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Malignant melanoma of the anterior mandibular gingiva: a case report

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MALIGNANT MELANOMA OF THE ANTERIOR MANDIBULAR GINGIVA: A CASE REPORT

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Abstract

Oral malignant melanoma is an infrequent neoplasm making up less than 1% of all melanomas; its behavior is more aggressive when compared to melanomas of the skin. We present a rare case of a 50-year-old male patient with a stage II oral malignant melanoma of the anterior mandibular gingiva treated with surgery and radiotherapy.

Keywords: Oral malignant melanoma - oral pigmentation - mucosal melanoma.

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MÉLANOME MALIN DE LA GENCIVE MANDIBULAIRE ANTÉRIEURE

Résumé

Le mélanome oral malin est une néoplasie rare représentant moins de 1% des mélanomes ; il présente un comportement beaucoup plus agressif que ceux de la peau. Nous présentons un cas rare de mélanome malin oral de la gencive mandibulaire antérieure chez un homme de 50 ans, traité par chirurgie et radiothérapie.

Mots-clés: Mélanome oral malin - pigmentation orale - mélanome muqueux.

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Introduction

Melanomas are malignant neoplasms arising from melanocytes, which originate from the neural crest cells and produce the melanin pigment of the epithelium's basal layer. These neoplasms are grouped under the name of "Dispersed Neuro-Endocrine System (DNES) tumors". Melanomas are present primarily in the basal portion of the epidermis at the dermal-epidermal junction [1].

Over 90% of melanomas occur on the skin with slightly more than 1% arising from mucosal surfaces [2]. The sites of predilection for mucosal malignant melanomas are commonly the rectum and the vulvo-vaginal regions. In the head and neck region, nasal and paranasal melanomas are three times more common than oral malignant melanomas (OMM) [3]. These latter have a much poorer prognosis than those developing on the skin [4]. Primary OMMs are rare, representing 0.2–8% of all melanomas [5] and accounting for 0.5% of all oral malignancies [6].

Case report

A 50-year-old male patient presented to our department with an asymptomatic pigmented lesion discovered on the mandibular gingiva nine months ago. Initially the patient had noticed the change in the color of the vestibular gums. Three months later, he noticed a swelling in the same region and stated that the adjacent teeth had become mobile with the swelling gradually increasing in size.

Patient's medical history was non-contributory. Thorough anamnesis and physical examination ruled out

the possibility of melanotic lesions elsewhere in the body; the oral lesions were considered "primary". On extraoral examination, submandibular lymphnodes were palpable on right and left sides. They were non-tender, about 1 cm in size, firm and freely mobile.
Intraoral examination showed a fungated, pigmented mass, measuring about 4×2.5cm on the labial gingiva extending to the lingual aspect of the anterior mandibular region (Fig. 1). It extended from the lower left lateral incisor region to that of the lower right canine, crossing the midline. Its surface was lobulated with a purplish-red discoloration of the overlying mucosa. Its consistency was non-tender and firm.
The dental panoramic x-ray revealed soft tissue shadow of the mass with bone loss extending from the region of the lower left central incisor to the lower right premolar. There was also loss of the lamina dura in relation to the lower left anterior quadrant, with migration of the left lateral incisor laterally whereas the left central incisor exhibited a floating tooth appearance [Fig.2].
Considering the history, the clinical examination and the radiological findings, malignant melanoma was the provisional diagnosis. Differential diagnosis of Kaposi's sarcoma, giant cell lesion and pyogenic granuloma were advocated. Based on clinical staging system for primary OMM, the present case was classified under stage II [7].

The routine blood and biochemical investigations were found to be within normal limits and the patient was non-reactive for HIV 1 and 2. Chest x-ray revealed no abnormality. Ultrasound of the abdomen ruled out liver metastasis. Incisional biopsy of the pigmented mass was done and histopathological findings were suggestive of malignant melanoma [Fig.3].

The surgical treatment consisted of marginal mandibulectomy and bilateral radical neck dissection. Histopathological examinations of the resected material showed malignant melanoma of the gingiva invading the mandibular bone. The patient was treated with radiotherapy to the tumoral and neck region. Patient is symptom-free for about a year now of follow-up.

