Intra-oral amelanotic malignant melanoma: Report of a case and review of literature

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Abstract
Primary malignant melanoma of the head and neck is a rare tumor, accounting for less than 1% of all melanomas. Rarely, melanoma may present itself without clinically evident pigmentation. Termed amelanotic melanoma, these lesions tend to have a worse prognosis because of delayed recognition and subsequent treatment. The use of radiotherapy alone has resulted in complete or partial responses, even though in the past malignant mucosal melanoma had been considered radio-resistant. Radiotherapy may be appropriate for patients with unresectable local disease, elderly patients who are poor surgical candidates or patients who refuse surgery. Here, we report a rare case of amelanotic malignant melanoma with regional metastasis, treated by radiotherapy which had a good treatment outcome.

Key words: Amelanotic, Malignant melanoma, Radiotherapy, Regional metastasis

Introduction
Primary malignant melanoma has been described in virtually all sites and organ systems into which neural crest cells migrate. Over 90% of melanomas occur on the skin.1 Primary malignant melanoma of the head and neck is a rare tumor, accounting for less than 1% of all melanomas. Half of such melanomas occur in the oral cavity, followed by the nasal cavity (44%) and sinuses (8%). In the oral cavity, the most frequent sites of occurrence are the hard palate and the maxillary gingiva. Oral malignant melanoma still represents a diagnostic challenge2.

Mucosal melanoma is derived from melanocytes present in the mucosa that had migrated as neuroectodermal derivatives in ectodermally derived mucosa. Due to its neuroectodermal origin it is now classified as a depressed neuroendocrine cell system (DNES). The same reason has been given to explain its low incidence in epithelia of endodermal origin (e.g. in larynx, nasopharynx and oesophagus)2.

Melanoma is a major health problem. When discovered early and fully excised, melanoma is highly curable. However, once metastatic disease develops, treatment options are limited and survival is generally measured in months. Patients with stage III melanoma (involvement of regional lymph nodes) have a 5-year survival of approximately 50%3.

Rarely, melanoma may present itself without clinically evident pigmentation. Termed amelanotic melanoma, these lesions tend to have a worse prognosis because of delayed recognition and subsequent treatment4.

Here we report a case of malignant melanoma of amelanotic variant.

Case report
A 54 year male patient referred to the Department of Oncology, Kasturba Medical College, Mangalore for opinion from a general dental practitioner. The patient presented with an ulcer in the maxillary right alveolar ridge in the posterior segment since 1½ years and swelling on the right side of the neck for the past 1 year. Biopsy of the neck lymph node was done at some other center 8 months back and was reported as tuberculosis.
The patient was treated with Anti-Tuberculosis Treatment for 6 months. The swelling did not subside. Pain on the neck region and fever was then noted for which he was hospitalized for 8 days at a primary health care center and antibiotics was given. Patient also had loose and painful tooth, which was extracted after the fever subsided. The socket did not heal following extraction rather the soft tissue of the alveolar ridge started to increase in size for which the patient was referred for opinion to our department.

On general examination, the patient’s built and nourishment were normal for his age. The vital signs were within normal limits. TMJ movements were bilaterally smooth, well co-ordinated and symmetrical. On examination lymph nodes, the right submandibular and superficial cervical groups of lymph nodes were palpable. The submandibular lymph node was approx 2 X 2cms, roughly oval, tender and fixed to the underlying structures. The superficial cervical group of lymph node was approximately 4cms X 2.5cms, elliptical, tender and fixed to the underlying structure. Overlying skin was normal.

On intraoral examination, there was a macular lesion on the right side of the hard palate which was roughly oval in shape of approximately 1.5cms². On palpation, it was non tender, had a smooth surface. On the right maxillary alveolar ridge, there was a nodular proliferative mass with ulceration of approximately 2cms X 1.5cms in size. On palpation of the area, it was tender and firm in consistency and bleeding was noted at some areas. No hyperpigmentation was noted in the area. No other lesions were observed in the oral cavity. Occlusal radiograph showed ill-defined radiolucency on the right side of the hard palate suggestive of erosion of the floor of maxillary sinus. Based on all these features, differential diagnosis of squamous cell carcinoma, lymphoma and malignant melanoma, were given.

