

## Case Report

### Oral Malignant Melanoma: A Case Report

Shwetha Vasanth Kumar, Niharika Swain

#### Abstract

Oral malignant melanomas are quite rare. They are considered more aggressive than the cutaneous melanoma and have a poorer prognosis. Early diagnosis can be achieved by histological examination and immunohistochemical staining. It is most commonly reported in the older age group, has a slight male predilection and is commonly seen in the palate and gingiva with the maxillary arch being more commonly affected than the mandibular arch. The aim of this paper is to describe clinical and microscopic features of oral malignant melanoma and its further confirmation by immunohistochemical staining with vimentin, S-100 and HMB-45 in a seventeen year old adolescent female patient in the lower anterior region of the mandibular arch.

**Key words:** Malignant Melanoma; Neuroendocrine Tumors; Neuroectodermal Neoplasms; HMB45, S-100; Vimentin; Cytoskeletal Proteins.

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#### Introduction

Malignant melanoma is a neoplasm arising from melanocytes which are present in the basal layer of the epidermis of the skin and the mucous membrane with squamous epithelium. Hence melanoma is found in oral cavity, eyes and meninges.<sup>1</sup> In contrast to cutaneous melanoma, Melanoma involving the mucosal surfaces of head and neck, typically present at a more aggressive vertical growth (nodular) phase with invasion of the underlying submucosa because of the advanced stage at the discovery.<sup>2</sup> Oral Malignant melanoma was first described by Weber, 1859.<sup>1</sup> The relative incidence of 0.07% of Oral Malignant melanoma was given by Hormia and Vuori (1969), while Pliskin (1979) stated that Oral malignant melanoma accounts for 0.2% to 8% of all malignant melanomas.<sup>3</sup>

The clinical features of Oral Malignant melanoma is often described as an asymptomatic swelling with occasional bleeding.<sup>4-7</sup> Histologically, it resembles squamous cell carcinoma, with large polyhedral cells with eosinophilic cytoplasm and sometimes exhibiting fusiform and mixed type of cells with downward invasion into the connective tissue.<sup>5,6</sup> Immunohistochemically, the typical melanoma is reactive for vimentin, S-100 protein, HMB-45, Melan-A, tyrosinase and microphthalmia transcription factor. Positivity for S -100 protein, seen both in nucleus and cytoplasm, although nonspecific, is of greater practical importance because it is negative in most of other tumors that enter into the differential diagnosis. HMB-45 is a

much more specific marker than S-100. HMB45 is a confirmatory and is reliably specific in 93% of melanocytic malignancies.<sup>8</sup> Thus we describe the histological and immunohistochemical analysis of oral melanoma in anterior mandibular gingiva in a 17 year old female patient which is a rare entity.

#### Case report

A 17 year old female patient reported with a complaint of pain in her lower right first molar. During a routine clinical examination, there was a single well defined growth around 3 × 2 cm in size at the lower gingiva in the 33, 32, 31, 41 region. The patient was relatively asymptomatic. The growth extended from 33 to 41 involving the marginal and the attached gingiva both labially and lingually with 32, 33 displaced lingually and distally (Fig 1). The overlying mucosa was rough with brownish blackish pigmentation. On palpation it was hard in consistency and fixed to the underlying bone. There was no other associated clinical signs and no apparent lymphnode involvement. Radiographic features suggested no trabeculae alterations, but only displacement of teeth was revealed. An incisional (punch) biopsy was done by in the Department of Oral Medicine under local anesthesia and the specimen was sent for histopathological analysis.

On microscopic examination, the hematoxylin & eosin stained section revealed neoplastic cells extending from the epithelium and infiltrating the underlying connective tissue stroma in nests and singly

(Fig 2). The cells are ranging from polygonal to spindle shaped having eosinophilic to brownish melanin pigmentation in the cytoplasm. (Fig 3) The presence of melanin pigment was confirmed by melanin bleach. Immunohistochemical studies were used to establish the final diagnosis at G.C.R.I, Ahmedabad. The tumor cells strongly expressed positivity for Vimentin (Fig 4), S-100 (Fig 5) and HMB-45 (Fig 6) antibodies. The patient was then advised a full body computed tomography and complete surgical resection. However the patient failed to turn up for further treatment and follow up.

