Case Report

# Oral mucosal melanoma: An enigma to the clinician

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**Abstract**

Oral mucosal melanoma is a rare oral malignancy with well defined clinical presentation of a pigmented brown macular to nodular lesion. The careful histopathological examination along with immunohistochemistry of the biopsy specimen was helpful in identification of this noxious lesion. A clear distinction between management and prognosis of benign gingival lesions and rarer lesions exists. Thus every general dental practitioner should advocate a mandatory histopathological examination of the each and every gingival growth. We present a unique case of oral mucosal melanoma masquerading as a benign gingival growth without any clinical presence of pigmentation in a 58-year-old male patient.

**Keywords:** Biopsy, melanoma, pigmentation

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## INTRODUCTION

Oral mucosal melanoma (OMM) is a highly malignant tumour of the oral cavity. The 2017 WHO classification of head and neck tumours states it as a malignant neoplasm of melanocytes.[1] OMM is biologically distinct from lesions of cutaneous origin. Epidemiologically OMM is a rare entity, accounting for just 0.5% of all melanomas with a slight male predominance and median patient age at diagnosis as 55-66 years. In the oral cavity this lesion often presents with baffling clinical appearance. The etiology of OMM is by unknown factors. The overall prognosis of OMM is poor, with a median survival of 2 years only. Prognosis and predictive factors of cutaneous melanoma e.g. Clark level of invasion and Breslow tumour thickness do not apply to OMM.[1] No standard treatment modality has been established so far and a combination of radical surgery with chemotherapy and radiotherapy is recommended.[2]

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Localized gingival enlargements are one of most common diagnosed gingival diseases. However due to their varied clinical presentations, the diagnosis and subsequent management of these entities becomes a challenge for the general dental practitioner. Here we present a patient with melanoma of the alveolo-gingival mucosa.

## CASE REPORT

A 58-year-old male with a complaint of swelling in the right back region of lower jaw since 2 months reported to Department of Oral Medicine. The swelling was slow-growing and asymptomatic except for hindrance in biting. The male was well built and adequately nourished with no relevant medical history. He gave a history of tobacco smoking (20 bidis/day for a period of 25 years). He had no other significant oral habit. On extra-oral examination nothing significant was noted. On intra-oral examination a pedunculated growth of size 2 × 1.5 cm



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was noted on the buccal side in between teeth 46, 48 extending over the tooth 47, with lingual extension, also brown pigmentations were noted on the mucosa. The overall oral hygiene was poor. The patient was advised for intra oral periapical radiograph (IOPA) of 46, 47 teeth region and provisional diagnosis of a gingival epulis or fibroma was made. The IOPA revealed no bony pathology roots of 46, 47 and 48. Routine blood investigations were found to be normal. No lymph nodes were palpable. So an en mass excision as well as atraumatic extraction of 47 was done under local anesthesia and the specimen sent for histopathological examination to Department of Oral Pathology. At the grossing table two soft tissue specimens with largest bit of size 1.6 × 1 cm and smaller one of 1 × 0.75 cm was processed into two separate paraffin blocks and stained with haematoxylin-eosin (H and E) stain [Figure 1b]. The H and E stained section shows stratified squamous epithelium overlying a fibrocellular connective tissue. One area of the section shows hyperplastic epithelium [Figure 2a], adjacent to it is an area with brown pigment containing epitheloid cells within the epithelium, along the basement membrane as well as within the connective tissue [Figure 2]. Under higher magnification, the large atypical powdery brown pigment containing cells resembling melanocytes are present at the epithelial-connective tissue junction as well as invading into the underlying connective tissue. Approximately more than 10 brown pigment containing epitheloid cell showing level 2 invasions into the lamina propria [Figure 2b]. Deeper part of fibrocellular connective tissue shows highly dysplastic spindle-shaped cells with no pigment, forming the bulk of the tumour mass [Figure 2c]. Some sectioning artifact is also present. A diagnosis of malignant melanoma, with a differential diagnosis of spindle cell variant of squamous cell carcinoma was considered. When the patient came for his follow-up examination the patient was re-examined clinically [Figure 1a]. Intra orally, a red erosive area and the now evidently pigmented residual alveolar ridge of 47, buccal side of attached and free gingiva of 48 was noted. Lingual side appeared to be normal.

