Case Report

Metastatic malignant melanoma of palate: A review of literature and report of an unusual case

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DOI: 10.4103/0975-5950.69165
www.njms.in

ABSTRACT

Oral malignant melanoma is a rare tumor, accounting 0.8to 1.8 % of all oral malignancies. It occurs most commonly in Japanese and Negros. Radical surgery is mainstay of the treatment. Prognosis is very poor with 5 years survival rate. We present a case of malignant melanoma in a 55 years female, metastatizing to liver spleen and vertebrae.

Key words: Melanoma, Mandible, Maxilla, Prognosis, Recurrence

Introduction

Primary oral malignant melanoma is rare, representing 0.2–8% of all melanomas.[1] The etiology of the mucosal malignant melanoma is unknown. It may present as a black macule; later it may develop as a nodule or ulceration, with asymmetry and irregular borders as clues to the diagnosis.[2] Oral melanoma frequently exhibits an extremely invasive behavior, with vertical growth, high index of metastasis, and poor prognosis.[3] Surgery, either alone or in association with radiotherapy, is the preferred treatment modality. Prognosis is poor with a 5-year survival rate varying from 0 to 55%.[1,4]

Case Report

A 46-year-old female reported to Department of Oral and Maxillofacial Surgery, CSM Medical University, Lucknow, with a complaint of black swelling in her palate. One year back, she had an excisional biopsy done in a local hospital, and histopathology of the lesion was suggestive of malignant histiocytoma (low grade). The patient underwent for radiotherapy, but after 6 months the lesion reappeared and the patient reported to us.

Intraoral examination showed nontender soft tissue swelling measuring 2.5 × 4 cm in dimension, extending from left maxillary canine to second molar teeth, crossing the midline [Figure 1]. Lymph nodes were nonpalpable, and medical history was noncontributory. Computed tomography (CT) of maxillary region revealed irregular lobulated lesion of soft tissue density arising from hard palate opposite left maxillary canine to second molar teeth and crossing the midline, measuring approximately 24 × 15 × 40 mm size and infiltrating the adjacent bone [Figures 2 and 3].

Infrastructural maxillectomy was done with safe margins of 1 cm. Histopathologic findings showed malignant neoplasm covered by stratified squamous epithelium showing flattening of rete ridges and focal ulceration [Figure 4]. A dermal lesion comprising pleomorphic and predominantly spindle shaped cells was seen. The cells were arranged mostly in fascicles. The cells had hyperchromatic nuclei with scant to moderate amount of cytoplasm. Intracellular granular black pigment was evident in fine to coarse granules. Foci of hemorrhage necrosis and lymphocytic infiltrations were evident. Fair number of mitoses was present. Intraepidermal spread of tumor was not present with some increase in normal appearing hyperpigmented melanocytes.

