Oral Mucosal Amelanotic Melanoma: A Rare Case Report

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Oral cancer is a major global health problem. It is ranked as the third most common cancer in India. More than 95% of oral cavity carcinomas are of squamous cell type. Melanoma is a major health problem and originates from the malignant transformation of melanocytes. Primary mucosal melanomas of the head and neck occur less frequently than their cutaneous counterparts. Among those, oral mucosal melanoma is extremely infrequent with an incidence of 0.5% of oral neoplasms. Less than 2% of all melanomas lack pigmentation, in the oral mucosa, however, up to 75% of cases are amelanotic melanomas. These are extremely rare variants and the most frequent sites in the oral cavity are the hard palate and the gingiva. Lesions that are suspected to be melanomas should be assessed both histologically and by immunohistochemistry, which are helpful in the diagnosis of amelanotic melanoma. They have a poorer prognosis than the pigmented melanomas because of the delay in diagnosis and in the initiation of treatment. This presentation is a rare case report of oral mucosal amelanotic melanoma.

Keywords: Amelanotic melanoma, Malignant melanoma, Oral mucosal melanoma

INTRODUCTION

Head and neck cancer is a collective term defined by topographical and anatomical bases to describe malignant tumors of the upper aerodigestive tract. It is a disease with high incidence and mortality occurring mainly in the oral cavity (lips, hard palate, tongue, gums, and floor of mouth), pharynx (naso-, oro- and hypopharynx) and larynx. It is considered to be the fifth most common cancer site worldwide, and is associated with low survival and high mortality rates, when diagnosed in advanced stages. Most cancers of the oral cavity are oral squamous cell carcinomas, and tobacco, alcohol, and betel use are the main risk factors for these and many potentially malignant disorders. The main high-risk groups are older adult males who use tobacco and alcohol. Primary malignant melanoma virtually occurs in all sites and organ systems into which neural crest cells migrate. Over 90% of melanomas occur on the skin. Primary malignant melanoma of the head and neck is a rare tumor, accounting for <1% of all melanomas. About 50% of such melanomas are seen in the oral cavity, followed by the nasal cavity (44%) and sinuses (8%). It is easy to arrive at a clinical diagnosis of pigmented melanomas based on red to black or brown color. Presentation of melanoma’s which without any clinical evidence of pigmentation is termed as amelanotic melanoma. It accounts for 5-35% of all the oral melanomas. Its prognosis is poorer when compared with pigmented melanomas due to delay in establishing the correct diagnosis and histological misdiagnosis, followed by delay in the initiation of the treatment.

CASE REPORT

A 68-year-old female patient reported to us with the chief complaint of bleeding gums and swelling of the upper right back tooth region since 6 months. Patient was apparently normal 6 months ago when she noticed bleeding gums and swelling in her upper right back tooth region on brushing, which gradually increased to the present size. Head and neck examination revealed melanosis on the bridge of the nose, right and left malar region. Right and left sub-mandibular lymph nodes were palpable, one each side, about 0.5 cm in diameter, freely mobile, firm in consistency and non-tender.

On clinical examination, a pink pedunculated growth was noticed involving right buccal maxillary gingiva and extending onto the palate with respect to 16, 17 and 18 region. The growth measured about 3 cm × 2 cm in dimension extending anteriorly from the distal aspect of 15 to 2 cm posterior to the distal aspect of 17. Medially, it extends 1 cm from the mid palatine raphe; laterally involving alveolar ridge of 16 and buccal marginal gingiva of 17 (Figure 1). Overlying mucosa appeared nodular with focal areas of bluish gray pigmentations on the proximal and palatal aspects of 17 and along palatine raphe (Figure 2).

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On palpation, growth was soft in consistency along the pigmented areas and firm along the palatal aspect. There was bleeding on probing and growth was non-tender. Grade I mobility of 17 and sharp distolingual cusp of 46 were noticed. Based on the clinical presentation, we arrived at a provisional diagnosis of pyogenic granuloma and a differential diagnosis of peripheral ossifying fibroma, peripheral giant cell granuloma, malignant melanoma were given. Patient was subjected to further investigations that included routine hematological investigations which were within the normal range except hemoglobin percentage of 10.8 g%, suggestive of anemia.

Intra-oral periapical radiograph in relation to 16, 17 and orthopantomogram showed edentulous space and erosion of the bone in relation to 16 region. Bony trabeculae show enlarged marrow spaces. Floor of maxillary sinus appears thinned and breach in continuity observed in relation to 16 (Figure 3a and b). Paranasal sinus view revealed increased radio-opacity in the floor of the right maxillary sinus (Figure 4).

