Case Report

Oral malignant melanoma: An aggressive clinical entity - Report of a rare case with review of literature

Shamimul Hasan, Sami Faisal Jamdar[1], Jogender Jangra[2], Sadun Mohammad Al Ageel Al Beaiji[3]

Department of Oral Medicine and Radiology, Jamia Millia Islamia, New Delhi, [1]Department of Oral and Maxillofacial Surgery, Teerthankar Mahaveer Dental College, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, [2]Department of Oral and Maxillofacial Surgery, Government Dental College, Post Graduate Institute of Medical Sciences, Pandit Bhagwat Dayal Sharma University of Health Sciences, Rohtak, Haryana, India, [3]Department of Conservative Dentistry and Endodontics, Specialist Dental Center, Hafer Al Batin, Saudi Arabia

Corresponding author (email: <shamim0571@gmail.com>)
Dr. Shamimul Hasan, C/O Mohd. Javed Khan, C-4, Duplex Quarters, New Sir Syed Nager, Aligarh, Uttar Pradesh, India.

Abstract

Melanoma is one of the most dreaded and aggressive neoplasms, being derived from epidermal melanocytes. The majority of melanomas are seen to involve the skin, and primary mucosal melanomas account for less than 1% of all melanomas. Oral malignant melanomas (OMM) are asymptomatic at the initial presentation, but later they become painful with growth and expansion. In the late stages, the patient may present with ulceration, bleeding, tooth mobility, paresthesia, ill-fitting prosthesis, and delayed healing of the extraction sockets. Diagnosis is often delayed due to asymptomatic clinical presentation, with silent progression of the lesion. OMM are associated with poor prognosis due to their invasive and metastasizing tendencies. The condition has poor survival rates, and metastatic melanomas show even worse prognosis. The 5-year survival rate for OMM ranges 4.5–29%, with 18.5 months being the mean survival rate. The tumor is best managed by wide surgical resection; however, consideration should also be made for adjunctive therapies such as chemotherapy, immunotherapy, and radiotherapy. Recurrences may be seen even 10–15 years after the primary therapy. This paper aims to present an interesting report of aggressive OMM in a 50-year-old male patient and emphasizes the role of dental professionals in maintaining a high degree of vigilance for the pigmented lesions of the oral cavity. Pigmented lesions of uncertain origin should be routinely biopsied to rule out malignancy. Early diagnosis of this dreadful entity entails thorough history taking, physical examination, and radiographic features coupled with histopathology.

Key words: *Melanocytes, oral malignant melanoma, pigmentary lesions*

INTRODUCTION

Melanoma is a malignancy of the melanocytic cells, which are derivatives of neural crest cells. The majority of melanomas originate from the skin; however, they may also originate from mucosal surfaces or other sites where neural crest cells migrate.[1] Primary oral malignant melanoma (OMM) is an uncommon malignancy, which is derived from melanocytes seen in the basal layer of the oral mucosa,[2] and contributes to 0.2–8% of all melanomas and 0.5% of all oral malignancies.[3,4] A change in the size, shape, or color of a mole is usually the first sign in melanomas.[5] Oral melanomas are associated with an extremely aggressive behavior, vertical growth pattern, high risk for

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metastasis, and poor survival rates.[6] Wide surgical excision with adequate negative margins with or without neck dissection forms the mainstay of treatment for malignant melanoma. Radiotherapy and chemotherapy have been attributed as adjunctive treatment modalities. Distant metastasis of the tumor may be minimized by the chemotherapy and immunotherapy.