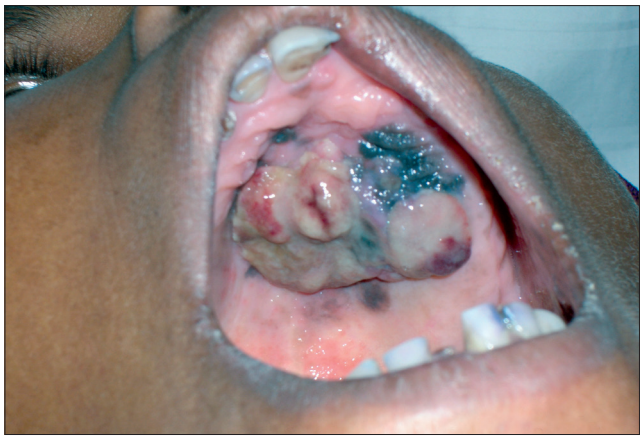

Figure 1: Intraoral view

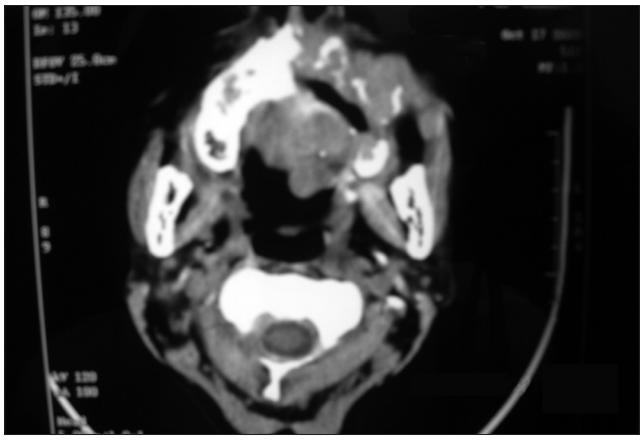

Figure 2: CT scan coronal view

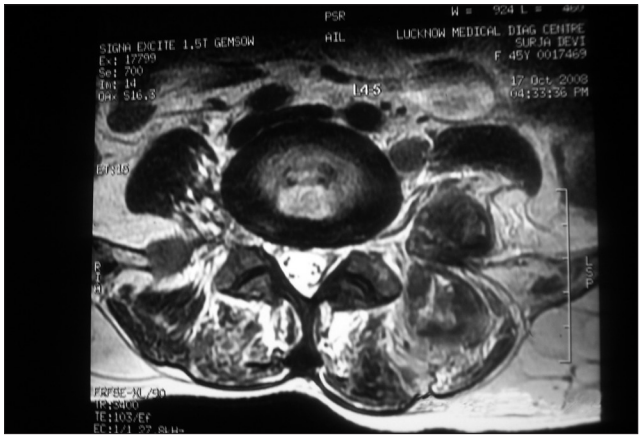

Figure 3: CT scan axial view

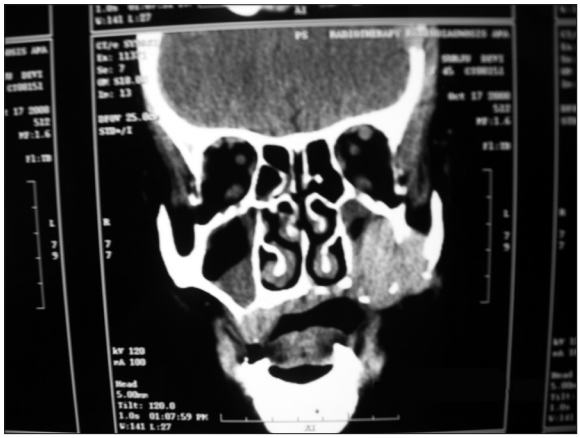

Figure 4: CT scan abdomen showing metastasis

The patient reported again after 8 months with complaints of ulcerated lesion at the same site, pain, paresthesia and weakness in both lower limbs. CT study of midface revealed partial maxillectomy with irregular mass lesion of soft tissue density at operated site infiltrating the antero-lateral wall of left maxillary antrum. Another focal well-defined intra-axial hyperdense Space occupying lesion (SOL) was seen in medial temporal lobe infiltrating the floor of pituitary fossa and extending into sphenoid sinus and infra temporal region. Magnetic resonance imaging (MRI) of lumbo-sacral spine revealed diffuse infiltrative metastasis in all visualized lumbar and sacral vertebrae, B/L sacral alae with large lobulated mass lesion in left paravertebral region extending from L4 to S1. L1 vertebral body was collapsed causing compression over conus medullaris with intramedullary compressive myelopathic changes extending from L1 to L2 level and extradural compression of cauda equina [Figure 5]. Ultrasonography of whole abdomen revealed focal echogenic space occupying lesion of ~27 × 28 × 24 mm size in segment III of liver and solitary significant peripancreatic lymphadenopathy of ~13 × 8 mm size was seen.

Discussion

Primary oral mucosal malignant melanoma is a rare neoplasm, developing from melanocytes found in the basal layer of the oral mucosa[5] and represents 0.2–8% of all melanomas and 0.5% of all oral malignancies.[6,7] Blacks, Japanese and Asian patients tend to be disproportionately more affected than Whites.[7] It can occur at any age, with an average of 56 years[7] and is extremely rare in people below 30 years.[8] Unlike cutaneous melanoma, the oral lesions are more common in men than women.[9] It occurs most frequently in the maxilla, with the palate as a common site (32%); maxillary gingiva is the second most frequent area of incidence(16%).[2,7]

The etiology of mucosal melanoma remains unknown.[9] Cigarette smoking, denture irritation and alcohol have been suggested as risk factors.[1] Clinical presentation of oral melanoma is variable, presenting as a dark brown, bluish black or black mucosal discoloration.[10] Pain was the most common referred symptom.[5] The lesions may be solitary or multiple, flat and/or elevated,[11]

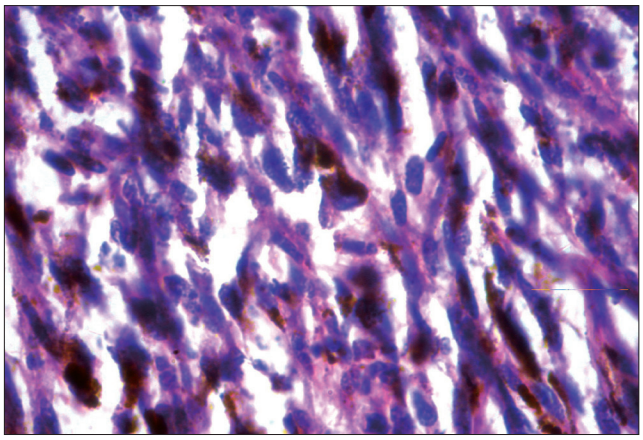

Figure 5: Histopathology of the lesion

borders are usually irregular, and no clear demarcation exists between the tumor and the adjacent tissues.[12] Rarely, melanoma may present itself without clinical evidence of pigmentation, in which case it is termed as amelanotic melanoma.[13] These lesions tend to have a worse prognosis because of delayed recognition and subsequent treatment [Table 1].[13]

Differential diagnosis includes other forms of pigmented oral pathology, diseases like Addison's disease, heavy metal poisoning[9] or smoking associated melanosis, oral melanotic macule, Kaposi's sarcoma, physiologic or racial pigmentation, melanocytic nevus and melanoacanthoma.[14]

Histopathologic examination of the lesion remains the most accurate diagnostic tool.[12] Adjunctive radiologic diagnostic methods such as CT, MRI and positron emission tomography are sometimes useful. In a study on the all groups of head and neck malignant melanomas, Goerres *et al*,[15] recently reported that positron emission tomography scanning may have some value for staging purposes.

