Case Report

Indian Journal of Dental Education
Volume 9 Number 1, January - March 2016
DOI: https://dx.doi.org/10.21088/ijde.0974.6099.9116.9

Malignant Melanoma of Oral Cavity: A Case Series and Review of Literature

Akhilanand Chaurasia*, Vaibhav Mishra**

Abstract

Primary oral malignant melanoma is a rare neoplasm of oral cavity accounting for 0.5% of all oral malignancies. The etiology of malignant melanoma is unknown however tobacco use and chronic irritation have some role. Clinically oral malignant melanoma can camouflage the other pigmented lesions of oral cavity. We are presenting 3 typical cases of oral malignant melanoma with an insight in literature.

Keywords*:* Pigmented Lesions; Malignant Melanoma; Oral Pigmentation.

Introduction

Malignant melanoma is a potentially aggressive tumor of melanocytic cell origin [1]. Oral melanomas are uncommon and thought to arise primarily from melanocytes in the basal layer of the squamous mucosa. The World Health Organization has defined mucosal malignant melanoma as a malignant neoplasm of melanocytes or of melanocyte precursors [2,3]. Malignant melanoma was first described by Weber (1859) however Lucke (1869) first recognized it as a distinct clinical entity and used the term 'melanotic sarcoma' [4]. The risk factors for mucosal melanomas are unknown. Mostly oral mucosal melanoma arises de novo from normal mucosa irrespective of chemical, thermal, or physical factors (smoking, alcohol intake, poor oral hygiene, irritation from teeth, dentures or other oral appliances) to which the oral mucosa is constantly exposed however 30% oral melanoma are preceded by oral pigmentations for several months or even [5,6]. The pigmentation varies from dark brown to blue-black color erythema is observed when the lesions are inflamed. Clinically oral malignant melanoma appears as elevation, color variegation, ulceration and satellite lesions that may have the appearance of physiologic pigmentation. Oral mucosal melanom is characterized by proliferation of malignant melanocytes along the junction between the epithelial and connective tissues as well as within the connective tissue. Oral melanoma may appear as pigmented macule, pigmented nodule, pigmented exophytic lesion or amelanotic variant of any of these three forms. It is characterized by marked aggressive and invasive behavior that manifests by both local and distant metastases to sites such as lungs, liver, brain, and bones [7]. Oral malignant melanomas demonstrate significant heterogeneity in morphological features, developmental process and biological behaviour. Hence oral malignant melanoma still represents a diagnostic challenge [8]. The oral malignant melanomas most commonly metastasize to tongue, parotid and tonsils [9,10]. Lymphatic metastasis at the time of diagnosis is a crucial prognostic factor for oral melanomas [11].

Case 1:

A 65 year old female patient reported with presenting complaint of black color growth in upper jaw since 8 months. The swelling was progressively increasing in size.The patient was average built and had normal gait and posture. She had no significant past medical and dental history. Extra-orally all structures were normal except the fullness of lip noted in maxillary anterior region. Intra-orally a black sessile growth of 3x3 cm is noted in maxillary anterior region which was extending from right maxillary lateral incisor to left maxillary central incisor. The surface of the outgrowth was smooth and glistening with bossing. The growth had typical grayish black color of melanoma(Fig.1, Fig.2). No lymphadenopathy was

Author's Affiliation: *Assistant Professor, **Junior Resident, Department of Oral Medicine & Radiology, Faculty of Dental Sciences, King George Medical University, Lucknow-226003 Uttar-Pradesh .

Reprints Requests: Akhilanand Chaurasia, Assistant Professor, Department of Oral Medicine & Radiology, Faculty of Dental Sciences King George Medical University, Lucknow-226003 Uttar-Pradesh.
E-mail: chaurasiaakhilanand49@gmail.com

noted in submaxillary nodes. On the basis of clinical presentation provisional diagnosis of oral malignant melanoma has been made. The patient was advised for maxillary occlusal radiograph to rule out any bony involvement. The maxillary occlusal radiograph(Fig.3) shows generalized bone loss. Patient was advised for incisional biopsy. The histopathology was suggestive of malignant melanoma.The patient was further referred to surgical oncology department where she is treated with surgical resection and radiotherapy.

Fig. 1: Intra-oral view showing black sessile growth of 3x3 cm is noted in maxillary anterior region which was extending from right maxillary lateral incisor to left maxillary central incisor. The surface of the outgrowth was smooth and glistening with bossing. The growth had typical grayish black color of melanoma

Fig. 2: Intra-oral view showing fullness of lip noted in maxillary anterior region.

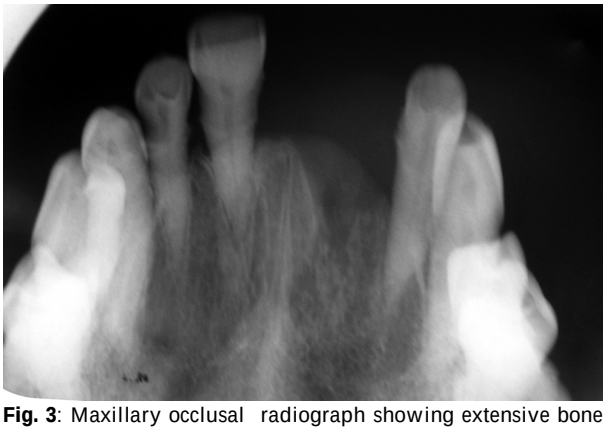

Fig. 3: Maxillary occlusal radiograph showing extensive bone resorption in maxillary anterior region

