Case Report

Malignant melanoma of gingiva: Report of a rare case

Ashok Vikey, Prakhar Kapoor, Rahul Kathariya¹, Deepali Vikey², Ipsita Kukreja³

Department of Oral Pathology and Microbiology, Sri Aurobindo Dental College, ²Private Practice, Indore, Madhya Pradesh, ¹Department of Periodontics and Oral Implantology, Dr. D. Y Patil Dental College and Hospital, Dr. D. Y Patil Vidyapeeth, ³Department of Oral Pathology and Microbiology, Bharati Vidyapeeth University Dental College and Hospital, Pune, Maharashtra, India

Abstract

According to the World Health Organization, oral malignant melanoma (OMM) is a rare disease, accounting for only 0.8% of all melanomas, 8% of head and neck melanomas, and up to 0.5% of all oral malignancies. OMM presents as a pigmented lesion with asymmetrical borders, irregular surface characteristics, and a distinct color. Melanoma-associated pigmented lesion of the oral cavity does not possess clinical specificity and frequently divert the clinical diagnosis; hence, differential diagnosis becomes mandatory. Furthermore, the unpredictable pathophysiological behavior and delayed detection, contributes for poor prognosis of the disease. As a result, the 5 years survival rate is only 10–25%. Commonly OMM is seen in maxillary gingiva of males. However, we report a rare case of a middle-aged female having pigmentations and growth over mandibular gingiva.

Key words: Cutaneous melanoma, melanoma, mucosal melanoma, oral malignant melanoma

INTRODUCTION

Continuous efforts by researchers and constant addition of literature minimized the aura of one of the deadliest disease, that is, oral malignant melanoma (OMM). As a result, the new innovative approaches came to existence and this became the first step to successful treatment against this disease. The disease is known since decades, but proper management is affected due to insufficient understanding regarding its pathophysiology and marked variation in its clinical findings.

Older literature attributes it as a deadly unsolved mystery. In 1856, the mucosal melanoma was discussed first, by Weber in Germany, and later on, the valuable information of head and neck mucosal melanoma was reported by Lincoln in 1885. In late 19th century, further studies were carried out, that focused to minimize the mortality and enhance public awareness towards the disease. Hence, an early detection and timely treatment is a key factor for its better prognosis.

Unlike OMM, there is a marked variation in the etiology and incidence rate of generalized cutaneous melanomas. The continuous global environmental changes result in over-exposure to ultraviolet (UV) radiation. Furthermore, the growing trends of sunbeds or tanning beds increased the risk of this disease. A sunbed is a device, which emits UV radiation (typically 97% UVA and 3% UVB, ± 3%) to produce a cosmetic tan.[1] Today the worldwide incidence of newly diagnosed melanomas range between 3% and 8%. Around 50% of mucosal melanomas affect the head and neck region, almost representing approximately 9% of all malignant head and neck tumors. Comparatively, mucosal melanomas show an aggressive biological behavior resulting in a 5 years survival rate of < 25%.[2]

The etiology of mucosal melanoma differs from its cutaneous counterpart, as there is no direct role of UV radiation. Primary causes are: Ill-fitting dentures, betel nuts, tobacco, formaldehyde, amalgam tattoo, nevi at traumatic regions, racial pigmentation, etc.[3] Some literatures explain that during embryologic development, melanocytes migrate from the neural crest to epithelial lining, which later show reactive changes by cytotoxic stimulant in the basal epithelial

Access this article online

Quick Response Code: 
Website: www.ijdentistry.com
DOI: 10.4103/0975-962X.163052

Address for correspondence:
Dr. Rahul Kathariya,
Department of Periodontics and Oral Implantology, Dr. D. Y. Patil Dental College and Hospital, Dr. D. Y. Patil Vidyapeeth (Deemed University), Pune - 411 018, Maharashtra, India.
E-mail: rkathariya@gmail.com
layer.\[4\] Though dendritic cells, derived from neural crest, produces the melanocytes but the exact mechanism of proliferation of these cells in melanoma is not known.\[5\]

Particularly, mucosal melanomas are asymptomatic in their initial phase, resulting in late diagnosis, thus allowing them to invade the deeper regions. The clinical characteristics include, dark brown/black in color, asymmetrical margins, and irregular surface, etc., Hence, the pigmented lesions of oral cavity; which does not possess clinical specificity need to be carefully evaluated for possibility of OMM.

Differential diagnosis include: Smoke related melanosis, drug pigments, physiologic or racial pigmentation, melanotic macule, Kaposi’s sarcoma, nevus or melanocanthoma, chronic leukemic, etc.\[6\]

Pigmentation is not the only criteria, as around 15% of the melanomas are nonpigmented. The OMM has distinct gender variation with majority of them showing male predominance. Among the oral melanomas; hard palate and maxillary gingiva are common sites. The lesion is rarely documented in female patients. Location wise, the involvement of mandibular gingiva is comparatively less.\[6\] Here, we report a case of OMM, in a 45-year-old female patient, who is conscious about the discoloration and growing bulk over mandibular anterior mucosa.

CASE REPORT

A 42-year-old Indian female with average height and moderate built reported to the dental office, complaining of blackish discoloration on the lower jaw since 6 months and difficulty while eating; especially with the lower front teeth. Intraoral examination revealed nontender and painless bluish-black growth with rough and irregular surface extending over the gingiva of 35–44 regions, which revealed no findings of ulceration and bleeding [Figure 1]. There was major involvement over the labial aspect of mandibular gingiva followed by anteroposterior extension into the vestibule and oral aspect of lip mucosa; but with minimal extension of the lesion on lingual aspect. The patient noticed a small blackish patch approximately 1 cm × 1 cm which gradually increased to present size with associated mobility of teeth. The mobility was appreciable in almost all mandibular anterior teeth. The overall general examination of the neck, back, extremities, and chest was insignificant except for nevi. Thus, the cutaneous part of melanoma was ruled out. During general examination, submandibular lymph nodes were enlarged but nontender approximately 1.5 cm × 1.5 cm in dimension. No history of trauma or tobacco in any form was reported. All vital signs were within normal limits. After evaluating hematological parameters, an incisional biopsy was performed under local anesthesia, for a confirmatory diagnosis.