### Discussion

Oral mucosal melanomas are highly malignant tumors with the tendency to metastasize or locally invade tissues more readily than other malignant tumors of the oral cavity. It accounts for only 0.5% of oral neoplasms and 0.2 to 8% of all malignant melanomas. They tend to have a worse prognosis than their dermal counterparts.<sup>9</sup> Due to its varied morphologic presentation the clinical diagnosis of oral melanoma is extremely difficult. The differential diagnosis of Oral melanoma include melanotic macule, amalgam tattoo, melano-acanthoma, Kaposi's sarcoma, Nevi, Addison's disease, Peutz-Jeghers syndrome, and other conditions which share similar macroscopic characteristics. Green et al proposed three criteria for the diagnosis of primary melanoma. 1. Demonstration of malignant melanoma in the oral 2. Presence of the so called junctional activity (melanocytes arranged along the basal layer of the surface epithelium) in the lesion. 3. Inability to show malignant melanoma at any other primary site.<sup>10</sup>

Melanocytes are derived from neuroectoderm and are usually found in skin, retina, uveal tract and other ectodermal derived tissues. Although their function is less understood, the presence of melanocytes in oral mucosa is well established. The etiology of Oral melanoma however is unknown unlike its cutaneous counterpart which is linked to chronic sun exposure. The role of ingestion of carcinogens such as tobacco use and chronic denture irritation has been suggested in its pathogenesis.<sup>11</sup>

According to the literature, the average age of Oral melanoma ranges from 50-60 years.<sup>5,6</sup> The incidence of Oral melanoma in

younger age (<20 years) is only 0.6% as given by Rapini et al (1985). There was also a significant male predilection. According to studies done by Chaudhary et al (1958) it was found that out of ninety three cases 75 (80%) occurred in the upper jaw. Of these, 38 (57%) were from hard palate, 20 (26%) were from alveolar ridge and 5 (8%) were from soft palate. Other sites affected, in the order of frequency were lower jaw, cheek, tongue and floor of the mouth. Further studies by Takagi and Berthelsen, it was verified that the gingival and hard palate were the most common sites. The second most common site was maxillary gingiva. Other sites included buccal mucosa mandibular gingiva, lip, tongue and floor of the mouth in the order of occurrence.<sup>4,5,7</sup>

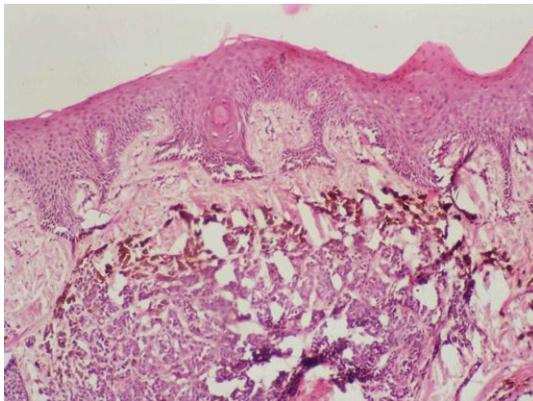
The majority of patients of oral mucosal melanoma lack early symptoms, thus leading to a delay in diagnosis. As the tumour enlarges, the patient may notice a swelling, loosening of teeth. Chaudhary, (1958) and Rapini, (1985) also reported that pre-existing melanosis was seen in one third of the patients.<sup>5,7</sup> Takagi et al, reviewed his patients and found that the most common initial symptoms were the development of the tumor and oral mucosal pigmentation (36%). Less than 10% of oral melanomas were described as amelanotic as described by various studies.<sup>2,12</sup> The clinical features of oral malignant melanoma, described by Berthelsen et al, were those of asymptomatic swelling, occasional bleeding and some cases pre existing melanosis. Pain was an unusual finding.<sup>4,6</sup> The American Joint Committee on Cancer does not have published guidelines on the staging of oral malignant melanomas. A clinical classification which was described by Westbury[1979] as, I - only primary tumor present, II - metastasis present (IIa - adjacent skin involved, IIb - regional lymph nodes involved, II ab - adjacent skin and regional lymph nodes involved) and III - metastasis beyond regional lymph nodes is the most common guideline followed during clinical assessment.<sup>3</sup> Our case however did not follow the typical clinical parameters of the neoplasm, as the lesion was found in the anterior gingival region of the mandible in a 17 year old female patient.

