

A Case of Oral Mucosal Malignant Melanoma in the Guise of Cervical Metastatic Lymphadenopathy with Apparently Unknown Primary

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ABSTRACT

Introduction

Primary malignant melanoma of the oral cavity is a rare neoplasm. The tumors tend to metastasize or locally invade tissue more readily than other malignant tumors in the oral region.

Case Report

A 55 year old male presented with left sided hard cervical lymphadenopathy with unknown primary with cytology of malignant melanoma. 18FDG-PET-C.T scan helped identification of the primary.

Discussion

The survival of patients with mucosal melanomas is less than for those with cutaneous melanomas. Tumor size and metastases are related to the prognosis of the disease. Early oral malignant melanomas can be clinically very difficult to distinguish from other benign oral pigmented lesions.

Conclusion

Any case presenting with cervical lymphadenopathy with a cytological diagnosis of Malignant Melanoma and without clinically identifiable primary, early detection using whole body 18FDG-PET CT is utmost important.

Keywords

Melanoma; Mouth Mucosa; Positron-Emission Tomography; Lymph Nodes

Malignant melanoma is a potentially aggressive tumor of melanocytic origin.¹ About 1–8% of all melanomas arise in the oral mucosa² and these account for 0.5% of all oral malignancies.³⁻⁵ The most frequently affected oral sites are the palate and the maxillary gingiva. The age of reported patients ranges from 20 to 80 years.¹⁻⁵ The neoplasm is more common in Japan and Africa than in Western countries.⁵

The etiopathogenesis of mucosal melanomas is poorly understood; however, it is well documented that the melanocytes migrate to both endodermally derived and ectodermally derived mucosa. The function of these melanocytes in the mucosa is not understood. Like their cutaneous counterparts, oral melanomas (OM) are believed to arise either from nevus, preexisting pigmented areas, Hutchinson's premalignant lentigo or denovo (30% cases).⁶

Case report

A 55 yrs old male from rural Bengal presented with left sided hard coalesced level-Ib,II, >6cm, cervical lymphadenopathy (N3) (Fig. 1). No definitive ulcerative or proliferative or endophytic growth could be detected anywhere in head and neck region by clinical/ endoscopic evaluation.

FNAC revealed metastatic malignant melanoma.

As primary was not detected by thorough clinical investigation, a whole body 18FDG-PET-C.T was done

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as the radiological investigation of choice to find the unknown primary.

PET-C.T found high FDG avid focus at left level-Ib, II L.N region and on left upper alveolus near 1st molar tooth (Fig. 2) Rest of the body was within normal limit .

Now retrospectively A small blackish <2cm patch noted over left upper gingiva adjacent to 1st molar tooth, without extension to hard palate or buccal mucosa(T1) (Fig. 3).

Final stage: c T1N3Mo(stage-II).

He underwent wide local excision of primary tumour with adjacent part of upper alveolar process and hard palate along with left sided type-1 MRND. Post op period was uneventful.



Fig. 1 Left sided hard coalesced level-Ib, II, >6cm, cervical lymphadenopathy (N3)

Final histopathology revealed clusters of spindle shaped cells with eosinophilic cytoplasm and large nuclei with prominent nucleoli. Immunohistochemically the cells are staining positive for S-100 and HMB-45. Surgical margins were free from tumour (>1.5cm). Neck dissection specimen showed lymph nodal metastasis.

He received adjuvant EBRT (66Gy; 2GY per# 6days a week for 6weeks). A post treatment whole body PET CT scan was done after three months, that

revealed no suspicious FDG avid area in oral cavity, neck or elsewhere. The patient is on monthly follow up during the last six months and is doing well without any obvious clinical feature suspicious of loco regional or cervical recurrence.

Discussion

The initial symptom and sign of oral mucosal melanoma is often a pigmented growth or swelling. The surface may be smooth, with an intact or ulcerated overlying mucosa. Satellite foci may surround the primary tumor. The color may be uniformly brown or black or may show variation of color, with black, brown, grey, purple, and red shades, or depigmentations.⁷ In amelanotic melanomas, pigmentation is absent.⁸ Oral malignant melanoma has an initial phase characterized by radial growth followed by a phase of invasion of the underlying tissues (the so-called “vertical growth phase”).

