Oral Malignant Melanoma – A Review

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Abstract
Pigmented areas in the oral cavity are often considered physiological but a practicing dentist must be aware of pigmentation secondary to oral melanoma which is rare, but life threatening. Melanoma represents one of the most life threatening cancers known. The etiology of oral melanoma is still unknown. Lesions are irregular and asymmetric, and commonly involve palate, gingiva, tongue, buccal mucosa and lips. Patients presents with rapidly spreading discoloration of the oral mucosa.

A thorough oral examination and high index of suspicion is needed for early diagnosis. Histopathology holds the key in discrimination of melanoma from lesions mimicking this disease. Prognosis of oral melanoma is comparatively poor and so an early diagnosis and follow-up is critical. This review aims to revisit this important disease.

Keywords: Melanoma, oral, malignant, focal, pigmentation.

Introduction
Ordinarily in the oral mucosa, it is the red and white lesions that are perceived as potentially dangerous. In the asian – african population dark pigmented areas are considered physiological; which is mercifully most often true. But a practicing dentist needs to be alert to the possibility of other rare causes of oral pigmentation like oral malignant melanoma.

Oral melanoma is exceedingly rare and cases have been reported in yellow, black races and in Indians of Asia. As management of oral melanomas have been observed to be challenging for doctors with a rapid metastatic rate, and relatively poor prognosis, a dentist’s knowledge about diagnosis of these lesions will abet efficient and improved treatment by early detection. Melanoma, a neoplasm of melanocytes represents one of the most life threatening cancers known. While certain risk factors have been identified for cutaneous melanoma (Table 1), no etiologic factor has been identified for primary oral melanoma (POM). However several risk factors have been mentioned (Table 2). POMs are known to arise from nevus, pre-existing pigmented area or de novo (30%).

Epidemiology
It is a lesion of adulthood and is rarely seen below 20 years of age. The mean age of occurrence is 56 years and male to female ratio is 2:1.
Clinical Features
POM presents themselves in an array of colors, ranging from light brown to dark brown, black to blue and red and can simulate a vascular or a salivary gland tumor or a reactive lesion like pyogenic granuloma. On the other hand, some of the lesions of POM are amelanotic and so are difficult to diagnose.

Oral lesions of POM are asymmetric, irregular in outline, and occasionally multiple. The surface architecture can range from macular to ulcerated and nodular. Rolled borders are usually absent in melanoma.

Commonly involved intraoral sites are hard palate (32%), maxillary gingiva (16%), mandibular gingiva (7%), tongue (7%), buccal mucosa (7%), upper and lower lip (7%). When the lesion is secondary or metastatic, they are more commonly present on tongue, parotid and tonsils.

Symptoms for which a patient seeks an oral physician's opinion is a rapid spreading discoloration of oral mucosa. Some other uncommon features include tooth mobility, paresthesia, swelling, ulceration, hemorrhage and pain in advanced cases. There has been a study demonstrating a practical and technically simple method for the clinical diagnosis of POM. The clinical test consists of rubbing the surface of the lesion with gauze with the objective of verifying if it stains black due to the presence of melanin pigment on its surface but the validity of the test in diagnosing POM is still in question.

Another clinical diagnostic criteria is known as ABCDE criteria (Table – 3).

Diagnostic challenges
Melanotic macule and Melanoacanthoma presents as pigmented macules but are actually innocuous. Oral melanomas are uncommon. POM remains asymptomatic for a long time and hence the diagnosis is often delayed. Amelanotic melanomas are not pigmented and so difficult to diagnose.

Differential diagnosis
There are a lot of 'mimickers' to this serious disease and some of these are themselves known to transform to melanoma. These lesions can be categorized under 3 broad subheadings: a. Pigmented lesions, which includes physiologic pigmentation, ecchymosis, nevus, melanotic macule, melanoacanthoma etc; b. Vascular lesions like those in Kaposi's sarcoma, and c. other lesions, which include lesions like amalgam tattoo.

Nevus can be macular, papular or nodular. Most Nevi starts to develop during childhood and evolve to be diagnosed in adults. Congenital nevus, as the name suggests is congenital and is seen in very small children. It has a very high chance of transforming to Melanocarcinoma. Oral melanotic macule, spitz nevus, acquired nevocellular nevus are usually <1cm in size.

In general, oral melanoma, oral melanotic macule, melanoacanthoma, blue nevus, congenital nevus, spitz nevus, acquired nevocellular nevus, are all closely related pigmented diseases which cannot always be clinically differentiated.

Kaposi's sarcoma is a vascular lesion which is an important differential diagnosis. If the colour of the lesion is bluish black, clinical differentiation will be based on the vascular nature of the lesion demonstrated either by aspiration, FNAC or biopsy. It may be borne outside (Africa, Kaposi's Sarcoma is strongly associated with AIDS.