Discussion

Oral malignant melanoma is a rare aggressive neoplasm of the melanocytes, located along the tips and peripheries of the rete pegs. The ratio of melanocytes to keratinocytes in gingiva is 1:15 [3]. Melanocytes differ from nevus cells and melanoma cells in showing features of pleomorphism, hyperchromatism, prominent nucleoli and mitotic activity [3].

In contrast to cutaneous melanomas etiologically linked to sun exposure, mucosal melanomas can occur either owing to certain risk factors, like tobacco use and chronic irritation, or may be de novo [6]. Some may arise from pre-existing nevi, especially atypical (dysplastic) nevi, and congenital hairy nevi [8]. Genes implicated in the development of melanomas include CDKN2A (p16), CDK4 (chromosome 12q15), RB1, CDKN2A (p19) and PTEN/MMAC1 [9]. OMM generally affects in adults between 55 and 65 years of age [10] and more commonly among the Japanese with a male to female ratio of almost 2:1. It often occurs in the hard palate and the maxillary gingiva [11]. As the palate is continuously exposed to the air while breathing, irritants and carcinogenic compounds in the air (such as components of tobacco smoke) may play a contributing role in the development of melanomas [10]. It is interesting that among pigmented lesions of the oral cavity, oral nevomelanocytic nevi (OMNs) are localized mostly in the palate and this finding may lead to the hypothesis that subtypes of OMNs could be precursors of the pathogenesis of OMM [12]. Less commonly, melanomas also affect lips, buccal mucosa, mandibular gingiva, tongue and floor of the mouth [4]. Our case report of OMM with respect to mandibular gingiva can therefore be regarded as a rare case seen in a male patient at the mandibular arch.

According to Tanaka et al. [13], oral melanomas could be classified into five types based on their clinical appearance: pigmented nodular, non-pigmented nodular, pigmented macular, pigmented mixed and non-pigmented mixed. The clinical coloration can appear as black, grey, purple or even reddish. The tumors are asymmetric, irregular in outline and occasionally multiple. Pain, ulceration and bleeding are rare until late stages of the disease. Lopez- Graniel et al. [14] stated that haemorrhage was the most common presenting symptom. Rolled borders are not a feature of oral mucosa melanoma because the atypical melanocytes exhibit a pagetoid mode of spread resulting in a uniform epithelial thickening [15]. No induration is observed which may be explained by the small, if not totally absent, inflammatory cell response at the lateral edges of the vertical growth phase [16]. In our case report, the patient presented with a pigmented, purplish-red, non-tender and non-indurated mass.

Adjunctive radiologic diagnostic methods such as computed tomography, magnetic resonance imaging and positron emission tomography (staging purposes) are sometimes useful [7] and should be undertaken to explore regional metastases to the submandibular and cervical nodes. Incisional biopsy is the method of choice for diagnosis [17].
An incisional biopsy was performed in our case, suggestive of OMM of the mandibular anterior gingiva.
Greene et al. [18] proposed three criteria for the diagnosis of primary OMM: 1) demonstration of malignant melanoma of the oral mucosa, 2) presence of so-called junctional activity (i.e. the melanocytes are arranged along the basal layer of the surface epithelium) in

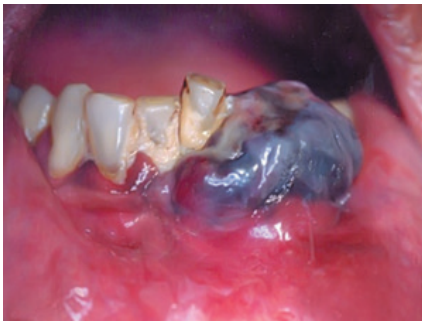

Fig. 1: Pigmented mass on anterior mandibular gingiva.