Other presenting signs and symptoms include bleeding, ill-fitting dentures, pain, increased mobility of teeth, and delayed healing of extraction sockets. The OM is more aggressive and the abundant blood supply of the oral cavity may permit blood vessel invasion and haematogenous dissemination early in the course of the disease.² Regional lymphadenopathy may be present and connotes a poor prognosis.⁹ Clinically, oral melanomas are classified into five types: pigmented nodular, nonpigmented nodular, pigmented macular, pigmented mixe and nonpigmented mixed.¹⁰

Early oral malignant melanomas can be clinically very difficult to distinguish from other benign oral pigmented lesions like oral pigmentations in Addison’s disease, blue naevi, ephelides (freckles), oral pigmentation of Kaposi Sarcoma, oral naevi , amalgam tattoo, graphite tattoo, oral melanotic macule, pigmentation of Peutz-Jeghers syndrome, physiologic pigmentation

When an oral pigmentation cannot be confidently diagnosed as benign on clinical grounds, a biopsy is mandatory. An excisional biopsy with a 1 to 2mm margin for small lesions or an incisional biopsy through the thickest or the most suspicious part of the tumor in case of a large lesion is required.¹¹ Fine needle aspiration

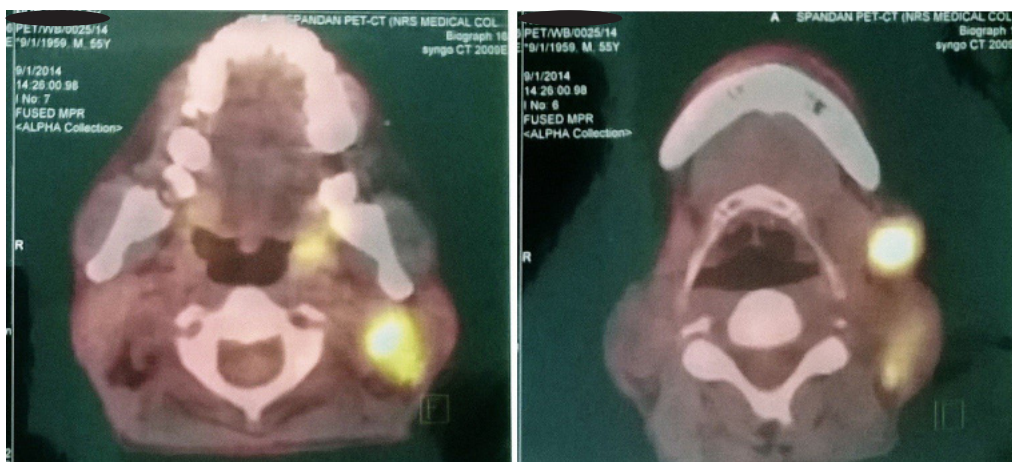


Fig. 2 FDG avid focus at left level-Ib, II LN region and on left upper alveolus near 1st molar tooth

or exfoliative cytology of primary pigmented lesions is contraindicated. It has been suggested that cutting into a malignant neoplasm during an incisional biopsy or other invasive procedure could result in accidental dissemination of malignant cells within the adjacent tissues (seeding) or even in the blood or lymphatic stream, with the subsequent risk of local recurrence, or regional or distant metastasis.¹ The most common sites of metastasis are lung, bone, brain, and liver, with widespread involvement occurring in advanced disease.²

Malignant cells of oral malignant melanoma show a

wide range of shapes, including spindle, plasmocytoid, clear cell, and epithelioid ones. These malignant cells possess considerable pleomorphism with large, irregular hyperchromatic nuclei, and prominent nucleoli, and have readily detectable mitotic activity. oral malignant melanoma can be histologically subclassified 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 the connective tissue; (3) melanomas with a combined pattern of invasive melanoma with in situ