For further definitive diagnosis, immunohistochemistry (IHC) markers panel of pan cytokeratins, P 63, Melan A, S-100 and Vimentin was carried out [Figure 3]. The keratinized stratified squamous epithelium was positive for pan cytokeratin marker while the atypical spindle cells were negative for pan cytokeratin and P 63 markers thus ruling out spindle-cell carcinoma. The brown pigment containing epitheloid cells were positive for S-100 and Vimentin. The strongly positivity for S-100 and Vimentin of the spindle shaped tumor cells in the deep connective tissue stroma confirmed the OMM diagnosis. Curiously this case was

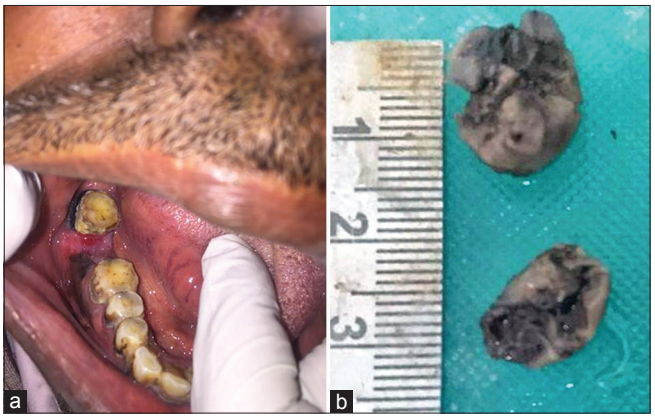


**Figure 1:** (a) Clinical photograph after excision of lesion and extraction of tooth 47 showing pigmented residual alveolar ridge of 47 and attached and free gingiva irt buccal side of 48. (b) Grossing picture: Two soft tissues as nodular masses with large tissue of size 1.6 cm × 1cm, brownish in colour and soft in consistency

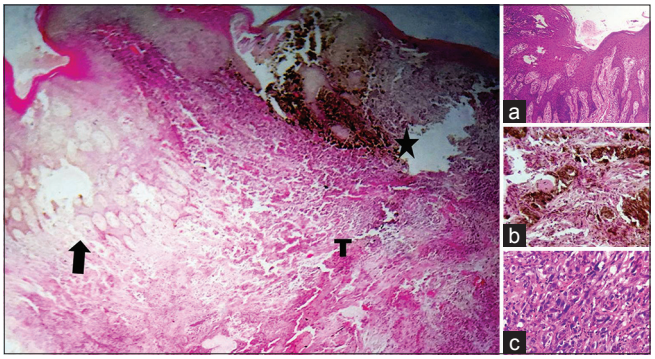


**Figure 2:** H and E stained sections showing the entire biopsy specimen in scanning view ×4 with - ⬆ hyperplastic epithelium, - ★ epitheliod cells at the epithelial connective tissue junction and as invasive nests with brown melanin pigment, T for tumor mass of spindle-shaped cells, (a) showing the hyperplastic epithelium at ×10; (b) showing brown melanin pigmented within tumour cells at ×40; (c) showing pleomorphism, hyperchromatism of infiltrative spindle-shaped tumour cells in deeper submucosa at ×40

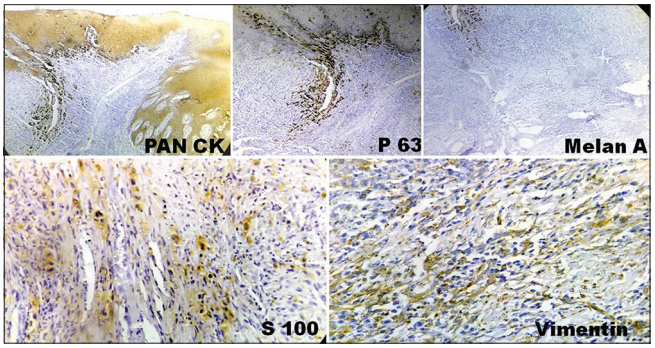


**Figure 3:** Immunohistochemistry panel for oral mucosal melanoma: Positivity for S-100 and strong positivity of spindle-shaped tumour cells in the connective tissue stroma for vimentin (×40, streptavidin-biotin-peroxidase), negativity for pan CK, P 63, Melan A seen in the spindle-shaped tumour cells (×10, streptavidin-biotin-peroxidase). Pan CK positivity noted in the superficial oral epithelium and melanin pigment seen in all sections

Melan A negative and the diagnosis of OMM was arrived by cumulative IHC findings.