Malignant melanoma of the skin has been classified into four major types.[16]

1. Lentigo maligna melanoma
2. Superficial spreading melanoma
3. Nodular melanoma
4. Acral lentiginous melanoma

The histologic appearance of the tumor is an invasive pattern of growth, with the tumor cells often appearing as densely packed epithelioid or sometimes sarcomatoid cells with eosinophilic cytoplasm. Varying degrees of cellular pleomorphism are seen throughout the specimen as may tumor invasion of blood vessels and lymphatics. The special stains (Fontana silver stain and the Prussian blue stain) are accurate in only about 75% of the cases. Demonstration of the neuronal specific

Table 1: Clinical staging system for oral malignant melanoma with histopathologic microstaging

Stages	Extension of lesion
I	Primary tumor present only (T any N0M0) Level I: Pure *in situ* melanoma without evidence of invasion or melanoma with "microinvasion" Level II: Invasion up to the lamina propria Level III: Deep skeletal tissue invasion into skeletal muscle, bone, or cartilage
II	Tumor metastatic to regional lymph nodes (T any N1M0)
III	Tumor metastatic to distant sites (T any N any M1)

Staging by Prasad *et al*.[6,8]

S-100 protein is a useful diagnostic indicator, especially if the tumor is of amelanotic type.[17] More recently, the application of monoclonal antibody techniques HMB-45 and Mart-1 (Melan A)[12] has increased the specificity of immunohistochemical diagnosis.[12] Ultrastructural examination of melanoma by electron microscopy[18] shows the presence of pre-melanosomes and melanosomes.

Radical surgery is the treatment of choice for oral melanoma, Elective neck dissection has also been advocated.[19] Management of clinically negative nodes remains controversial.[1,4] Radical surgery in combination with radiotherapy and chemotherapy or radiotherapy alone is preferred in inoperable tumors or in the elderly.[1] Immunochemotherapy has been shown to be useful as an adjuvant to surgical resection.[1]

Guidelines have been established for recommended excisional margins for melanomas of various thicknesses.[20] Melanoma *in situ* should have a 0.5–1.0 cm margin, thin melanomas (<0.76 mm) should have a 1.0–2.0 cm margin, and intermediate and thick lesions (>0.76 mm) should have a 2–3 cm margin.[21] Tumor-free margin of 1–2 cm, generally required and accepted for cutaneous melanoma, can be applied only rarely in the oral cavity.[22]

Chemotherapy is generally reserved for proven metastatic disease. Morton *et al*,[23] demonstrated temporary tumor regression following the intralesional injection of cutaneous melanoma with BCG vaccine. Kirkwood *et al*,[24] reported that melanoma is one of the human cancers which respond to interferon anti-tumor therapy. A combination of cimetidine with interferon appears to be more effective than interferon alone.[25] The future promise of tumor-directed antibodies labeled with cytotoxic drugs may offer hope for improved survival.[9]

Malignant melanoma generally has been considered a poorly radiosensitive malignancy.[11] Primary radiotherapy appeared to be more effective than surgical treatment when the 5-year cumulative survival rates were compared.[26] Postoperative radiotherapy

could be of some use; postoperative radiotherapy using fractions of 6 Gy twice a week for a total dose of 30 Gy was given by Meleti *et al*.[12]

There was a correlation between tumor thickness and the incidence of cervical lymph node metastasis. The tumor thickness in Stage I patients was 3–9 mm (average: 5.7 mm), while that in Stage II patients was 5–24 mm (average: 12.8 mm).[16] Metastatic spread via the bloodstream may occur early to the lungs, liver, brain or bone, and later metastatic spread to the local lymph nodes occurs. Distant metastatic spread occurs within 6–78 months. The pattern of lymph node metastasis of oral melanoma has not been well documented. Umeda *et al*,[16] stated that there is an apparent relationship between tumor thickness and the incidence of neck metastasis. When the tumor thickness is more than 5 mm, neck lymph nodes are likely to be involved. The most common sites of metastasis are the submaxillary and upper jugular lymph nodes, which is the same as for squamous cell carcinoma of the oral cavity.

The prognosis of oral lesions is worse than skin lesions, with 31% of patients with localized disease surviving for 5 years, falling to 5.2% if cervical metastasis is present. A more likely reason for the worse prognosis of oral mucosal melanomas is the late presentation of patients with locally advanced disease. The rich vascularity and lymphatic drainage of the mouth favors earlier metastatic spread to regional lymph nodes and to distant sites such as the lungs and vertebral column.[27]

Early diagnosis is essential for successful treatment and is perhaps the key factor in improving the prognosis of OMM, but this remains to be proven. Surgery is the mainstay of therapy. New adjuvant immunotherapeutic modalities and chemotherapy protocols have been used to improve the survival of patients with more advanced disease.

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