Dacarbazine (DTIC) and interferon-alfa-2b (IFNa2b) are used for chemotherapeutical and immunotherapical treatments, with the first line of drug being DTIC, either alone or in combination with nimustine hydrochloride and vincristine, or different combinations of bacillus Calmette–Guérin (BCG) and recombinant interleukin 2 (IL-2)[7]

CASE REPORT

A 50-year-old male patient of low socioeconomic status reported to the outpatient department of Oral Medicine and Radiology, with a chief complaint of a painless, slow-growing swelling in the right maxillary teeth region for the past 5 months. The swelling was initially small and had gradually increased to the present size. There was no associated history of trauma and pain. The medical history was noncontributory. The patient gave negative history for smoking and other deleterious habits. Extraoral examination revealed diffuse swelling in the anterior region of the right maxilla. The swelling extended anteroposteriorly from the tip of the nose to 3 cm lateral to the right ala of the nose, and suprainferiorly extended up to the ala-tragus line to the lower border of the upper lip. The swelling caused mild deviation of the tip of the nose to the left side with obliteration of the right nasolabial fold. On palpation, the swelling was nontender and firm in consistency [Figure 1]. A single, firm, fixed, and tender right submental lymph node was also appreciated on palpation. On intraoral clinical examination, a lobulated, pigmented (purplish-black) growth, measuring 5 × 4 cm^2 was noticed between the maxillary right central incisor and the maxillary right first molar. The growth was seen to involve the marginal, attached, and interdental gingival region on the labiobuccal aspect of the maxillary alveolus. However, there was no palatal extension of the growth. Palpatory findings were suggestive of a firm, nontender growth, which bled when probed. The maxillary right canine and the first and second premolars were clinically missing with slight displacement of the maxillary right lateral incisor [Figure 2]. The patient presented with poor oral hygiene. Thorough clinical examination ruled out the presence of any other primary site of the lesion. A provisional diagnosis of primary OMM was assigned, based on the history and clinical features. Differential diagnosis of lymphoma and squamous cell carcinoma was taken into consideration. Complete blood cell count as well as biochemical and urine analysis were insignificant and within normal limits. Distant metastasis of the lesion was ruled out on the clinical, radiographic, and ultrasonographic examination. The pantomogram revealed partially edentulous jaws and an irregular radiolucent lesion with ill-defined margins, extending from the maxillary right canine to the maxillary first molar [Figure 3]. Magnetic resonance imaging (MRI) morphology suggested a mass lesion involving the anterior wall of the right maxillary sinus and right maxillary alveolar arch up to the second molar and extending to involve the gingivobuccal sulcus and the buccinator muscle, and the zygomatic prominence laterally with extension into the adjacent anterior part of soft tissue with heterogenous postcontrast enhancement [Figure 4]. Histologic section showed a piece of tissue with pigmented connective tissue stroma under a thin, irregular, and ulcerated epithelium. Under higher magnification, connective tissue showed

