INTRODUCTION

Oral melanoma (OM) is a malignant neoplasm of melanocytic origin. Melanocytes are dendritic cells of neural crest origin that migrate to the basal layer of oral mucosa during embryogenesis. Melanin, a pigment, produced by melanocytes is either phagocytosed or deposited into adjacent epithelial cells. A melanocyte and the group of epithelial cells that it provides with melanin are collectively described as epithelial-melanin unit. In a single tissue section of gingiva, melanocytes are found in the ratio of 1 melanocyte to 15 keratinocytes. Malignant transformation of melanocytes into melanoma cells produces marked changes in morphology, organization and biologic characterization of melanocytes. Melanoma cells are round or spindle shaped cells with no dendritic process and they possess irregular, hyperchromatic nuclei. These cells attain the ability to invade the superficial layers of epithelium and the underlying submucosa.

OM develops most commonly in the fifth to sixth decades of life and rarely occurs below 20 years of age. Nearly 80% of the cases occur in maxillary mucosa with highest prevalence in hard palate and gingiva. Most of the OMs are asymptomatic but some may present with ulcerated epithelium or bleeding from the lesion. Pain is usually reported at the later stage of the disease. Surgical excision of the lesion with a wide margin is the accepted mode of treatment. In contrast to cutaneous counterpart, prognosis of the OM is considered to be poor. Survival rate of less than 20% for 5 years has been reported in the literature.

CASE REPORT

A 42-year-old male reported to the outpatient department of Ragas Dental College and Hospitals, Chennai with the chief complaint of bleeding from extraction socket in the right lower posterior teeth region for the past 4 days. History revealed that the patient had mobility of 45 for past one month and the tooth was extracted 5 days back. The day after extraction, the patient had bleeding from the extraction socket. The past medical history was not contributory. General examination did not reveal any abnormality. On extra-oral examination, a diffuse swelling was present in the right lower region of the mandible.

Table 1: Differences between melanocytes and melanoma cells

| Melanocytes                                      | Melanoma cells                                      |
|-------------------------------------------------|-----------------------------------------------------|
| Dendritic cells, possessing dendritic process through which melanin is deposited to epithelial cell | Round to spindle shaped cells, lack dendritic process |
| Small regular nuclei                             | Large, irregular hyperchromatic nuclei with prominent nucleoli |
| Solitary cell arrangement with no contact between two such cells. (Contact inhibition.) | Loss of contact inhibition |
| Located along the basal layer of epithelium      | Invade the superficial layers of epithelium (Pagetoid spread) or even underlying submucosa |
| Rare mitotic activity                             | Remarkable mitotic activity                         |
the face extending, 2 cm from corner of the mouth to 1 cm in front of the angle of the jaw [Figure 1]. The swelling was soft and nontender on palpation. There was no lymph node enlargement. On intra-oral examination, a well-defined reddish black nodular growth was observed at the extraction site of 45, measuring 2×1 cm in size. Surface of the growth appeared lobulated [Figure 2]. The lesion was firm and nontender. Orthopantomogram (OPG) did not show any abnormality. The presence of a reddish black exophytic growth in the gingiva and a history of recent extraction made us consider the following lesions in the differential diagnosis: epulis granulomatosa, traumatic neuroma, malignant melanoma, angiosarcoma and Kaposi’s sarcoma.

An incisional biopsy of the lesion was performed which showed parakeratinized stratified squamous epithelium and the underlying fibrovascular connective tissue. Within the connective tissue there were proliferation of epithelioid and spindle shaped cells with basophilic nuclei and prominent nucleoli arranged in sheets and organoid pattern. Pigmented granules suggestive of melanin were seen both intracellularly and extracellularly throughout the lesional tissue. [Figures 3-5]. The histopathological features were suggestive of oral melanoma.

