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Malignant Melanoma of Mandibular Gingiva: Case Report of a Rare Clinical Entity.

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ABSTRACT
Oral melanoma is a rare cancer of oral mucosa with either no early symptoms, or mere symptoms such as an area that is black or brown, with areas of gray, red, purple, or loss of pigment. Primarily Oral melanoma is a rare neoplasm of melanocytic origin, accounting for only 0.5% of all oral malignancies. The "chameleonic" presentation of a mainly asymptomatic rare condition, poor prognosis, and the necessity of a highly specialized treatment are the reasons behind our case report. Here we have presented a case of Oral Malignant Melanoma in an 83 years old male patient affecting the gingival mucosa of right lower posterior tooth region.

Keywords ;- Oral Melanoma, Melanocytic origin, Oral Malignancy, Gingival mucosa.

I. INTRODUCTION

Even though oral conditions with increased melanin pigmentation such as melanotic macules, smoker's melanosis, amalgam and graphite tattoos, racial pigmentation, and vascular blood-related pigments are common; however, melanocytic hyperplasias are rare. They are thought to arise primarily from melanocytes in the basal layer. In the oral mucosa, melanocytes are observed in a ratio of about 1 melanocyte to 10 basal cells. Melanoma cells retain some features of nevus cells, such as lack of dendritic processes, round to spindled shape, and loss of contact inhibition and show considerable pleomorphism, with large, irregular hyperchromatic nuclei, prominent nucleoli, and detectable mitotic activities[1].

Melanoma of the head and neck account for around 25% of all melanomas while Oral mucosal melanomas accountfrom 0.2% to 8% of all melanomas[2].Around 80% of oral malignant melanomas develop in the mucosa of the upper jaw and palate with rare occurrence on the lips, gums, or tongue[3].

Age of occurrence lies in between 30 and 90 years of age, with a higher incidence in the 6th decade and a mean age of 56 years[4]. Higher prevalence is noted in blacks, Japanese, and Indians of Asia due to more frequent finding of melanin pigmentation in oral mucosa of these races. Clinically these are mostly asymptomatic and detected only when there is ulceration or hemorrhage of the overlying epithelium . The delayed detection may be the cause for the poor prognosis with a 5-year survival being between 15% and 38%[5].The purpose of this article is to present a case of oral malignant melanoma involving the mandibular gingiva, as well as to emphasize the necessity for early recognition and treatment of such.

II. CASE REPORT

An 83-year-old male patient reported to the Department of Oral Pathology with chief complaint of pain and bleeding from swelling in the lower right gums. The patient noticed the black swelling 4 months back. The patient had a habit of smoking for the last 30-40 years but had no familial cancer background. The clinical examination revealed a large mass of 8 × 3 cm in dimension on lingual aspect of right mandibular alveolus involving marginal, attached, and interdental gingiva with little buccal involvement [Figure 1]. The growth was blackish gray with intact smoothsurface and well defined margins. Anteriorly, it extends from the gingiva of mesial surface of 43 (canine), to the gingiva in relation to 46(first molar) posteriorly. There was also regional tooth mobility.

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Figure 1

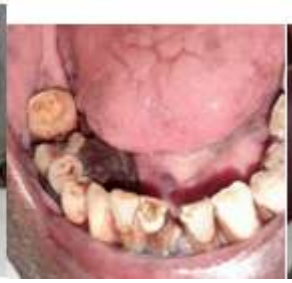
Figure 2a


Figure 2b

The palpatory findings revealed afirm consistency lesion with mild pain that bleeds on slightest provocation. A large 3cm mobile right submandibular lymph node was palpable. Complete examination of the lesion revealed no other primary site of the lesion. [Figure 2a and 2b] OPG showed radiolucency invoving the peri-apex of 43 and 46 with generalized bone destruction. [figure 3]

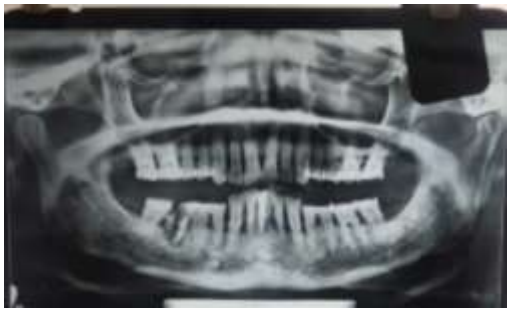
Figure 3

Correlating all clinical features, provisional diagnosis of primary malignant melanoma of oral cavity and D/D of Pyogenic granuloma was given.