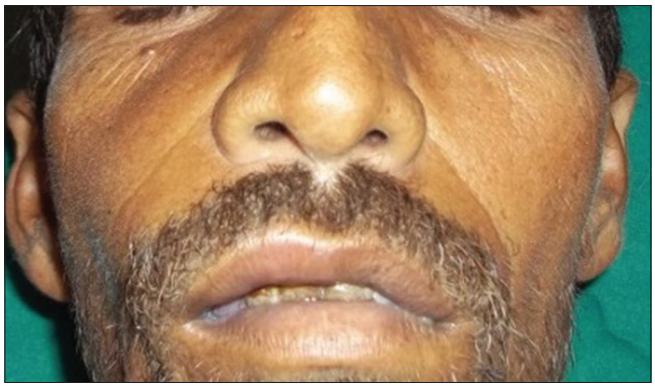

Figure 1: Diffuse extraoral swelling in the right maxillary anterior region

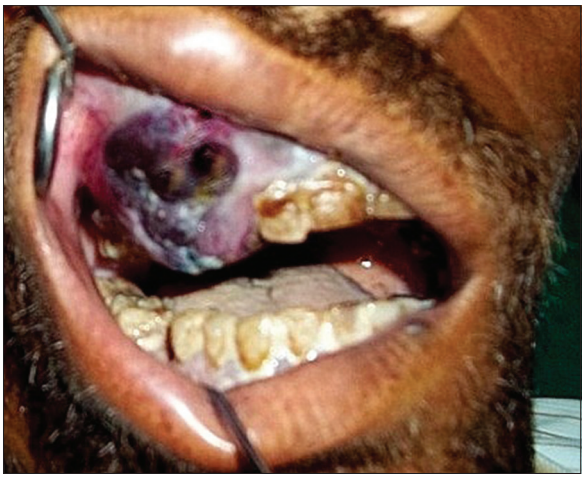

Figure 2: Pigmented, lobulated growth in the right maxillary alveolus region

clusters of tumor cells in small foci and in sheets. Cells are spindle-shaped with large nuclei, prominent nucleoli (suggestive of melanocytes), and pigmented cytoplasm. Tumor cells are seen to invade and ulcerate the overlying stratified squamous epithelium. The deeper connective tissue showed dense chronic inflammatory infiltrate and endothelial-lined blood vessels with red blood cells (RBCs) [Figure 5]. The clinical, radiological, and histological features confirmed the diagnosis of malignant melanoma. The tumor cells showed strong positivity for immunohistochemical marker HMB-45, thus reconfirming the diagnosis [Figure 6]. The patient and his family members were informed about the diagnosis, treatment plan, and prognosis of the condition. However, the patient declined the invasive treatment and did not appear for regular follow-up.

DISCUSSION

Weber was the first to report a case of OMM as early as in 1856.[8] The etiology of malignant melanoma remains obscure. However, the predisposing factors are the following: Excessive exposure to sunlight [ultraviolet (UV) radiation]; psoralen and UV A radiation (PUVA) therapy; tanning salons; skin (freckles) and hair color; large, atypical nevi; xeroderma pigmentosum, immunosuppression; ill-fitting denture; and environmental exposure to chemicals, tobacco, petroleum, and printing products. Primary oral melanomas originate either from a nevus or preexisting pigmented lesion, currently most thought to arise *de novo*.[9-11]

The mucosa of the upper jaw accounts for nearly 80% of oral melanomas, with the keratinizing mucosa of the palate and the alveolar gingiva being the most common sites of occurrence.[12] The disease has a male preponderance (male-to-female ratio 2.8:1) and the age range is 20–83 years with an average age of 56 years.[13] Japanese, black Africans, American Indians, and Hispanics are the most commonly affected ethnic groups.[14]

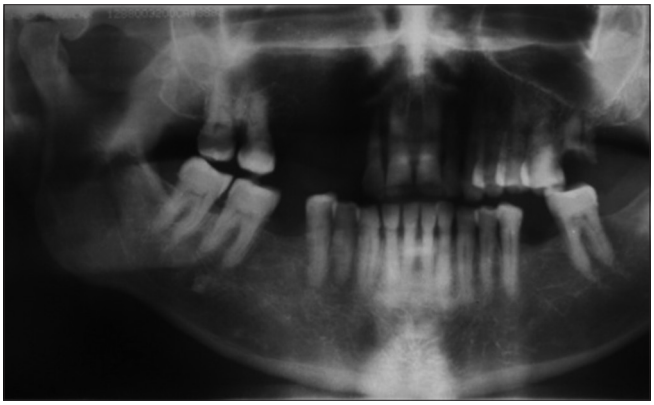

Figure 3: Cropped pantomogram showing a radiolucent lesion with ill-defined margins in relation to maxillary canine to maxillary first molar

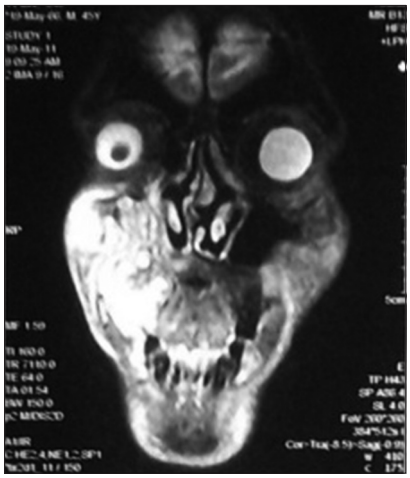

Figure 4: MRI showing a hyperintense lesion involving the right maxillary sinus and right maxillary alveolar arch with extension to gingivobuccal sulcus

