Primary oral malignant melanoma - a case report

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Abstract

Melanoma arising from mucosal surfaces of the head and neck is a very rare neoplasm and it is considered among the most deadly of all human neoplasms. Although skin melanomas comprise 1.3% of all cancers, oral malignant melanoma accounts for only 0.2 to 8% of all reported melanomas, common sites of occurrence being palate and maxillary gingiva. Due to its presence at relatively obscure areas in the oral cavity, most oral malignant melanomas are diagnosed at a late stage and are associated with poor prognosis. Early diagnosis is essential for successful treatment and perhaps the key factor in improving the prognosis of oral malignant melanoma. This paper reports a case of a 42year old woman with primary malignant melanoma at a rare site, the left retromolar region involving the left side of the mandible, up to level IV ipsilateral cervical lymph nodes. The patient was treated with left hemimandibulectomy with radical neck dissection and was followed up for two years and 3months without any local recurrence or distant metastasis. It is suggested that any pigmented lesion that are suspected of undergoing changes in their clinical appearance should be biopsied.

Keywords: Malignant melanoma, palate, maxilla, gingiva, oral cavity.

Introduction

Malignant melanoma is a neoplasm of melanocytic origin that arises from a benign melanocytic lesion or de novo from melanocytes with otherwise normal mucosa or skin[1]. The etiology of skin melanoma is associated with sun exposure and it comprises 1.3% of all cancers[2]. Malignant melanoma of oral cavity accounts for only 0.2% to 8% of all reported melanomas and 0.5% of all oral malignancies[3,4]. Oral malignant melanoma has been reported as having higher incidence in Japan, India and Africa than in western countries[5]. A striking male prediction is noted in mucosal melanomas, with men being affected 3.5 times more frequently than women[6]. It can occur at any age, with an average of 56 years[4]and is extremely rare in people below 30years[2]. The most frequently affected oral sites are the palate and maxillary gingiva[2]. Intra oral malignant melanomas are easy to diagnose clinically as they are pigmented and have irregular shape and outline.

The oral mucosal melanomas are classified by histologic pattern as in situ, invasive and combined in situ and invasive[7]. Most oral melanoma lesions (85%) are invasive or have both an invasive and in situ pattern[7]. Criteria for diagnosis of primary oral melanomas include demonstration of melanoma in oral mucosa, presence of junctional activity and inability to demonstrate extraoral primary melanoma[8].

The treatment of oral malignant melanoma is by multidisciplinary approach including surgery, radiotherapy and immunotherapy[3]. The prognosis remains poor with 5 year survival rate reportedly varying from 0% to 55%[9].

This paper, reports a case of a 42year old woman with primary malignant melanoma in the left retromolar region involving the left side of the mandible and up to level IV ipsilateral cervical lymphnodes and briefly reviews the relevant literature about the lison.

Case report

A 42 year old woman reported to the Department of Oral Medicine & Radiology, Institute of Dental Sciences, Bareilly, Uttar Pradesh India, with the complaint of painless

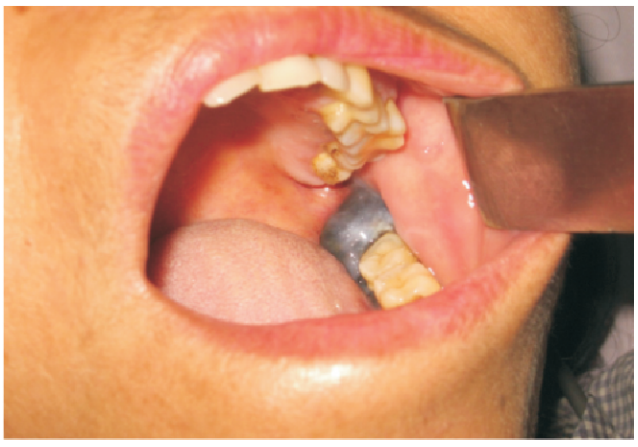

Figure.1. Intra oral photograph showing malignant melanoma in the left retromolar region

swelling in the left posterior region of the mandible and difficulty in opening the mouth that had begun two months earlier. The patient had no history of any systemic illness or trauma to neck and face region. The patient did not have any tobacco (chewing or smoking) or drinking (alcohol) habits.