In microscopic examination, the H and E stained section revealed in situ melanotic pigments [Figure 2]. The section showed large cells with pleomorphic vesicular nucleus and brown pigment, few abnormal mitoses, and altered nucleocytoplasmic ratio invading into the connective tissue in the form of sheets, cords, and islands [Figure 3]. The tissue was also immunohistochemically stained for human melanoma black-45, a specific marker for melanocytes that also revealed cytoplasmic positivity of malignant melanocytes for the antibody [Figures 4 and 5]. After confirming the diagnosis as malignant melanoma, segmental resection, and bone grafting was performed by medical personnel. In posttreatment follow-up, patient reported with some other problems such as difficulty in eating and speech. The intraoral examination revealed uneven healing of resected part and further development of the bluish-black patch on left posterior mandible. Due to severe trismus and discomfort, we were unable to take a postoperative photograph. Wide excision of the growth and node biopsy was done and the patient is being recalled for follow-ups every 6 months. The patient is asked to notify any sign of recurrence.

DISCUSSION

The oral mucosal melanoma is a rare entity with incidence rates of <1% of all melanomas and among head neck tumors it is 1.6%. The worldwide incidence
rate is about 0.5%.[7] According to Andersen et al., the head and neck mucosal melanomas accounted for 0.8% of all melanomas and 8% of head and neck melanomas. They reviewed 2.5 million individuals in Denmark over a 30 years period and found that OMM mostly occur between the fourth and seventh decades of life, with a mean age of 55–57 years. It shows vague gender predilection accounting male to female ratio 3:1. The etiopathogenesis is poorly understood. Melanocytes are dendritic cells that have migrated as neuroectodermal derivatives in the ectodermally derived mucosa.[4] Some studies also suggest familial inheritance specially, along with dysplastic nevus syndrome where; p16 and differences in DNA repair impairments contributes to carcinogenesis of malignant melanoma. In such circumstances, the damaged DNA, activates the proto-oncogenes or inactivates the tumor suppressor genes.[8] Majority of patients show history of preexisting oral pigmentation before the diagnosis of oral melanoma.

Moreover, common primary sites include; the nasal cavity, paranasal sinuses and in the oral cavity; most commonly in the maxillary alveolar ridge and hard palate, whereas it is rarely seen on the mandibular gingiva.[9] So far some studies have documented, relationship between free radicals, and melanoma cells, resulting into increased levels of reactive oxygen species. This is due to the metal binding properties of melanin and loss of structural integrity of melanosomes.[10]

At present it is accepted that, OMM is very aggressive tumor and various factors contribute to its aggressiveness, such as late detection, poor resectability, and early metastasis. This not only limits the 5 years survival rate up to 10–25%, but also affects prognosis. Melanoma is notoriously resistant to chemotherapy, but the other approaches can be carried out during its treatment. According to oncosurgeons; treatment of choice for malignant melanoma is surgery. Stage 1, melanomas are excised.
along with 1 mm margins and T2aN0M0 (Stage 1B) needs sentinel lymph node biopsy. Stage 2 cases are treated with wide excision and node biopsy, whereas for stage 3 it needs wide excision with 2 mm margins and node dissection and the radiation or chemotherapy is given post-operatively. Stage 4 is really the challenge, it is treated with surgery and chemotherapy; interferons (IFNs), interleukins (ILs), vaccines, and different biochemotherapeutic agents serves as adjuncts. Today’s new technology has opened new hopes. As a result, biotherapies including IFNs and IL-2 provide intriguing avenues for further evaluation and treatment. The mechanism of clinically effective IL-2 therapy may be the direct action of IL-2 on a biologically distinct subset of melanoma cells, leading to up-regulation of tumor suppressor IL-24.[11]

The favorable prognosis of the lesion lies in its early diagnosis. Hence, to avoid future complications the suspected oral pigmentation should be planned for biopsy. Moreover, in some extent; criteria given by Green et al.,[3] may be helpful to clinicians, that suggests; demonstration of melanoma in the oral mucosa, presence of junctional activity and inability to demonstrate extra oral primary melanoma. Further, some studies have classified the disease for prediction of its prognosis, that is, Stage 1: When the lesion is confined locally, Stage 2: Have positive metastasis and Stage 3: With hematogenous spread. In the later stage; distant metastases may be found in a variety of sites, including the lungs, bones, liver, brain, and skin.

CONCLUSION
A detailed case history, thorough clinical examination, and suspicious eye to the irregular intraoral pigments can help the clinician for early diagnosis. Sometimes patients ignore the symptoms that may reflect indirectly on health care provision and result in a poor prognosis. Any physiologic pigmentation to hormones, medication or pigmentation other than amalgam tattoo should be biopsied. The treatment promoted by thorough oral examination and biopsy should be well planned to improve patient prognosis and avoid chances of recurrence.

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How to cite this article: Vikey A, Kapoor P, Katharya R, Vikey D, Kukreja I. Malignant melanoma of gingiva: Report of a rare case. Indian J Dent 2015;6:161-4.

Source of Support: Nil. Conflict of Interest: None declared.