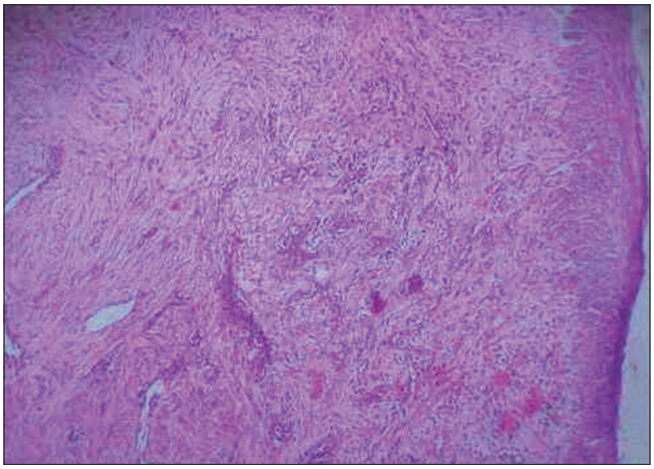

Figure 5: Histopathology showing spindle-shaped melanocytic cells with large nuclei, prominent nucleoli, and pigmented cytoplasm invading and ulcerating the epithelium

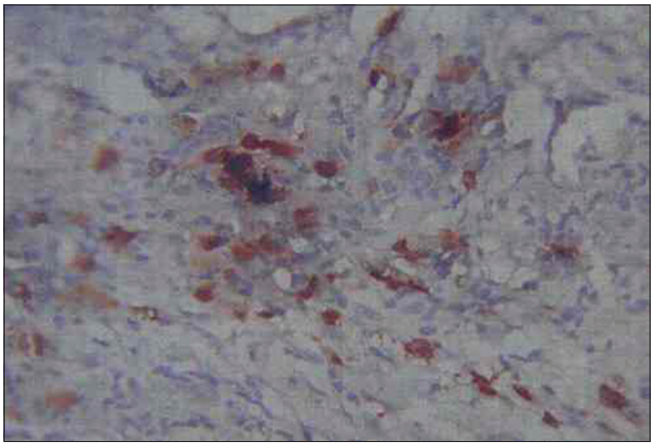

Figure 6: Immunohistochemistry showing strong reactivity of tumor cells to HMB-45

OMM usually has an asymptomatic clinical appearance and progresses unnoticed by the patient, and this results in a delayed diagnosis. Pigmented growths or swellings are usually the early presenting features in most cases of OMM. The surface may be smooth, with an intact or ulcerated overlying mucosa. OMM are usually uniformly brown or black in color or may show color variation (black, brown, red, purple, and grey shades) or depigmentation.[15] Bleeding, faulty prostheses, loosened teeth, late healing of tooth sockets, and, rarely, pain are some of the reported uncommon manifestations.[16] About 78% of cases are associated with widespread bone destruction.[17]

The clinical features of OMM may be summarized by the ABCDE rule: Asymmetry, where one half show variation from the other; Border irregularity, with blurred, notched, or ragged edges; Color disparity, with varied pigmentation, such as black, brown, tan, red, white, or blue; Diameter more than 6 mm; and Elevated surface of the lesion.[10]

Malignant melanoma usually manifests in the following five clinical types: Pigmented nodular type, nonpigmented nodular type, pigmented macular type, pigmented mixed type, and nonpigmented mixed type.[12,13]

Atypical melanocytes (usually larger than normal melanocytes, along with nuclear pleomorphism and hyperchromatism), high density of melanocytes, and atypical cells in the biopsy of melanotic lesions of the oral mucosa contribute to the histopathology of OMM.[18] Based on its histopathological pattern, the Western Society of Teachers of Oral Pathology (WESTOP) classifies OMM into: (a) Melanoma *in situ*, in which the tumor cells are seen in the epidermis and its interface with the connective tissue; (b) invasive melanomas, in which the tumor cells invade the connective tissue; and (c) melanomas with a combined pattern between invasive and *in situ*.[15]

Immunohistochemistry studies show a strong reactivity of tumor cells to S-100 protein, melan- A, and HMB-45, and are beneficial in distinguishing oral melanomas from other malignancies.[18]

Clinical staging of tumor, node, metastases (i.e. TNM) in association with histopathological microstaging is a beneficial factor in the prognosis of OMM, as given below.[3,19]

Stage I: Presence of primary tumor (Tany N_0 M_0)
- Level I: Pure *in situ* melanoma with either absence of invasion or *in situ* melanoma with "microinvasion"
- Level II: Involvement of the lamina propria
- Level III: Invasion into the deep skeletal tissue (skeletal muscle, bone, or cartilage)

Stage II: Metastasis of tumor to regional lymph nodes (Tany N_1 M_0)

Stage III: Metastasis of tumor to distant sites (Tany Nany M_1).