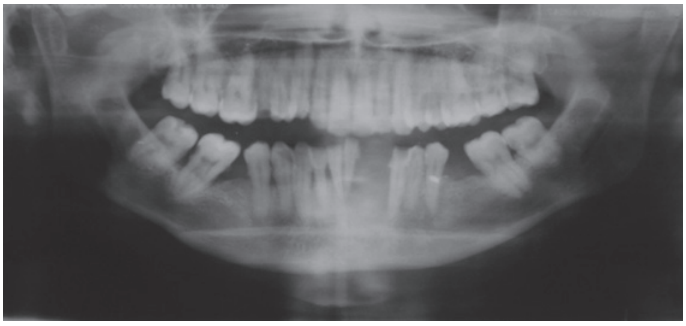

Fig. 2: The orthopantomogram revealed loss of the lamina dura in relation to the lower anterior quadrant, with migration of 32 laterally; the 31 exhibited a floating tooth appearance.

the lesion, and 3) the inability to show malignant melanoma in any other primary site. Based on these criteria, our case was diagnosed as primary OMM.

Clinical staging system for primary oral melanoma with histopathological microstaging is as follows [7]:

Stage I: Primary tumor present only (N0M0).

Level I: Pure in situ melanoma without evidence of invasion or in situ melanoma with microinvasion.

Level II: Invasion up to the lamina propria.

Level III: Deep tissue invasion into the skeletal muscle, bone or cartilage.

Stage II: Tumor metastatic to regional lymph nodes (T any N1M0).

Stage III: Tumor metastatic to distant sites (T any M1). Some authors reported a survival rate of 30% in tumors having a thickness of <5 mm, dropping to 18% in tumors with >5 mm thickness, and to 10% in patients with tumor thickness >1 cm [19]. Based on this, our case would belong to the group of patients having 10% survival rate as the tumor thickness is more than 1 cm.

The mainstay of treatment is wide surgical resection aiming at complete resection of the primary tumor and any positive cervical lymph nodes.

A sentinel lymphnode is the first lymphnode(s) to which cancer cells are most likely to spread from a primary tumor [20]. A sentinel lymphnode biopsy (SLNB) can be used to help determine the extent or stage of cancer in the body. Because SLNBs involve less extensive surgery and the removal of fewer lymph nodes than standard lymphnode surgery, the potential for adverse effects or harms is lower.

A negative SLNB result suggests that cancer has not acquired yet the ability to spread to nearby lymphnodes or other organs. A positive SLNB result indicates that cancer had reached the sentinel lymphnode and may be present in other nearby lymphnodes (called regional lymphnodes) and possibly, other organs. This information can help determining the stage of the cancer (extent of the disease within the body) and developing an appropriate treatment plan.

SLNBs may be done on an outpatient basis or may require a short stay in the hospital. In addition to helping doctors stage cancers and estimate the risk of spread to other parts of the body, SLNB may help some patients avoid more extensive lymphnode surgery. Removing additional nearby lymph nodes to look for cancer cells may not be necessary if the sentinel node is negative for cancer. All lymphnode surgery can have adverse effects and some of these effects may be reduced or avoided if fewer lymphnodes are removed. The potential adverse effects of lymphnode surgery include the following:

- Lymphedema or tissue swelling.
- Seroma or the buildup of lymph fluid at the site of the surgery.
- Numbness, tingling, or pain at the site of the surgery.
- Difficulty moving the affected body part.

SLNB like other surgical procedures can cause short-term pain, swelling, and bruising at the surgical site and can increase the risk of infection. In addition, some patients may have skin or allergic reactions to the blue dye used in SLNB. Another potential harm is a false-negative biopsy result which gives the patient and the doctor a false sense of security about the extent of cancer in the patient's body. Researchers have investigated whether patients with melanoma whose sentinel lymphnode is negative for cancer and who have no clinical signs of other lymph node involvement can also be spared more extensive lymphnode surgery at the time of primary tumor removal [20].

Sentinel-node biopsy or lymphoscintigraphy, beneficial in staging of cutaneous melanomas, has less value in staging or treating oral melanomas. Complex and ambiguous drainage patterns may result in the bypass of some first-order nodes and in the occurrence of metastasis in contralateral nodes [21].