Intra oral clinical examination revealed a non-tender mass on the left retromolar region about 2x2 centimeters diameter in size. The mass was sessile with smooth surface and well defined margins. The color of the overlying mucosa of the mass was dark bluish-black in colour **(Figure1).** The left submandibular lymph node was palpable, approximately 2x1 centimeters in diameter, non-tender and fixed to the inferior border of the mandible. There was no other pigmented area in the oral mucosa or any suspicious cutaneous lesions on any of the part of the body.

Orthopantomograph was taken to evaluate possible bone destruction, but no abnormality was detected **(Figure 2).** Whole body scanning included computerized tomograms of head, neck & brain, radiographs of chest and long bones, abdominal ultrasonography revealed no definite distant metastasis. Haematological and urine examinations did not reveal any significant findings. Complete excision of the lesion along with 2 centimeter of underlying bone was resected (Marginal resection) and submitted for histopathological examination.

Hematoxylin and eosin stained sections of the lesion showed islands and nests of atypical melanocytes within the connective tissue with chronic inflammatory cell infiltrates **(Figure 3A)**. The melanocytes were round to oval in shape with hyperchromatic nuclei, eosinophilic cytoplasm and melanin pigmentation. Areas of mitotic figures were frequent **(Figure-3A).** The atypical melanocytes were seen invading into stratified squamous epithelium and were also irregularly distributed in junctional area **(Figure3B).** Immunohistochemistry was used to establish the final diagnosis. The tumor cells were strongly expressed S-100 protein and HMB-45 monoclonal antibody **(Figure 4A&B)** suggesting malignant melanoma.

Based on physical, radiological and histopathological examination (presence of tumour nests in overlying squamous epithelium), a final diagnosis of primary oral malignant melanoma (Combined in-situ and invasive type) was made.

All the margins of the primary lesion and resected bony margins were positive for tumor invasion suggesting aggressive nature of the lesion.

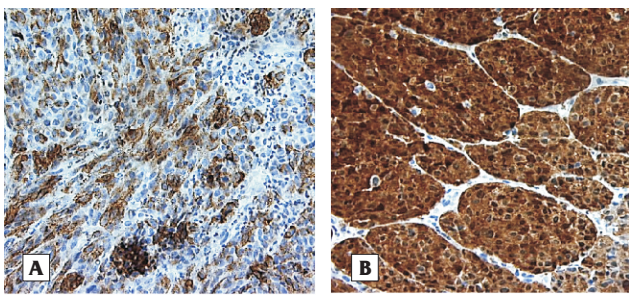

Figure 4. Photomicrograph showing S-100 (A) protein and HMB-45 (B) positivity expressed by tumour cells (20X)

