Primary Oral Malignant Melanoma

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INTRODUCTION

Melanoma is a malignant neoplasm of melanocytes which are derived from the neural crest cells that constitute the melanin pigment of the basal layer of the epithelium. Although most melanomas arise from the skin, they may also arise from the mucosal surface or at other sites wherein neural crest cells migrate.

Melanoma is the third most common skin cancer accounting for 1.3% of total cancers. Oral melanomas comprise much less than 0.2 to 8.0% of all melanomas and approximately four times more frequently in the oral mucosa of the upper jaw, usually on the palate and anterior gingiva. Some rare cases of involvement of lip, mandibular gingiva and buccal mucosa were also reported previously. Here, we are presenting a case of oral malignant melanoma (OMM) involving mandibular gingiva in a 60-year-old male patient.

CASE REPORT

A 60-year-old male patient farmer by profession, reported to the Department of Oral Medicine and Radiology, Modern Dental College, Indore, India, with a complaint of swelling in lower right back teeth region since 2 months.

His present illness revealed fracture of lower right posterior tooth while chewing food later associated with swelling of gums with the same region which was increased gradually to the present size. Swelling was associated with intermittent and throbbing type of pain. On mastication, intermittently he noticed bleeding from tooth while chewing food later associated with swelling of gums in the occlusal plane extending up to lower buccal vestibule with bulk of the swelling predominantly in the lingual gingiva and buccal vestibule. Superficial mucosa over the swelling was thin and erythematous with polarity in the premolar region with indentations of the antagonist teeth. The anterior portion of the swelling in a lingual vestibular region showed dark bluish black pigmentation, and posterior part of swelling showed dark red color. The swelling was not pulsatile. Sublingual veins showed varicosities (Fig. 1). On palpation, swelling was pedunculated, exophytic, nodular, nontender and firm in consistency with its base lying on gingiva of fractured 45 region. It was noncompressible, nonfluctuant and bleed on manipulation. Tooth (45) associated with swelling had tenderness on palpation with grade III mobility.

There was no lymphadenopathy present elsewhere in the body except right submandibular lymph node which was enlarged, nontender not fixed to underlying tissue.

Intraorally, a single, pigmented, nodular, irregular exophytic growth of size 4 × 3 cm, present over the right lower alveolar region which was extending anteriorly from mesial aspect of 43 to 47 region posteriorly and superioinferiorly from 1 cm above, the occlusal plane extending up to lower buccal vestibule with bulk of the swelling predominantly in the lingual gingiva and lingual vestibule. Superficial mucosa over the swelling was thin and erythematous with polarity in the premolar region with indentations of the antagonist teeth. The anterior portion of the swelling in a lingual vestibular region showed dark bluish black pigmentation, and posterior part of swelling showed dark red color. The swelling was not pulsatile. Sublingual veins showed varicosities (Fig. 1). On palpation, swelling was pedunculated, exophytic, nodular, nontender and firm in consistency with its base lying on gingiva of fractured 45 region. It was noncompressible, nonfluctuant and bleed on manipulation. Tooth (45) associated with swelling had tenderness on palpation with grade III mobility.

The case was taken up for extraction of 45 and 46, and incisional biopsy was taken.

Histopathologically, the hematoxylin and eosin stained section showed dysplastic spindle-shaped melanocytes and melanin...
pigment which is interspersed within connective tissues stroma which was suggestive of an OMM (Fig 3).

To rule out metastasis radiographs of chest and long bones, computed tomography, magnetic resonance imaging and sonography of neck and abdomen were done, which were normal. But fine-needle aspiration cytology of right submandibular lymph node was suggestive of metastatic infiltration MM.

Later, patient was taken up for right hemimandibulectomy with radical neck dissection. Patient was kept under observation with regular follow-up for 1 year.

DISCUSSION

MM is an extremely rare neoplasm of epidermal melanocytes. OMM is typically very aggressive and is accompanied by poor prognosis.8

The most frequent head and neck site of occurrence of mucosal melanoma is the conjunctiva followed by sinonasal cavity, oral cavity, pharynx, larynx and upper esophagus (in decreasing order of frequency). Moore and Martin in a series of 1546 melanomas found 26 arising in upper respiratory tract and oral cavity, of these only 12 were primary oral melanomas.9

OMM affects all races. In Japan, India and Africa malignant melanoma of mucosal surface have been reported as having a higher incidence than in Western countries. Takagi reported that oral melanomas comprise 7.5% of all MM in Japan.10 Mucosal melanomas tend to present at an advanced stage are more aggressive and present in a vertical growth (nodular) phase of diseases. The oral mucosal melanomas are classified by histologic pattern as in situ and invasive. Most oral melanomas lesions (85.0 %) are invasive or have both an invasive and in situ pattern. Criteria for primary oral malignant melanomas (POMM), as described by Greene et al include:

1. Demonstration of melanoma in oral mucosa
2. Presence of junctional activity
3. Inability to demonstrate extraoral primary melanoma.11

The etiology of OMM remains unknown in contrast to cutaneous melanoma which is linked to sun exposure. Nevi are considered as potential source of some oral melanomas but sequence of events is poorly understood. Currently, most melanomas are thought to arise de novo. Many genes are implicated in the development of melanoma, including CDKN2A (p16), CDK (chromosome 12q15), RB1, CDKN2A 9 (p19) and PTEN/MMAC1.12