Amelanotic melanomas can resemble many different mesenchymal neoplasms, and immunohistochemical stains must be used for diagnosis. The

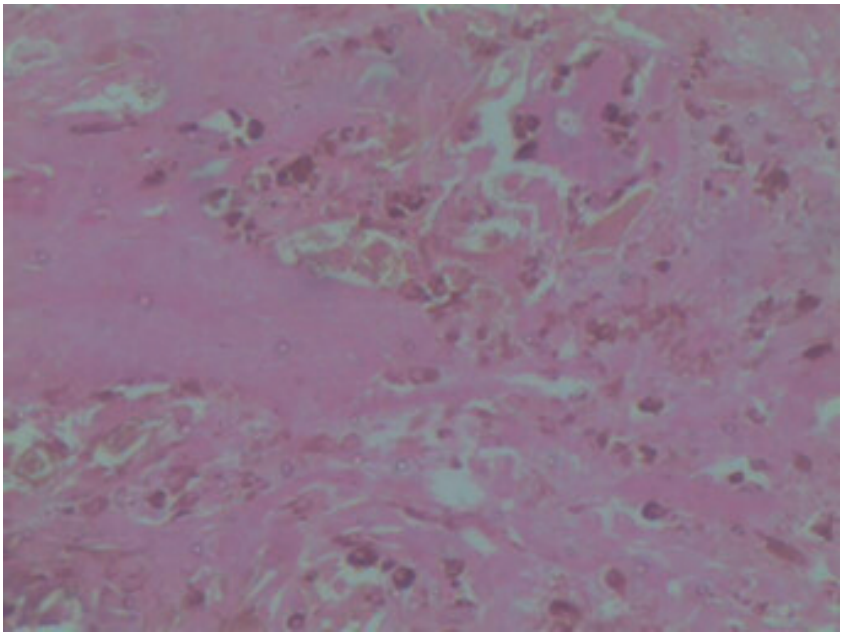

Fig. 3: Haematoxyllin and Eosin sections revealed numerous atypical melanocytes within the epithelium and invasion into the connective tissue. These cells are epitheloid to spindle in shape, with vesicular, hyperchromatic nuclei and prominent nucleoli.

pathologist should look for evidence of a lymphocytic reaction within the connective tissue and an increased number of melanocytes in the basal cell layer as an indication for immunohistochemical staining.

Leukocyte common antigen and Ki-1 are used to identify the lymphocytic lesions. Cytokeratin markers, often cocktails of high– and low–molecular-weight cytokeratins, can be used to help identifying epithelial malignancies.

The positivity to S-100 protein and homatropine methylbromide antigen (HMB-45) is characteristic of, although not specific for melanomas. S-100 protein is frequently used to highlight the spindled, more neural-appearing melanocytes whereas HMB-45 is used to identify round cells. Immunohistochemical tests revealed that there was intense and widespread positivity for NKFC3- associated melanoma antigens and focal positivity for vimentin and cytokeratin. Melanomas, unlike epithelial lesions, are identified by using vimentin, a marker of mesenchymal cells.

Microphthalmic-associated transcription factor (MITF), tyrosinase, and melanoma antigen (Melan-A) immunostains have been used to highlight melanocytes. The inclusion of these stains in a panel of stains for melanoma may be beneficial [2]. The use of at least 2 different immunostains is recommended for diagnosis.

MITF has value in decorating amelanotic melanomas and desmoplastic melanomas when other immunohistochemical stains have failed. S-100 protein and tyrosinase show the highest percentage of positivity. MART-1/Melan-A is reported to be much more useful than HMB-45 for highlighting melanocytic tumors, but because it is a marker of melanocyte lineage, benign lesions such as melanocytic nevi also stain [21]. Reddy et al. in their case showed that special stains like Masson's Fontana silver stain and Melanin Bleach technique are also helpful in the diagnosis of malignant melanoma for which they were positive [22].