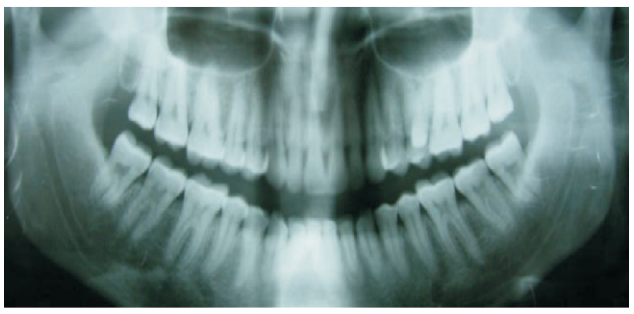

Figure.2. Orthopantamograph showing no abnormality

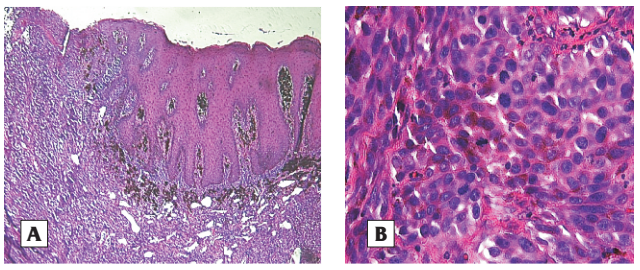

Figure.3. H & E stained photomicrograph showing, (A) Sheets of atypical melanocytes within connective tissue and mitotic figures(arrow) (40X), (B) atypical melanocytes invading into oral epithelium and also irregularly scattered in the junctional area (10X).

Treatment and follow up

An aggressive treatment was planned as all margins of the primary lesion and bony margins were positive for tumor invasion. The patient was treated with wider excision of the lesion margins, partial hemimandibulectomy of the left side along with radical neck dissection. Histopathological examination of the resected specimen revealed, all the tumor margins and the left parotid and submandibular glands free of tumour invasion and cervical lymph nodes up to level IV positive for tumour invasion. The postoperative recovery of the patient was uneventful. The patient was followed up for 2 years and 3 months without any recurrence or distant metastasis.

Discussion

Primary oral malignant melanoma is a rare neoplasm, developing from melanocytes found in the basal layer of the oral mucosa[10]and represents 0.2-8% of all melanomas and 0.5% of all oral malignancies[3,4]. In a study by Moore and Martin [11] of 1546 melanomas, 26 were found arising in the upper respiratory tract and oral cavity; of these only 12 were primary oral melanomas. The race most commonly affected by oral melanomas are black Africans, Japanese, Asians and Hispanics[9]. Takagi reported that oral melanomas comprise 7.5% of all malignant melanomas in Japan[5]. A striking male predilection is noted in mucosal melanoma, with men being affected 3.5 times more frequently than women[6]. It can occur at any age, with an average of 56years[4]and is extremely rare in people below 30years[2]. It occurs most frequently in the maxilla, with the palate as a common site (32%) followed by maxillary

gingiva (16%)[4]. In the patient in this report, the lesion was in the left retromolar region which is a rare location.

The aetiology of oral malignant melanoma is unknown, in contrast to cutaneous melanoma, which is linked to sun exposure[12, 13]. Nevi are considered a potential source of some oral melanomas, but the sequence of events is poorly understood. Currently, most melanomas are thought to arise de novo[8,12]. The role of inhaled and ingested carcinogens from tobacco use and chronic irritation from ill fitting dentures has been suggested in their pathogenesis, similar to squamous cell carcinoma. It is possible that physical and/or chemical stimulation play a role in physiologic oral pigmentation.

Pigmentation is usually the initial symptom of most oral melanomas otherwise they are asymptomatic. Oral melanomas may be uniformly brown or black or show variation in colour with black, brown, gray, purple and red shades or even depigmentation[9]. Focal pigmentation preceding development of actual neoplasm frequently occurs several months to years before clinical symptoms appear[12,14,15]. In the late course of the disease, pain, ulceration and bleeding may be present. The oral melanoma shows uniform epithelial thickening instead of rolled borders because the atypical melanocytes exhibit pegatoid mode of spread[8,14]. The relative inaccessibility of the mucosa to self examination often delays diagnosis, leading to late detection and poor survival. At presentation, approximately 13% to 19% of patients have lymph node metastasis and another 16% to 20% are likely to develop metastasis subsequently. The aggressive biologic behavior of oral malignant melanoma is particularly problematic[8,15,16] .The ABCDE checklist (Asymmetry, border irregularities, colour variations, diameter greater than 6mm and elevation, a raised surface), which is used in the identification process of cutaneous melanomas could also be of some help in diagnosis of oral melanomas[12].