Like Cutaneous melanoma, oral mucous membrane (OMM) probably has in many cases an initial phase characterized by radial growth followed by a phase of invasion of the underlying tissues (the so-

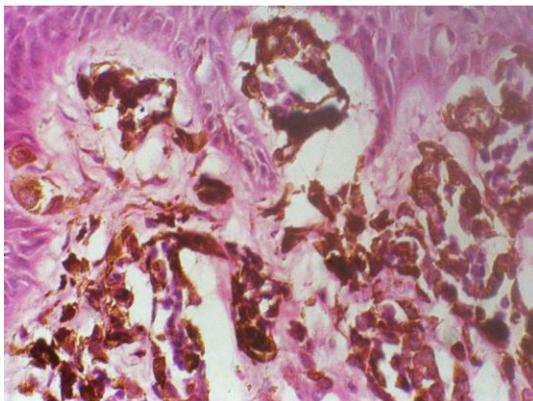
called 'vertical growth phase'). OMMs can be histologically sub classified into: (1) in situ melanoma, which is limited to the epithelium and the epithelial-connective tissue interface; (2) melanomas with an invasive pattern, in which the neoplasm extends into connective tissue; (3) melanomas with a combined pattern of invasive melanoma with in situ component.<sup>13</sup>



**Figure 1:** Well defined pigmented growth at the lower gingiva extending from 41,31,32,33 regions.

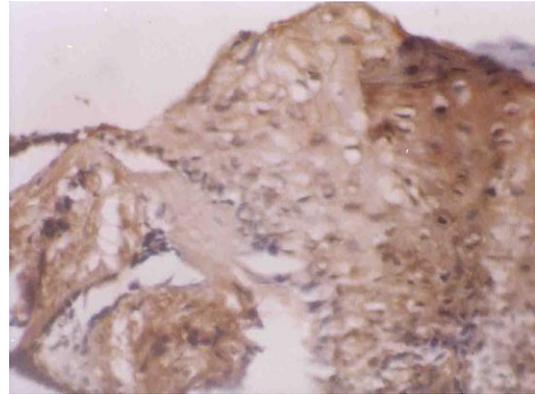


**Figure 2:** Neoplastic cells extending from the epithelium and infiltrating the underlying stroma in single and nests [20x]

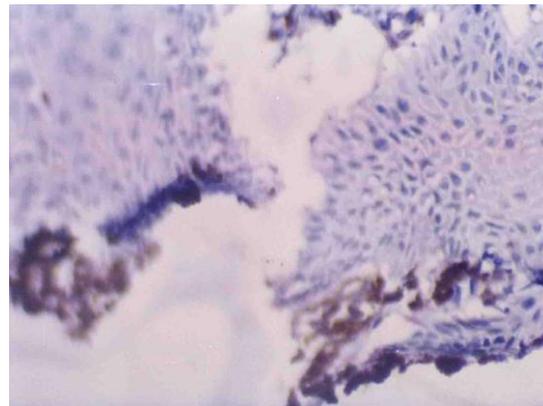


**Figure 3:** The cells range from polygonal to spindle shaped having eosinophilic to

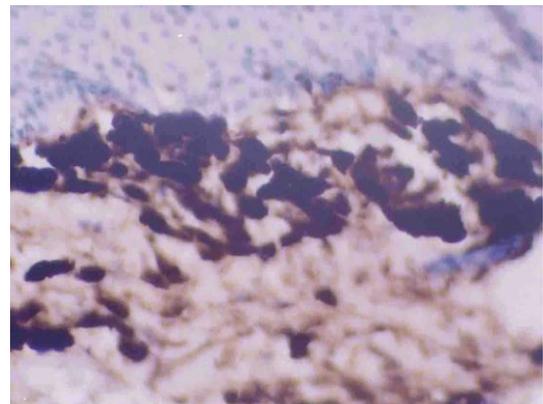
brownish melanin pigmentation in the cytoplasm [40x]