An incisional biopsy of the lesion was done under local anesthesia and the specimen was sent for histopathologic examination. The hematoxylin and eosin-stained section showed mucosa covered tissue showing a melanin-producing tumor, consisting of atypical irregularly elongated spindle and oval-shaped melanocytes, exhibiting uniformly dark, enlarged and irregular nuclei [Figure 4a. 4b, 4c]. The tumor ulcerates the overlying epithelium at places.

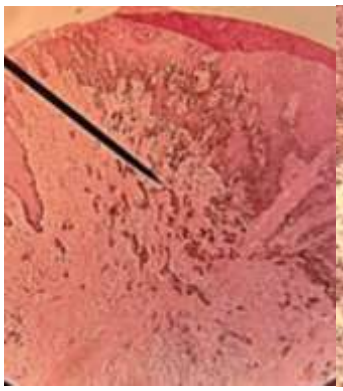
Figure 4a

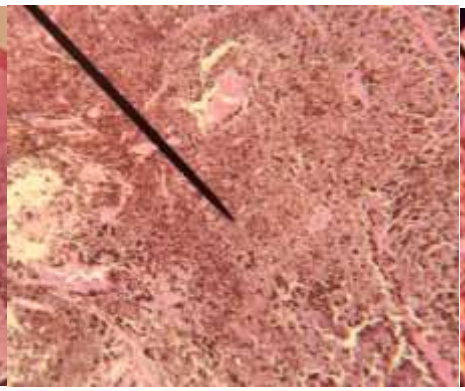
Figure 4b

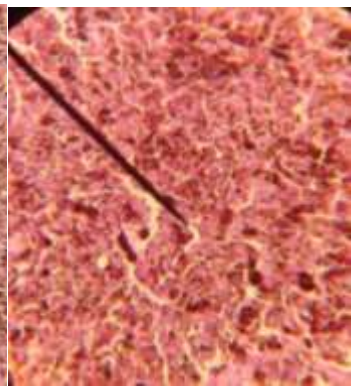
Figure 4c

The diagnosis of malignantmelanoma was made and the patient was referred to the Dept of Oral and maxillofacial surgery for required therapy.

III. DISCUSSION

Oral melanoma is a very rare rapidly progressing particularly aggressive malignancy. Compared to other melanomas, mucosal melanomas have the lowest percentage of

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5-year survival rate, probably due to delayed detection[6],[7],[8],[9] .The clinical aspect of oral melanoma is varied from being presented as a black-brown patch to macule, or nodular lesion of grey, red, purple, or areas of depigmentation[10]. Amelanotic lesions have also been reported[11]. Almost a third of patients shows lymph node metastasis at the time of diagnosis[10], as it is asymptomatic in the early stages[12]. Pain, bleeding, and ulceration are late symptoms in the disease. Primary oral melanomas have a strong preference for the maxilla, mainly in the hard palate, gingiva, or alveolar ridge[10]**.** Secondary oral melanomas (even rarer than primary tumors) commonly occur in the tongue[13].

The risk factors, etiologyand pathophysiologyare not clearly understood. Biopsy is still the gold standard for diagnosing oral melanomas[11], and radical surgical excision is the treatment of choice with radiotherapy, chemotherapy, and immunotherapyas additional treatment modalities. Though oral mucosa melanomas mainly originate de novo up to 37% are preceded by pigmented lesions lasting for months to years[10] .Denture irritation, infection, and tobacco smoking can be the risk factors, but a direct relationship has not yet been established[11].

The exact pathophysiology of mucosal melanomas is still not well understood but some pathways have been identified like mutations in c-KIT and BRAF.