Routine blood investigation, were within normal limits. CT scan revealed erosion of the floor of maxillary sinus, mass lesion in the right hard palate, compressing right jugular vein and indurating posterior aspect of right submandibular gland and level IIa necrotic lymph node seen lateral to right submandibular gland.

Incisional biopsy revealed sheets of spindle to polygonal cells with vesicular nuclei and prominent eosinophilic nucleoli. The stroma between cells was scanty with blood vessels. The overlying mucosa showed parakeratosis and hyperplasia suggestive of spindle cell variant of squamous cell carcinoma with a differential diagnosis of amelanotic melanoma. On immuno-histochemistry, it was negative on Cytokeratin AE1/AE3 but strongly positive in cytoplasm of all tumour cells on Homeatropine Methyl-bromide (HMB)-45. Based on all these features a final diagnosis of amelanotic variant of malignant melanoma was given.

Since right jugular vein was compressed and induration on the posterior aspect of right submandibular gland was noted, radiotherapy was planned before surgery to reduce the size of the lymph nodes. External Beam therapy of total of 60 Gy in 30 fractions (200cGy per fraction) for a period of 6 weeks (5 days a week) was given. A field size of 18 X13 cms was selected with 13cms separation and a depth of 6.5cms for (0.84 X 2) secs by parallel opposite technique.

Patient developed radiation induced mucositis after 2 weeks and dermatitis after 4 weeks of therapy which subsequently subsided with the palliative treatment after a period of 4 weeks of radiation therapy. The size of the lymph nodes had significantly reduced after the therapy. Follow-up of the patient was done every 2 weeks for a period of 6 months and the lesions had regressed with no recurrence.
Malignant melanoma was first described by Weber in 1859. It was recognized as a distinct clinical entity and named as “melanotic sarcoma” by Lucke in 1869. Despite being first reported over 150 years ago, mucosal melanoma of the head and neck remains a mystery.

Unfortunately, research related to oral melanoma is limited, because of its rare occurrence and there is a lack of large series of cases with long follow-up. No long term research has been conducted which limits the information primarily to case reports.

Mucosal melanomas are rare, comprising less than 1% of all melanomas. Due to its rarity, the origin of oral melanomas and the risk factors are largely unknown.

It is possible that physical or chemical stimulation due to smoking may play a role in the physiologic oral pigmentation. In addition, in an experimental study assessing the influence of cigarettes, it has been seen that chemical and physical stimulation causes hyperproduction of melanocytes in the oral epithelium leading to oral pigmented lesion. Tobacco smoke may play role in the development of melanoma in the palate, which is the commonest site of the lesion. Other possible etiologic factors are formaldehyde exposure, presence or absence of dysplastic nevi, tobacco use etc. Age ranges from 35-80 years with a male preponderance.

The incidence of oral malignant melanoma demonstrates racial differences. A high incidence of mucosal melanoma is observed in Asian population while low among Caucasians.

Clinical presentation varies widely. One third of the patients are asymptomatic at the time of diagnosis. The lesions may be incidentally observed by the patient or the physician.

The palatal mucosa is the most commonly affected area in the oral cavity, followed by maxillary gingiva (77% from these sites).
Oral melanoma can be dark brown, bluish black or black. Rarely it may present itself without clinically evident pigmentation (5%)\(^2\). The specific cause for the lack of melanotic pigmentation of these lesions is unclear. Speece et al. proposed that there is a deficiency of tyrosine and an enzyme required for melanin production. Others believe that this enzyme system is intact and can produce melanin but the quantity is insufficient to be seen with histologic methods\(^7,10,11\). The latter explanation seems convincing because electron microscopy does reveal the presence of melanosomes in all amelanotic melanomas reported till date\(^4\). Amelanotic variant have a worse prognosis because of delayed recognition and subsequent treatment.

Main contribution of this case report is an alarm to the oral physician and the medical personnel who may not be able to diagnose these lesions because of their asymptomatic behaviour. The oral cavity being the most accessible area for examination, all the medical personnel should examine the oral cavity without fail and should be able to elicit the changes within it. Since the amelanotic variant may present diagnostic dilemma, proper investigations have to be performed to come to a definitive diagnosis and to plan the treatment thereafter.

References