**Figure 4:** Tumor cells showing positivity towards for Vimentin



**Figure 5:** Tumor cells showing positivity towards for S 100



**Figure 6:** Tumor cells showing positivity towards for HMB 45

Histologically malignant melanoma resembles squamous cell carcinoma, with large polyhedral cells with eosinophilic cytoplasm. In other pattern it simulates fibrosarcoma with tumor cells being spindle shaped with elongated nuclei. Takagi et al described histologically out of 18 patients there were 10 cases with polygonal cell types, 2 with fusiform cell types and 6 with

mixed type. The cytoplasm contained melanin pigment and downward invasion of the cells in the connective tissue and in 2 cases intra epithelial spread was seen. Pseudo-epitheliomatous down growth of rete pegs was sometimes observed.<sup>6</sup> The malignant cells often found in nests or groups arranged in an organoid fashion; however, single cells can predominate. The melanoma cells have large nuclei, often with prominent nucleoli, and show nuclear pseudo inclusions due to nuclear membrane irregularity. The abundant cytoplasm may be uniformly eosinophilic or optically clear. Occasionally, the cells become spindle or neurotize in areas. This finding is interpreted as a more aggressive feature, compared with findings of the round or polygonal cell varieties. In the oral mucosa, the prognosis is dismal for patients with any type of malignant cell.<sup>14</sup> Immunohistochemistry helps in establishing and confirming that the melanocyte as the cell of origin. Melanomas, unlike epithelial lesions, are identified by using vimentin, which is a marker of mesenchymal cells. Since melanocytes are derived from the neural crest these cells are reactive for S-100 but these are not specific. Melanosome marker, Homatropine methylbromide (HMB-45) is a monoclonal antibody which binds to immature melanosome associated epitope in melanoma. It is highly sensitive and specific. S-100 protein and HMB-45 antigen positivity are characteristic of, although not specific for, melanoma. The other melanocyte specific antigens are MART1 and tyrosinase.<sup>12</sup>

In cutaneous melanoma, the important prognostic factors are the depth and the level of invasion. However the level of invasion is difficult to judge in oral melanomas because the presence of muscle bundles and the lack of a true dermis make the assessment of the level of invasion difficult if not impossible.<sup>6</sup> Hematic and lymphatic dissemination is possible especially in the tumors with vertical growth. The profuse vascularization could influence in the elevated incidence of metastasis.<sup>15</sup> The proliferation may reach bone tissue, lung, liver and brain. Survival after 5 years mentioned in the literature is less than 20%. In the review by Rapini et al.<sup>1</sup> over 101 patients it was 13%. In the series by Lopez Graniel et al. was 6,6% and both the average from the series of Delgado Azañero et al. as that of Hicks et al. was 15% (2009). Gingival melanoma (18%) has a slightly

greater 5 year survival than that for palatal melanoma (11%) with a considerable longer median survival period. Nodal involvement reduces the median survival period.<sup>2,16</sup>

The primary mode of treatment for malignant melanoma is wide surgical excision with ample margins. Adjuvant chemotherapy and radiation is used as a supplementary mode of treatment after surgery. The prognosis has been poor for the case of malignant melanoma of the oral cavity for the following reasons.<sup>3</sup> Firstly Lesion is difficult to diagnose in early stages, secondly it is asymptomatic thirdly, prone to ulceration and infection and finally complete excision is difficult. A careful oral examination and biopsy will usually result in early diagnosis thus improving the prognosis. Clinicians must carefully examine the oral cavity and any growing pigmented lesion must be biopsied.

### Conclusion

Mucosal Melanoma is a rare tumour of the oral cavity which can metastasize rapidly. The purpose of this article is to emphasize early diagnosis. Hence, the presence of a pigmented lesion in the mucous membrane of the oral cavity should raise the suspicion of malignant melanoma and all such lesions should be histopathologically examined.

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