## DISCUSSION

The various differential diagnosis for consideration for OMM are Melanotic Macule, smoking associated Melanosis, post-inflammatory pigmentation medication induced Melanosis, Melanoplakia, Melanoacanthoma, Nevi, Addison's disease, Peutz-Jeghers syndrome, Amalgam tattoo, Kaposi's sarcoma.[3] Histopathological differential diagnosis for brown pigmented cells found at the junction of epithelium and connective tissue include junctional nevus and Amalgam tattoo.

The lack of understanding of biology, clinical characteristics, and prognostic factors of OMM makes it a mystery entity with a well recognized cutaneous counterpart. Guevara-Canales *et al*., discussed the various possible etiological factors as pre-existing long-term melanosis (involving 33 to 55% head and neck melanomas), mechanical trauma such as denture irritation, use of tobacco, exposure to formaldehyde and alcohol.[4]

The clinical characteristics of OMM seem to be greatly variable from appearing as macular lesions, plaque type to nodular non discrete gingival growth. The lesion colors vary from dark blue to black and sometimes no pigmentation with regular or irregular edges. OMM occurred mostly in the hard palate, upper gingival mucosa, lower gingival mucosa, buccal mucosa, tongue and floor of mouth.[5]

Song *et al*., reviewed retrospectively various pathological parameters of cell type (non-epithelioid and epithelioid), level of invasion, ulceration, mitotic rate, pigmentation, necrosis, tumour-infiltrating lymphocyte, vascular invasion. They described histopathology of typical OMM as atypical melanocytes at the junction (*in situ*) and/or invasive nests, and single cells infiltrating the submucosa. These cells were usually epithelioid, with prominent nucleoli, but could be spindled cells with long, oval-shaped nuclei appearing to be highly cohesive. They found the cell type to be a statistically significant independent prognostic factor in a multivariate analysis.[2] Based on the level of invasion assessment by Prasad *et al*.,[6] our case shows level 2 invasion into the lamina propria with more the 10 atypical melanocytes at the epithelial connective tissue interface.

Immunohistochemistry (IHC) plays an important role for a definitive diagnosis. Our case showed IHC markers discrepancy. Immunohistochemically, the typical melanoma is reactive for vimentin, S-100, HMB-45, and Melan-A, tyrosinase, and micropthalmia transcription factor. Of these, Vimentin is the more consistent and the least useful diagnostically. Positivity for S-100 proteins although nonspecific, is of greater practical importance because it is negative in most of other tumours that enter into the differential diagnosis. HMB-45 is much more confirmatory marker than S-100 but S-100 protein is frequently used to highlight the spindled, more neural-appearing melanocytes as was own case. Specifically, OMM and desmoplastic variant of melanoma are HMB-45 negative. Pan cytokeratin and p16 are used to differentiate tumors of epithelial and HPV basis.[7]

Appropriate management of localized gingival growth depends on correctly diagnosing the etiopathogenesis of the enlargement. However, the skills of a clinician is put to test when arriving at a particular diagnosis among the myriad of gingival enlargements that can be classified according to etiology and pathologic changes, location, size and distribution.[8] The commonly occurring localized gingival growth includes Fibroma, Irritation/Inflammatory Fibroma, Peripheral Ossifying Fibroma and Peripheral Giant Cell Granuloma. This case report serves as a reminder for proper histopathological examination for all major or minor gingival lesions. From the histopathologist point of view, grossing of the lesion and processing of multiple tissue bits cannot be over emphasized as in this case where the pigmented area was localized to one area and the epithelial hyperplastic area could have been mistaken for a 'Benign Gingival Hyperplasia'.

Oral cavity is the most accessible part of the body for oral visual examination by self and by any medical/dental practitioner, so a high degree of suspicion, careful history taking and a complete physical examination is warranted for all the involved multidisciplinary health providers. This would help even the initial or atypical signs and symptoms to be diagnosed.

### Declaration of patient consent

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

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## Conflicts of interest

There are no conflicts of interest.

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