To confirm the diagnosis, special staining and immunohistochemistry were done. Masson-Fontana stain showed positivity for the neoplastic cells [Figure 6] and immunohistochemical evaluation of the tissue specimen showed positive stain for Homatropine methylbromide-45 (HMB-45) antibody [Figure 7]. Chest radiograph, computed tomography of head and neck region and ultra sound of abdomen was performed to rule out any secondary lesions. Based on the histopathology and immunohistochemical findings, a final diagnosis of primary oral melanoma was made. Segmental mandibulectomy with level I nodal dissection was done along with fibula graft replacement. The patient was free
of disease at the end of first year follow-up and was lost to follow-up thereafter.

**DISCUSSION**

Oral melanoma was first reported by Weber in 1859.\(^9\) OM accounts for 0.5% of all oral malignant neoplasms and 0.2% - 8% of all melanomas.\(^{1,4,5,10}\) Rapini et al. found that the highest percentage of OM reported was in the age range of 41 - 60 years.\(^5\) The lesion does not show any gender predilection, but is slightly more common in males than females.\(^{8,11}\) Aguas et al. in their review of 177 cases, reported that OM occurs in 53.1% of males and 46.9% of females. Hard palate and maxillary gingiva are the most common sites of occurrence, followed by mandibular gingiva, buccal mucosa, tongue and lip.\(^{3,6-9}\) Table 2 shows the reported site predilection for oral melanomas.

**Table 2: Site predilection for oral melanoma\(^{[2,5-8,11]}\)**

| Authors                      | No. of cases | Maxilla (Palate and gingiva) | Mandible | Tongue | Lip | Buccal mucosa | Other sites |
|------------------------------|--------------|-----------------------------|----------|--------|----|---------------|-------------|
| Tanaka et al, (1994)         | 20           | 18                          | 1        |        |    |                |             |
| Patton et al, (1994)         | 15           | 2                           | 5        | 2      | 3  |                | 3           |
| Manganaro et al, (1995)      | 4            | 3                           | 1        |        |    |                |             |
| Westop Banff workshop Barker BF et al, (1997) | 50          | 35                          | 8        | 1      | 4  |                | 2           |
| Dimitrakopoulos et al, (1998) | 1            | 1                           |          |        |    |                |             |
| Lopez Graniel et al, (1999)  | 15           | 12                          | 1        | 2      |    |                |             |
| Umeda et al, (2002)          | 15           | 13                          | 1        |        |    |                | 1           |
| Chiu et al, (2002)           | 1            | 1                           |          |        |    |                |             |
| Garcia et al, (2004)         | 2            | 2                           |          |        |    |                |             |
| Aguas et al, (2009)          | 10           | 8                           | 2        |        |    |                |             |
| Reddy et al, (2010)          | 1            | 1                           |          |        |    |                |             |
| **Total**                    | **134**      | **92**                      | **16**   | **8**  | **8** | **5**          | **5**       |

100% 68.6% 11.9% 5.9% 5.9% 3.7% 3.7%
Rapidly enlarging mass

Tanaka et al., described the clinical presentation of OM and classified them into five types: (a) pigmented nodular, (b) nonpigmented nodular, (c) pigmented macular, (d) pigmented mixed, (e) nonpigmented mixed. The pigmentation of the lesion may vary from light brown to dark brown and from black to blue. In our case, the lesion presented as reddish black nodular growth (pigmented nodular). Most of the OM are asymptomatic with some lesions presenting with ulcerated epithelium or bleeding from the lesion. Pain is usually reported at the later stage of the disease.

Differential diagnosis of oral melanoma includes pigmented lesions of melanotic and nonmelanotic origin. Oral melanotic macule, melanoacanthoma, melanocytic nevi, smoking associated melanosis, postinflammatory pigmentation, drug induced pigmentation and intraoral pigmentation associated with systemic diseases like Peutz-Jeghers syndrome, Cushing syndrome and Addison’s disease have to be considered in the differential diagnosis of oral melanoma.

In our case, recent dental extraction and rapidly enlarging reddish black mass in relation to extraction site made us to consider the following lesions in the differential diagnosis.

Epulis granulomatosa (EG), a variant of pyogenic granuloma, featured first in our differential diagnosis. It is an exorbitant proliferation of granulomatous tissue occurring in response to bony sequestra left in the extraction socket. In our case the reddish nodular mass in the recent extraction site produced the suspicion of EG but closer examination revealed attachment of the mass to the gingiva rather than to extraction socket.