Recent data indicates that c-KIT (CD117) is overexpressed in many mucosal melanoma cases and melanomas unrelated to sun exposure[14]. Drugs working on the tyrosine kinase activities, such as imatinib, seemed effective in treating mucosal melanomas expressing the c-kit protein, but treatment failure has also been reported[14]. BRAF protein mutations are reported inless than 10% of cases whereas in cutaneous melanoma, BRAF mutations are found in up to 80% of cases. Dabrafenib and vemurafenib are used for patients exhibiting BRAF mutation-positive melanoma[13].

The characteristic histopathological feature of mucosal melanomas is the presence of atypical melanocytes (hyperchromatism and nuclear pleomorphism) in the epithelium and connective tissue junction. This along with positive S-100 and HMB-45 markers, is confirmatory of mucosal melanoma[15].

Mucosal melanomas can show three principal histopathological patterns.

1. An in situ melanoma is in the epithelium[16];15% of cases of oral melanoma
2. A deeply invasive or nodular melanoma extending to the underlying connective tissue; 30% of cases
3. A combined pattern is characterized by an in situ or radially growing pattern combined with a nodular component; 55% of cases.[16]

Early diagnosis is essential for aggressive Oral Melanoma with a poor prognosis. Clinical examination supported by dermoscopy can be an approach but has technical limitations[10]. Incisional biopsy from the thickest part of a large lesion and excisional biopsy of small lesions remains the gold standard[13]. Ultrasound or CT scan of the head and neck and thoracoabdominal regions can be used to stage the tumor correctly[10].

Melanoma staging

Tumor, T[17]

No T1 or T2 in mucosal melanoma.

- T3: Tumors limited to the mucosa and immediately underlying soft tissue, regardless of thickness or greatest dimension; for example, polypoid nasal disease, pigmented or non-pigmented lesions of the oral cavity, pharynx, or larynx
- T4: Moderately advanced or very advanced
- T4a: Moderately advanced disease involving deep soft tissue, cartilage, bone, or overlying skin
- T4b: Very advanced disease involving the brain, dura, skull base, lower cranial nerves (IX, X, XI, XII), masticator space, carotid artery, prevertebral space, or mediastinal structures

Lymph Nodes, N

- NX: Regional lymph nodes not assessed
- N0: No regional lymph node metastases
- N1: Regional lymph node metastases present

Distant Metastases, M

- M0: No distant metastasis
- M1: Distant metastasis

Differential Diagnosis:-Oral Melanoma needs to be differentiated from different focal and diffuse oral pigmentations. The following are included in the differential diagnosis of an oral melanoma:[10]

Serial number	Focal Oral Pigmentations	Diffuse Oral Pigmentations	Systemic Diseases
1.	Amalgam tattoo (exogenous pigment)	Physiological/racial pigmentations	Peutz–Jeghers syndrome
2.	Melanoacanthoma	Smoker's melanosis	Laugier–Hunzikerdisease
3.	Melanotic macules	Drug-induced hyperpigmentation	Leopard syndrome
4.	Melanocytic nevi	Postinflammatory hyperpigmentation	Carney complex syndrome
5.			McCune-Albright syndrome
6.			Adrenal gland diseases

PROGNOSIS

Oral melanomas are often diagnosed at a late stage and have a very poor prognosis[18]. The five-year survival rate is 25.5% for mucosal melanomas in the head and neck[13]. Around a third present lymph node metastasis at the moment of diagnosis[10].The expression of bcl-2 is linked to a better prognosis while aberrant expression of p53 protein and loss of expression of p16 protein are associated with a poor prognosis of Oral Melanomas[19].Even after complete surgical excision, relapse rate is 20%[15].

IV. CONCLUSION

Primary mucosal melanomas are exceedingly rare but rapidly lethal and aggressive tumors. Dentists have a unique rolein prompt diagnosis of Malignant Melanoma, thereby improving the patient's prognosis. Asymptomatic irregular melanotic lesions should raise concern and be further investigated [15], especially those in sites most common to oral melanoma.Here lies the importance of our case report of a rare mucosal entity that needs to be diagnosed at an early stage because of its aggressive nature and poor prognosis.

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