Original magnification: **a.** $\times 10$; **b.** $\times 40$.

Differential Diagnosis

Differential diagnosis of melanoma includes oral melanotic macule, smoking associated melanosis, medication induced melanosis (antimalarial drugs and minocycline), melanoplakia, Cushing's syndrome, postinflammatory pigmentation, melanoacanthoma, melanotic nevi of oral mucosa, blue nevi, Addison's disease, Peutz-Jeghers syndrome, amalgam tattoo, Kaposi's sarcoma, physiologic pigmentations, and many other conditions sharing the same macroscopic characters[8]. Moreover, it is necessary that OMM should be differentiated from other malignant entities, such as poorly differentiated carcinoma and large anaplastic lymphoma. Amelanotic malignant melanoma without radial growth phase may be misdiagnosed as epulis or squamous cell carcinoma.

Treatment

Traditionally, wide surgical excision with adequate negative margins with or without neck dissection is the treatment of choice for malignant melanoma, with radiotherapy and chemotherapy as adjunctive treatment methods. In case of OMM, if the disease is localized it can be controlled by radiotherapy, in contrast to cutaneous melanoma. Chemotherapy and immunotherapy may play a role to prevent distant metastasis.[9] Dacarbazine (DTIC) and interferon-alpha-2b are used for chemotherapeutic and

immunotherapeutic treatments with the first line of drug being DTIC, alone or in combination with nimustine hydrochloride and vincristine. or different combinations of bacillus Calmette-Guerin and recombinant interleukin-2.

Prognosis

Most oral melanomas are large at presentation and have a poor prognosis than cutaneous melanoma. The reported 5 years survival rate for OMM has ranged from 4.5%-29% with a median survival rate of 18.5 months after initial diagnosis. In general, the survival rates are poor and worse for those with metastasis.

3. Conclusion

The oral cavity is a common site for pigmented lesions, most of them benign. Dentists should keep the possibility of malignant melanoma in mind during any differential diagnosis of a pigmented lesion. When in doubt, the dentist should refer the patient to a specialist or perform a biopsy. Prevention and screening for malignant melanoma include annual evaluation of pigmented lesions of oral mucosa. Early diagnosis is promoted by careful oral examination and early biopsy of pigmented and suspicious non pigmented masses along with advanced surgical techniques and considerations to chemotherapy, radiotherapy, immunotherapy, and combined therapy may help in

improving the prognosis of patients with malignant melanoma.

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