Traumatic neuroma (TN) is a reactive proliferation of damaged nerve trunk usually occurring after trauma, dental extraction or other surgical procedures. Most common intraoral locations are mental foramen, lower lip, and tongue. In our case, history of extraction of lower second premolar advocated the possible occurrence of TN but pain or sensory anomalies like paresthesia, anesthesia and hyperpathia which are typical presentation of TN were missing in our patient.

Angiosarcoma is a rare malignant neoplasm of vascular endothelium. Only 4% of tumors are reported in the intraoral sites with tongue and mandible being the predominant sites. The tumor occurs more commonly in the elderly individuals, usually above 65 years. Trauma, long-standing lymphoedema, and irradiation of benign vascular lesion are some of the predisposing factors. Reddish nodular growth with the lobulated surface supported the clinical diagnosis of angiosarcoma, but the occurrence in the younger age group, as in our case was unusual.

Kaposi’s sarcoma (KS) is a malignant vascular tumor considered to be caused by Human Herpes Virus-8. Clinically, KS occurs in four variants - classic, endemic (African), epidemic (AIDS related), and posttransplant (immunosuppression associated). The classic variant occurs mainly in older patients involving skin of the lower extremities. The oral KS is a rare neoplasm occurring as brownish red to violaceous macule or papule on the palate, which increases slowly to nodular growth. In our case the lesion occurred on the mandibular gingiva, which is an unusual site for Kaposi’s sarcoma and the patient also complained of rapid growing of the nodular swelling rather than slow growing one.

Rapidly enlarging pigmented growth on the mandibular gingiva led to a diagnosis of a malignant tumor of pigmented cell, the melanocyte. Oral melanoma occurs between the age group of 41-60 years. Maxillary gingiva and hard palate being the primary site, cases of mandibular gingiva, buccal mucosa and tongue have also been reported.

Microscopically, our case showed the presence of atypical melanocytes within the epithelium, sheets of epithelioid and spindle shaped neoplastic cells with prominent nucleoli in fibrous stroma, extensive accumulation of intracellular and extracellular melanin pigmentation, suggestive of oral malignant melanoma.

Special stains such as Masson-Fontana and melanin bleaching aid in the diagnosis of melanoma. Oral melanoma shows positivity for immunohistochemical markers such as HMB-45, S-100 and MART-1/Melan A. HMB-45 recognizes a 10-kDa antigen localized in premelanosomal vesicles. It is considered to be more specific than other markers as the antibody does not stain normal adult melanocytes or intramucosal nevi. Our case showed positive results for Masson-Fontana stain and HMB-45 antibody.

Treatment of choice for oral melanoma is complete excision with adequate negative margins. Wide resection with free margin of 2-5 cm is usually practiced for cutaneous melanoma, but this is difficult to achieve in oral melanomas because of anatomical limitation. Radiotherapy and chemotherapy play an important role in the management of unresectable tumors.

Prognosis of OM is poor when compared to its cutaneous counterpart. The 5-year survival rate for oral melanoma ranges from 7 to 13%. The poor prognosis of OM is attributed to its common site of occurrence, maxillary gingiva and hard palate areas being difficult for self examination, absence of symptoms in the early stages, rapid invasion of the lesion to underlying bone and incomplete removal of the lesion due to anatomical limitation. The rich vascular supply of oral cavity may contribute to early metastasis and multiple primary lesions make their management difficult. Prasad et al., showed that the presence of vascular invasion was an important adverse prognostic finding for melanomas.
CONCLUSION

In spite of wide surgical excision, prognosis of oral melanoma is still worrisome. Early diagnosis of the lesion is considered as the prime mode of preventing morbidity and mortality. The dental practitioners should meticulously follow up pigmented oral lesions and biopsy should be performed for the lesion that rapidly grows in size or that shows alterations in color and surface irregularity. Reporting of cases from different ethnic group are encouraging and lead for better understanding of the lesion in future.

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