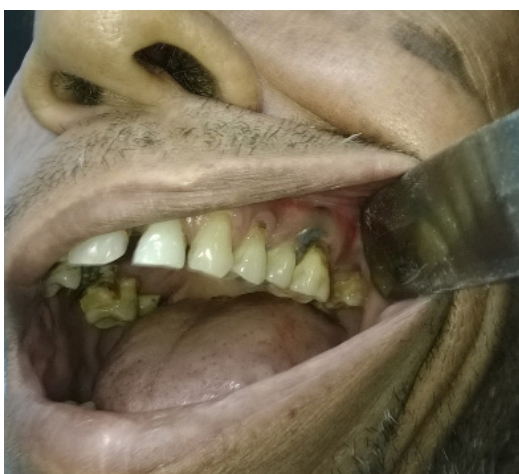


Fig. 3 A small blackish <2cm patch noted over left upper gingiva adjacent to 1st molar tooth, without extension to hard palate or buccal mucosa (T1)

component.⁷

A simple TNM clinical staging, recognizing three stages, has been shown to be of prognostic value. A recent histopathological microstaging for Stage I subclassifies it into three levels^{1,12,13}: Stage I: Primary tumour present only (Tany N0M0). Level I: pure in situ melanoma without evidence of invasion or in situ melanoma with "microinvasion," Level II: invasion up to the lamina propria, Level III: deep skeletal tissue invasion into skeletal muscle, bone, or cartilage. Stage II: Tumour metastatic to regional lymph nodes (Tany N1M0). Stage III: Tumour metastatic to distant sites (Tany Nany M1).

Treatment of oral malignant melanoma is still controversial. Excision of the primary lesion, preferably using an intraoral approach and involving at least 1.5 cm of healthy tissue, is recommended.¹⁴ Patients with primary oral malignant melanoma present lymph node metastasis in 25% of cases.¹³ Neck dissection should be reserved for cases with preoperatively confirmed lymph node metastases and the choice of the neck dissection modality should be guided by the extent and the level of the nodes.⁸

Surgery could be combined with radiotherapy, chemotherapy, or immunotherapy even though the effectiveness of such therapies is mostly unknown. Postoperative radiotherapy is generally recommended if poor prognostic pathologic features are present, such as multiple positive nodes, or extranodal spread of metastatic melanoma, even though oral malignant melanomas are regarded as poorly radiosensitive. Other irradiation modalities such as intraoral mould (⁶⁰Co, ¹⁹²Ir, or ¹⁹⁸Au), intraoral electron beam or interstitial brachytherapy have also been used.¹⁵

Dacarbazine, platinum analogues, nitrosoureas, microtubular toxins, dimethyl triazeno imidazole carboxamide (DTIC), nimustine hydrochloride, or vincristine have been used as adjuvant therapy or postoperative chemotherapy. IFN-2b, IL-2, BCG, anti-Fas antibody, IL2, and cytokines have shown varied results.¹

The prognosis of oral malignant melanoma is poor. A tumor thickness greater than 5 mm, presence of vascular invasion, necrosis, polymorphous tumor cell

morphology and the inability to properly resect the lesions with negative margins have been associated with poor survival in patients with primary oral malignant melanoma.¹ Gingival melanoma has a better 5-year survival rate than palatal melanoma.³ Recurrences may occur even 10–15 years after primary therapy. Distant metastases to the lungs, brain, liver, and bones are frequently observed.¹⁶

Conclusion

Primary oral mucosal melanomas are exceedingly rare and biologically aggressive malignancies. Oral malignant melanomas clinically mimic many other pigmented lesions of the oral cavity.

Any case presenting with cervical lymphadenopathy with a cytological diagnosis of Malignant Melanoma without any clinically obvious pathology in head and neck region suspicious of the primary lesion, an urgent PET CT scan should always be indicated to seek for the primary because early oral malignant melanomas can be clinically very difficult to distinguish from other benign oral pigmented lesions.

Early detection can be life saving by quick initiation of treatment as survival of patients with mucosal melanomas is less than their cutaneous counterpart.

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