Other focal pigmentation include ecchymosis, which has a history of trauma preceding the occurrence of lesions and resolves within few days with characteristic color changes from red to blue to greenish to yellow and finally fades out. Amalgam tattoo is diagnosed by its presence in vicinity of a tooth restored with amalgam.

A protocol should be followed while approaching a suspected case of POM:

Lesion should be photographed to study the rate of growth/changes in the lesion.

Incisional Biopsy should be performed to look for presence of melanoma, and if present, to look for type, thickness and level of invasion, as melanoma can metastasize via blood as well as lymphatic channels. It has the ability to metastasize to any organ, including the heart.

If cervical lymphadenitis is present, FNAC should be performed to check for neoplastic cells.

Chest radiograph should be obtained to check metastasis to lungs. The spread may cause one or more tumors in the lungs and might cause fluid collection around lungs.
This fluid called pleural effusion which is seen in the chest X-ray. CT scan and MRI should be done to evaluate neck for regional disease or to look for distant metastatic foci. Lymphoscintigraphy, sentinel lymph node (1st node to be involved) mapping, skeletal scintigraphic surveys and PET scan can also performed to check for distant spread. Thus all oral pigmentation which are large or irregular or have recently appeared or increased in size should be biopsied, as the clinical differentiation is often difficult and histopathology holds the key.

**Histological Features**

The presence of atypical melanocytes, usually larger than the normal melanocytes and having varying degree of nuclear pleomorphism and hyperchromatism in the epithelial and connective tissue junction in the biopsy of the melanotic lesions of the oral mucosa are suspicious for oral malignant melanoma. Histologic techniques such as bleaching of the section before staining can aid in studying the details of the tissue and likewise immunohistochemistry can also be useful.

**Management**

According to ‘Westop Banff Workshop Proceedings, 1995’, surgery is considered to be the primary treatment for malignant melanoma and since oral melanomas have a grave prognosis, radiotherapy and chemotherapy serve as adjuvants. Radiotherapy is administered especially in the early stages of Melanoma using 15MeV linear accelerator. Normally a dose of 62 to 68 Gy is usually given. Chemotherapy can be induced using: Daccarbazine – DTIC & INF α-2b DAV protocol

D- Dimethyltriazeno-Imidazole-Carboxamide
A- ACNU (Nimustine Hydrochloride)
V – VCR (Vincristine)

Recent and innovative treatment modality includes ‘immunotherapy’ which includes OK 432 and interferon α-2. OK 432 is a biologic response modifier consisting of lyophilized powder made from low virulence Su-strain human streptococcus pyogenes which have been treated with penicillin. Bacille Calmette Guerin (BCG) has also been tried with the intent of activating killer T cells and inhibits suppressor T cells thereby improving the host’s immunity.

**Prognosis**

The 5 year survival rate of POM is poor (15%) as compared to cutaneous melanoma (80%).

Six variables are to be identified for assessing prognosis: histologic regression, tumor thicknes and lymphocytes infiltrating tumor, presence of satellite lesions, site, mitotic rate and sex of the patient. There can be several reasons for poor prognosis in POM:

1. Late diagnosis,
2. Anatomic limitations making radical surgery difficult,
3. Mucosal tumors show rapid invasion to deeper structures,
4. Vascularity of oral mucous membrane,
5. Mucous membrane is thinner than skin because of thinner lamina propria due to thin papillary dermis and absence of reticular dermis, thus most mucosal melanomas progress quickly to vertical growth phase and gain access to the rich vascular and lymphatic network more quickly.

**Conclusions**

A Protocol has been highlighted for approaching a patient with oral pigmentation: 1. all oral pigmented lesions that could not be clinically diagnosed should be biopsied, 2. biopsy should be performed from the thickest & darkest region of the lesion, 3. pathologists should be provided with complete clinical information for biopsies, and 4. follow-up of the patient should be done which includes thorough checkup, chest X-ray and clinical photographs.

**References**


Table 1  Risk factors for Cutaneous Malignant Melanoma

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<tr>
<th>1. Family history</th>
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<tr>
<td>2. Fair complexion</td>
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<td>3. Light &amp; red hair</td>
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<td>4. Blue or Green eyes</td>
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<td>5. History of sun burns in childhood</td>
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<td>6. Indoor occupation with outdoor recreational habits</td>
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Table 2 - Suspected risk factors for Oral melanomas

| 1. Mechanical trauma from ill fitting dentures. |
| 2. Infection. |
| 3. Oral habits. |
| 4. Self medications. |
| 5. Melanoma related antigens (gp100, melanin A) |
| 6. Cytogenetic defects |

Table 3  ABCDE Criteria for POM

| A - Asymmetry |
| B - Border irregularity |
| C - Color variation |
| D - Diameter >6mm |
| E - Evolving |