Computed tomography (CT) revealed the presence of small soft tissue in right upper first molar region with minimal enhancement. Mild erosion of underlying alveolar process was observed. Soft tissue measured about 1.2 cm and was localized. Mild mucosal thickening was seen in the right maxillary sinus. Floor was minimally thinned, but intact (Figure 5a and b).
Positron emission tomography CT reveals an enhancing soft tissue lesion of 1.9 cm × 1.8 cm × 0.8 cm in the hard palate, extending along the right palate arch with focal erosion of the inner cortex of the alveolar process of adjacent right maxillary arch and right hard palate. Sub centimeter metabolically active right Level II cervical lymph node-metastatic. A peripheral pleural based nodule of 4 mm along the right posterolateral costal pleura of right upper lobe and another irregular 6 mm nodule along the medial portion of the right oblique fissure (Figure 6).

An incisional biopsy of the growth was carried out under local anesthesia (Figure 7). Biopsy specimen was subjected to histopathological examination of H and E stained tissue sections revealed biphasic lesional cells composed of spindle to epithelioid shaped cells, few dendritic cells with scanty connective tissue stroma (Figure 8). Subsequently, the tissue was subjected to a series of immunohistochemical markers. S-100, HMB 45 and MELAN A which showed intense positivity for lesional cells.

Ki 67-intensely positive, suggesting highly proliferative lesion and negative for CK and CD 34.

After correlating the clinical presentation, histopathological features, immunohistochemical findings of the lesion and radiographic findings established final diagnosis of amelanotic melanoma of the hard palate and gingiva in relation to 16, 17, 18 region.

Patient was referred to a regional oncology center for further treatment where she underwent hemimaxillectomy and chemotherapy. The patient is doing well post-operatively and awaits prosthetic rehabilitation.

**DISCUSSION**

Primary malignant mucosal melanoma of the head and neck is a rare entity. Mucosal melanoma was first described by Weber, in Germany in 1856. Despite being first reported over 150 years ago, mucosal melanoma of the head and neck remains an enigma. Research related information about oral melanomas remains limited with only information confined to case reports. This may probably be due to its rare occurrence and lack of long-term follow-up. In oral mucosa, melanocytes are located along the tips and peripheries of the rete pegs. No etiologic factors have been identified to date for oral melanomas, but factors such as family history, syndromes, cytogenetic defects, growth factors, pre-existing lesions, mechanical trauma, denture use, infection, oral habits, self-medication, eating disorders, smoking habits...
and exposure to formaldehyde and other carcinogenic substances have increased risk in the development of oral melanomas. It is most commonly seen in the age range of 35-80 years with a male prevalence. The incidence of oral melanoma shows racial differences. In Asian population incidence of oral malignant melanoma is high and it is low in Caucasians. The lesion is much more common in the upper jaw than the lower jaw. In the upper jaw palate is the most common location followed by maxillary gingiva. The mandible is only involved in 20% of cases. Other sites include the buccal mucosa, mandibular gingiva, lip, tongue and floor of mouth. Clinical presentation of oral melanomas varies widely with one third of the patients being asymptomatic at the time of diagnosis but may become ulcerated and painful in advanced lesions. Based on the clinical presentation the tumors are classified into five types: I - pigmented nodular, II - non-pigmented nodular, III - pigmented macular, IV - pigmented mixed, and V - non-pigmented mixed Type I and II. Clark et al. (1975) documented two phases in the growth of primary melanoma: A radial growth phase, where the neoplastic process is confined within the epithelium, and a vertical growth phase, in which the neoplastic cells migrate into the underlying dermis. Metastasis will occur if the melanomas enter into the vertical growth phase. Oral malignant melanomas can be dark brown, bluish or black in color, but amelanotic melanomas lack pigmentation both clinically and histopathologically. Less than 2% of all melanomas lack pigmentation making it difficult to diagnose. The specific cause for the lack of melanin pigmentation in these lesions is unknown. Speece et al., proposed that there is a deficiency in tyrosine an enzyme required for melanin production. Histopathologically, oral malignant melanoma shows undifferentiated and high cellular activity. On pathologic grounds, an amelanotic lesion should be distinguished from poorly differentiated carcinoma, small cell carcinoma, lymphoma, sarcomas, and metastasis from a primary skin melanoma. Therefore, immunostaining for S-100 protein, HMB-45 and Mart-1 should be used to establish correct diagnosis. The most common sites of metastasis are lymphnodes, liver and lung. The recommended treatment for oral malignant melanoma is surgery in combination with chemotherapy and to a lesser extent immunotherapy or irradiation therapy. Amelanotic melanomas have a particularly disastrous prognosis. The survival rate of oral amelanotic melanoma is very poor because of delay in diagnosis, due to lack of pigmentation, biologic aggressiveness, rapid growth, a high incidence of local recurrence, high vascularization of maxillofacial region, the age of the patient, and lastly by lack of defined treatment guidelines.

CONCLUSION

Since the oral cavity is the most accessible area, examination should be done thoroughly to elicit the changes within it. As amelanotic variant may present a diagnostic dilemma, proper investigations have to be performed to come to a definitive diagnosis and to plan the treatment. Early diagnoses by histological examination together with immunochemistry are the keys to improving the survival for patients with oral amelanotic melanoma.

REFERENCES


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