Although melanoma is classically not radiosensitive, occasional patients have shown a good response to radiation therapy. Immunotherapy has been successfully used but chemotherapy has demonstrated a relatively low response rate. Dacarbazine-DTIC, INF-γ and INF-α-2b have been described as chemotherapeutical and immunotherapeutical treatments associated with Bacillus-Calmette-Guerin vaccine and recombinant interleukin-2 (rIL-2) in different combinations. Anecdotal reports describe success with IFN-α or hyperfractionated radiation therapy. Many cancer centers follow surgical excision with a course of IL-2 as adjunctive therapy to prevent or limit recurrence. Peginterferon alpha-2b (Sylatron™) has been approved by the FDA for melanomas with microscopic or gross nodal involvement within 84 days of definitive surgical resection including complete lymphadenectomy. Clinical trials of ipilimumab, a human monoclonal antibody, have shown encouraging results in therapy for metastatic melanoma. The drug blocks regulation of cytotoxic T-lymphocytes and allows sustained immunologic activity against melanomas and other malignancies. Ipilimumab body (Yervoy™) is now approved by the US

Food and Drug Administration (FDA) and is indicated for unresectable or metastatic melanomas [21].

The protocol of immunochemotherapy includes DTC (dimethyltriazeno-imidazole-carboxamide), ACNU (nimustine hydrochloride) and VCR (vincristine) which is also known as DAV protocol [23], coupled with OK-432 which is a biologic response modifier consisting of penicillin treated Streptococcus pyogenes and INF -α2.

Other immunotherapeutic drugs that are occasionally used include interferon and cimetidine, which, when used together, are believed to activate killer T cells and inhibit suppressor T cells, resulting in reduction of the size of the melanoma.

For patients with evidence of multiple positive lymphnodes or with extracapsular spread, post-operative radiation therapy after neck dissection seems to be appropriate [2]. In our case also, patient was treated by radiotherapy post-operatively. Radiation can also be used palliatively for metastatic disease [2]. Although radiation alone is reported to have questionable benefit (particularly in small fractionated doses), this therapy is a valuable adjuvant in achieving relapse-free survival when high-fractionated doses are used [21].

The melanoma-associated antigen (MAGE) family consists of a number of antigens initially recognized by cytotoxic T lymphocytes, which are currently being investigated for immunotherapy of patients with metastatic melanomas and other tumor types. Expression of MAGE mRNA in melanocytic tumors is said to be restricted to invasive malignant tumors and absent in nevi. Recently, a monoclonal antibody (57B) has become available to examine MAGE protein expression in archival material. Because tumor-infiltrating lymphocytes in melanomas are associated with longer survival, their findings suggested a potential prognostic role for MAGE. Furthermore, the seeming restriction of immunopositivity to invasive malignant tumors suggests a potential diagnostic role for the antibody 57B in confirming the malignant potential of a melanocytic tumor [24].

One reason for the poor prognosis of OMM is early invasion of the underlying tissue, increasing the likelihood of metastasis [13]. The five-year survival rate for OMM ranges from 9.4–15.6% even after radical treatment. It depends on whether there is lymphnode involvement (18 months) or not (46 months) [6] and worsens with distant metastasis. The most common sites of metastasis are lymphnodes, liver and lung with widespread involvement occurring in severe cases.

Conclusion

The present case emphasizes the importance of early diagnosis and management which could improve the survival rate in patients with OMM. In our case, one year survey speaks about and weighs little the importance of patient counseling. Educating and motivating the patients for follow-up play a very important role in increasing his/her life span and must be stressed upon to the patient.

Early identification of oral melanomas should be promoted by careful oral examination and early biopsy of pigmented and non-pigmented suspected masses since early diagnosis and intervention results in better prognosis [22].