Jaw bone involvement by primary and secondary melanoma radiographically are very rare[16]. However, when they do involve the bone, they are indistinguishable from osteomyelitis. While others have an appearance found with any other lytic malignant tumour[17]. The clinical differential diagnosis of pigmented lesions of oral mucosa include tattoo (Amalgam, Graphite), Oral melonptic macule, Nevi, Melanoacanthoma[8].

In the histopathologic distinction, Billings et al[18]found all metastatic lesions lacked evidence of junctional activity in the overlying mucosa and showed no epidermal migration. This is in contrast to primary lesions, in which 44% and 38% had juntional activity and epidermal migration respectively. A relatively common feature seen in the primary lesions (25%) is the presence of extensions of the melanotic pigment into the minor salivary glands[18]. However, these findings may be inconsistent and the diagnosis of a primary oral mucosal melanoma requires the careful search for and exclusion of any suggested cutaneous or mucosal lesions[19]. In the patient in this report, there was no history of melanoma-like lesion excision or cutaneous lesions suggestive of malignant melanoma over her body, extremities, head and neck. There was no evidence of secondary or distant metastatic lesion radiographically and the histological findings revealed scattered tumour nests present in the overlying squamous epithelium. Hence, both physical and histopathological features suggested that the tumor was primary oral malignant melanoma. The immunohistological profile of oral malignant melanoma is similar to that of cutaneous melanoma, with the exception that no oral malignant melanoma is positive for cytokeratins[20]. HMB-45 shows greater specificity for melanoma than S-100 protein[21]. The immunoperoxidase stains of our patient showed strongly positive finding in S-100 protein and HMB-45 stains.

The treatment policy for oral malignant melanoma is unclear and many authors think it is left to the discretion of the surgeon[22]. Traditionally, wide surgical excision with adequate negative margins with or without neck dissection is the treatment of choice for oral malignant melanoma. The radiotherapy and chemotherapy are used as adjunctive treatment methods. In case of localized disease, it can be controlled by radiotherapy. But local failure is common and may indicate risk of metastasis[23]. In this patient, the excised margins of the lesion, mandible were positive for tumour invasion suggesting wider involvement of the bone and possible regional lymph node metastasis (Left submandibular lymph nodes were palpable and fixed). This aggressive behaviour of the lesion prompted surgeons to go for left hemimandibulectomy with radical neck dissection. All the level IV cervical lymph nodes were positive for tumour invasion on histopathological examination of excised specimen and no local recurrence or distant metastasis for 2years and 3months of follow up justify our decision for radical neck dissection. The patient was not advised radiotherapy, chemotherapy or immunotherapy, as many authors consider melanoma is a radio resistant neoplasm and it is frequently used for palliation[24]. Chemotherapy is generally reserved for proven metastatic lesion[25]and immunotherapy is still in experimental stage and has not improved survival or local regional control rates in patients with mucosal melanomas[24].

There is no effective treatment for distant metastasis in malignant melanomas. Radiotherapy is associated with prolonged remission. Chemotherapy and immunotherapy may play a role to prevent distant metastasis[24].

The prognosis of patients with oral melanoma is very poor and certainly related to the biologic behavior of the disease. The reported 5 year survival rate for oral malignant melanoma has ranged from 4.5% to 29% with the median survival rate of 18.5 months after initial diagnosis[15]. The median survival is affected by whether there is lymph node involvement (18months) or not (46months). In the case reported here, there was nodal metastasis up to level IV lymph nodes, which may reduce the survival duration of the patient.

Early diagnosis is essential for successful treatment and perhaps the key factor in improving the prognosis of oral malignant melanoma. Any pigmented lesions that are suspected of undergoing changes in their clinical appearance should be biopsied. Though surgery is the mainstay of therapy, new adjuvant immunotherapy, biochemotherapy with interferon, interleukins and vaccine therapy protocols[26]are being used and hold promise for the future to improve the survival of patients with more advanced disease.

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