The average age of occurrence is 55 years, most cases occurring between 40 and 80 years with documented cases as early as age of 7 years and as late as 95 years.4,5,12,13 Many investigators reported that there is predilection for males with male to female ratio almost 2:1.4,5,12 Palate and alveolar mucosa are involved in 80% of cases followed by buccal mucosa, mandibular gingiva, lips, tongue and floor of mouth in decreasing incidence.4,5,12,13

Most of the melanomas are asymptomatic; swelling with pigmentation is usually initial sign of OMM. It may be uniformly brown or black or show variation in color with black, brown, gray, purple and red shades or depigmentation.14 According to Tanaka et al, OMM could be classified into five types based on their clinical appearance: Pigmented nodular, nonpigmented nodular, pigmented macular, pigmented mixed
The patient may not be able to determine the duration and rate of growth. Pain, ulceration and bleeding are rare until late in disease. Rolled borders are not a feature of oral melanoma because the atypical melanocytes exhibit pagetoid mode of spread resulting in uniform epithelial thickening. In our case, we found that anterior portion of the swelling in a lingual vestibular region showed dark bluish-black pigmentation and posterior part of swelling showed dark red appearance; which make clinical diagnosis confusing to call OMM, peripheral giant cell granuloma and/or pyogenic granuloma.

Amelanotic melanoma type of variety shows various types of clinical appearances like erythematous or pink, some time eroded and nodular. This tumor is often confused for other tumors, and only the histological examination provides the right diagnosis. The so-called ABCDE checklist (asymmetry, border irregularities, color variations, diameter > 6 mm, and elevation, a raised surface), which is used in the identification process of cutaneous melanoma, could also be of some help in the diagnosis of oral melanoma. About 10% of the cases are amelanotic. More than 95% of the lesions are anti S-100 antigen positive, and more specific markers include HMB45, Melan-A and antityrosinase. Special stains like Mason’s Fontana and melanin bleach are also helpful in the diagnosis of MM.

Radiographically, primary and secondary melanomas very rarely involve the jaw bones. However, when they do involve the bone, they are indistinguishable from osteomyelitis, while others have appearance which is to be found with any other lytic malignant tumor. In our case, we found that there was irregular interdental bone loss with mandibular second premolar and first molar making radiographic diagnosis confusing. Radiographically, such type of interdental bone loss can be seen in early benign condition (reactive lesion), early malignant lesion as well as in pulp and periodontal diseases, it will be difficult to diagnosed OMM radiographically when lesion is an early period or small in size.

The differential diagnosis of OMM includes tattoo (amalgam, graphite), oral melanotic macule, nevi, melanoacanthoma, local patch of melanoplakia, focal hemosiderin deposit in peripheral giant cell granuloma.

The clinician who must choose from these entities with only the information available from the patient examination has difficulty arriving at a working diagnosis.

On clinical examination, the early nodular melanoma may be difficult or impossible to differentiate from an intramucosal, compound or blue nevus; a pigmented fibroma or a peripheral giant cell granuloma that contains a large amount of hemosiderin. Occasionally, the nodular melanoma has an irregular, fissured, or ulcerated and bleeding surface (as seen in our case) features that strongly suggest malignancy. Rapid growth is a feature of melanoma.

Although the rapidly enlarging pigmented exophytic variety is not easily confused with other entities, the clinician may be confronted with a lesion in a patient being seen for the first time. The patient may not be able to determine the duration and rate of growth.

OMM has a predilection for metastasis to lungs, liver, brain and bones. Documented cases of metastasis to oral cavity are rare, but include secondary lesions of the gingiva, palate, tongue and tonsils. Approximately 13 to 19% of patients have lymph node metastases, and another 16 to 20% are likely to develop metastases subsequently.

The recommended treatment for oral melanoma is wide surgical excision with adequate negative margins with or without neck dissection but it can be difficult due to anatomic restrictions. However, melanoma is not radiosensitive, but sometimes patients show a good response in early or in situ melanomas. Immunotherapy has been successfully used but chemotherapy has demonstrated a relatively low response rate. Dacarbazine-DTIC, INF-gamma and TNF-alpha-2b have been described as chemotherapeutical and immunotherapeutical treatments associated with Bacillus Calmette-Guerin vaccine and recombinant interleukin-2 in different combinations.

The prognosis of oral melanoma is far worse than cutaneous melanoma.3,8 Use of Clark’s criteria for degree of invasion and prognosis are not applicable to oral melanoma because there is no intraoral counterpart of reticular and papillary dermis.4,5,13 The reported five-year survival rate for OMM has ranged from 4.5 to 29% with a median survival rate of 18.5 months after initial diagnosis, whereas 5 years survival rate for patients with cutaneous melanoma range from 35 to 45%.5

Poor prognosis may be due to late diagnosis and special anatomic considerations of oral cavity which include:

1. Early invasion of deeper structures due to proximity of bone and muscles.
2. Invasion of bone which often results in incomplete excision increasing likelihood of metastasis.
3. Rich vascular supply of oral cavity further constituting in dissemination of melanoma.5,13 According to Batsaki et al, invasion of > 0.5 mm indicates poorer prognosis.

POMM is exceedingly rare and biologically aggressive malignancy. Clinically, it mimics like many other pigmented lesions of the oral cavity, so it should include in the differential diagnosis of pigmented lesions. Successful treatment of oral melanoma is dependant on detail history, thorough oral examination and biopsy with other necessary investigations of any suspicious oral pigmentation because early diagnosis and intervention results in better prognosis. The above case is presented in view of its rarity in involvement of oral cavity and mandibular gingiva.

**REFERENCES**