References

1. Pandey M, Abraham EK, Mathew A, et al. Primary malignant melanoma of the upper aero- digestive tract. Int J Oral Maxillofac Surg. 1999;28:45–9.
2. Ebenezer J. Malignant melanoma of the oral cavity. Indian J Dent Res 2006;17:94-6.
3. Strauss JE, Strauss SI. Oral malignant melanoma: a case report and review of literature. J Oral Maxillofac 1994;52:972-6.
4. Garzino-Demo P, Fasolis M, Maggiore GMLT, et al. Oral mucosal melanoma: a series of case reports. J Craniomaxillofac Surg. 2004;32:251–7.
5. Hashemi MS. Malignant melanoma of the oral cavity: A review of literature. Indian J Dent Res 2008;19:47-51.
6. Meleti M, Leemans CR, Mooi WJ, et al. Oral malignant melanoma: a review of the literature. Oral Oncol. 2007;43:116–21.
7. Prasad ML, Patel SG, Huvos AG, Shah JP, Busam KJ. Primary mucosal melanoma of the head and neck: A proposal for microstaging localized, Stage I (lymph node-negative) tumors. Cancer 2004;100:1657-64.
8. Bork, Hoede, Korting, Burgdorf, Young. Diseases of the oral mucosa and the lips. Philadelphia: W.B. Saunders; 1996. p. 336-40.
9. Rajendran R, Sivapada Sundaram B. Benign and Malignant tumors of the oral cavity. In: Shafer, Hine, Lavy, editors. Shafer's Text book of oral pathology. India: Elsevier; 2009. p. 120-7.
10. Gorsky M, Epstein JB. Melanoma arisinig from the mucosal surfaces of the head and neck. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1998;86:715–9.
11. Chidzonga MM, Mahomva L, Marimo C, et al. Primary malignant melanoma of the oral mucosa. J Oral Maxillofac Surg. 2007;65:1117–20.
12. Buchner A, Merrel PW, Carpenter WM. Relative frequency of solitary melanocytic lesions of the oral mucosa. J Oral Pathol Med. 2004;33: 550.
13. Tanaka M, Mimura M, Ogi, K, et al. Primary malignant melanoma of the oral cavity: Assessment and outcome from the clinical records of 35 patients. Int J Oral Maxillofac Surg. 2004;33:761-5.
14. Lopez-Graniel CM, Ochoa-Carrilo FJ, Menese-Garcia A. Malignant melanoma of the oral cavity: diagnosis and treatment experience in a Mexican population. Oral Oncol.1999;35:425–30.
15. Manganaro AM, Hammond HL, Dalton MJ et al. Oral melanoma: Case reports and review of literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1995;80:670.
16. Batsakis JG. Pathology of tumors of the oral cavity. In: Thawley SE, Panje WR, Batsakis JG et al(eds). Comprehensive management of head and neck tumors. Philadelphia: PA, Saunders; 1999:651-655.
17. Greenberg MS, Glic KM. Burket's oral medicine. 9th ed. BC Decker: Hamilton; 2003;131-2, 214-5.
18. Greene GW, Haynes JW, Dozier M, Blumberg JM, Bernier JL. Primary malignant melanoma of the oral mucosa. Oral Surg Oral Med Oral Pathol 1953:6(12)1435-43.
19. Lourenno SV, A MS, Sotto MN, Bologna SB, Giacomo TB, Buim ME, et al. Primary oral mucosal melanoma: A series of 35 new cases from South America. Am J Dermatopathol. 2009;31:323-30.
20. Sentinel Lymph Node Biopsy - National Cancer Institute. www.cancer.gov/ cancertopics/ sentinel-node-biopsy.
21. Collins II BM, Barnes Jr EL. Oral Malignant Melanoma. http://www.misc.medscape.com.
22. Reddy BVR, Sridhar GR, Anuradha CH, Chandrasekhar P, Lingamaneni KP. Malignant melanoma of the mandibular gingiva: A rare occurrence. Indian J Dent Res. 2010; 21: 302-305.
23. Rapidis AD, Apostolidis C, Vilos G and Valsamis S. Primary malignant melanoma of the oral mucosa. J Oral Maxillofac Surg.2003;61:1132-1139.
24. Busam KJ, Iversen K, Berwick M, Spagnoli GC, Old LJ, Jungbluth AA. Immunoreactivity with the anti-MAGE antibody 57B in malignant melanoma: Frequency of expression and correlation with prognostic parameters.Mod Pathol. 2000 Apr;13(4):459-65.