A simple and practical method for the clinical diagnosis of OMM was proposed by Delgado-Azañero and Mosqueda-Taylor, and 84.6% of OMM cases may be diagnosed by this method. In this test, the lesion is rubbed with a gauze piece and observed for black staining (lesional melanin pigment attributes for the black staining). The method is highly sensitive and aids in diagnosis.[20]

Metastasis to the regional submandibular and cervical lymph nodes may be demonstrated by the computed tomography and MRI. However, incisional biopsy remains as the gold standard for diagnosis.[21] Exfoliative cytology and fine-needle aspiration of the primary pigmentary lesion may cause the malignant cells to not only spread within the adjacent tissues, but also cause hematogenous and lymphatic spread. This may contribute to a higher risk of local recurrence and metastasis to the regional or distant sites.[14]

In this case, MRI showed a hyperintense lesion involving the right maxillary sinus and right maxillary alveolar arch with extension to the gingivobuccal sulcus.

According to Greene *et al*., the following three parameters aids in the diagnosis of primary oral melanoma:[22]
- Presence of malignant melanoma in the oral mucosa
- Positive "junctional activity"
- Absence of malignant melanoma at any other primary site.

The lymph nodes, liver, and lungs are the common sites of metastases. The tumor is best managed by an excisional biopsy followed by a wide surgical excision. Radiotherapy and chemotherapy are used as adjunctive treatment modalities.[9]

Surgical exploration forms the cornerstone for the management of malignant melanoma, and vigorous surgical extirpation of local disease may result in extended disease-free survival.[23,24] However, preoperatively confirmed cases of lymph node metastases should be managed with neck dissection.[5] The enblock resection minimizes the chances of local recurrence, with insignificant effect on metastasis and survival.

Melanoma was earlier considered to be radioresistant in nature, but radiotherapy is now believed to be a significant adjuvant in attaining local control and may even have merit as a primary treatment option.[25] In addition, primary irradiation is considered as a possible substitute for surgery for inoperable cases.

A breakthrough in the evaluation and management of malignant melanoma has been achieved by the use of biotherapy including interferons (IFNs) and IL-2. IL-2 may have a direct action on a biologically distinct subset of melanoma cells, thus, leading to upregulation of tumor suppressor IL-24.[26]

Minimal success has been achieved by the use of imunotherapeutic agents, such as BCG, which aims at activation of the host immune response. IFN and cimetidine are the other immunotherapeutic drugs, which act synergistically on killer and suppressor T cells, thereby causing a reduction in the tumor size.

The patient in the present case declined the invasive surgical treatment and did not follow up.

Oral melanoma is associated with poor prognosis. Anatomical considerations (proximity of bone and muscles) facilitate the early invasion of deeper structures, thus increasing the chances of metastasis. Another contributing factor in the dissemination of melanoma is the rich vascular supply of oral cavity.[27]

CONCLUSION

OMM is a rare tumor of melanocytic cells. It is considered a dreaded condition because of its rapidly invasive and metastatic nature. The primary objective of reporting this rare case is to emphasize the need for vigorous scrutinizing of the indolent pigmented lesions and highlighting the significance of biopsy as an aid in the prompt diagnosis of OMM. The bizarre morphological features, extreme rarity of occurrence (less than 1%), and an unpredictable and aggressive behavior necessitate that such cases should be reported, thus facilitating the timely diagnosis, treatment, and better prognosis of this uncommon pathology. This case report is unique in the sense that the primary lesion is seen on the maxillary gingiva, and metastatic lesion has been ruled out by thorough clinical and radiographical examination.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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