Case 2

A 45 year old patient (Fig.1) complaint of black color mass in left side of upper jaw since 4 months. Previously it was a small black growth on palate which was progressively increasing in size. He was normally built and has normal gait and posture. Extra-orally no significant finding noted(Fig.1). Intra-orally a black color growth extending from anterior palate (maxillary central incisor region) to posterior palate involving the left maxillary alveolar ridge and tuberosity region(Fig.2). The surface of growth was ulcerated and covered with yellowish necrotic slough. The left side maxillary molars were mobile and extensive sub-maxillary lymphadenopathy is noted. On the basis of clinical presentation provisional diagnosis of oral malignant melanoma has been made. The patient was advised for panoramic radiograph which showed extensive bone destruction which extends from left maxillary 1st molar to 3rd molar involving same tuberosity area with tooth floating appearance of maxillary 1st, 2nd and 3rd molar(Fig.3). The patient was advised for incisional biopsy. The histopathology was suggestive of

Fig. 1: Profile view of patient

Fig. 2: Intra-oral view showing black color growth extending from anterior palate (maxillary central incisor region) to posterior palate involving the left maxillary alveolar ridge and tuberosity region

Fig. 3: Panoramic radiograph showing extensive bone destruction which extends from left maxillary 1st molar to 3rd molar involving same tuberosity area with tooth floating appearance of maxillary 1st, 2nd and 3rd molar

malignant melanoma. The patient was further referred to surgical oncology department where he is treated with surgical resection and radiotherapy.

Case 3

A 70 year old male(Fig.1) reported with presenting complaint of pain in right side of upper jaw and blackish growth. The black mass was progressively increasing in size. He was poorly built and had normal gait and posture. There was no significant finding extra-orally(Fig.1). Intra-orally (Fig.2) a black color growth of 3x3 cm noted which was extending from maxillary 1st molar to maxillary tuberosity region. The growth was extending buccally involving buccal sulcus and palate. There were a number of blackish macular area involving anterior and posterior palatal area noted (Fig.3). There was extensive sub-maxillary lymphadenopathy noted. On the basis of clinical presentation a provisional diagnosis of oral malignant melanoma has been made. The patient was advised for panoramic radiograph which showed extensive bone destruction which extends from right maxillary 1st molar to right maxillary tuberosity area with tooth floating appearance of 1st molar (Fig.4).The patient was advised for incisional biopsy.

Fig. 1: Profile view of patient

Fig. 2: Intra-oral view showing a black color growth of 3x3 cm noted which was extending from maxillary 1st molar to maxillary tuberosity region

Fig. 3: Intra-oral view showing blackish macular area involving anterior and posterior palatal area

Fig. 4: Panoramic radiograph showing extensive bone destruction which extends from right maxillary 1st molar to right maxillary tuberosity area with tooth floating appearance of 1st molar

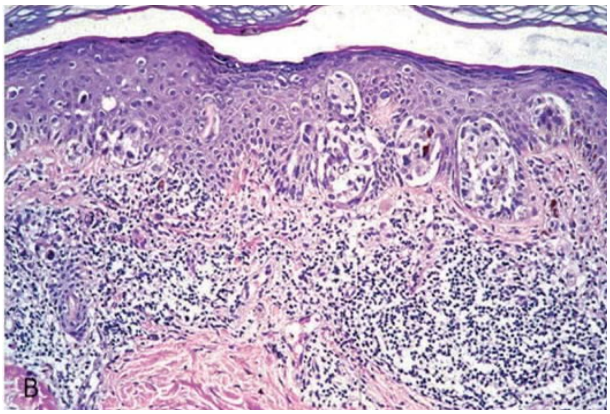

Fig. 5: Histomicrograph showing abundant spindle shaed melonocytes infiltrating oral mucosa

The histopathology was suggestive of malignant melanoma. The patient was further referred to surgical oncology department where he is treated with surgical resection and radiotherapy.

Discussion

Malignant melanoma is a potentially aggressive tumor of melanocytic cell origin [1]. Oral melanomas are uncommon and thought to arise primarily from melanocytes in the basal layer of the squamous mucosa.The etiology of oral malignant melanoma essentially unclear till date however tobacco, chronic irritation from ill-fitting dentures, ingested and inhaled environmental carcinogens at high internal body temperature can be predisposing factors [12,5,13]. Malignant melanoma of oral cavity have a variety of genetic expression at molecular level. The of loss of heterozygosity at 12p13 and loss of p27KIP1 protein expression contribute to melanoma progression [14]. However melanoma-associated antigens are expressed during the transformation process from a benign melanocytic nevus to malignant melanoma. Most of these are related to the melanin production process and most are HLA-restricted [4]. The p53 protein alterations have been identified in about two-thirds of oral malignant melanoma [15]. A recent study concluded that cytogenetic analysis and evaluation of melanocyte-specific gene-1 (MSG-1) appears to be very helpful for understanding the pathogenesis of oral malignant melanoma [16,17]. Oral malignant melanoma is largely a disease of older age group (40 years) and it is rare in patients younger than 20 years. The average age at diagnosis is 56 years. Oral malignant melanoma is commonly diagnosed in men aged 51-60 years whereas it is commonly diagnosed in females aged 61-70 years. A male predilection exists with a male-to-female ratio of almost 2:1. Oral malignant melanoma is diagnosed approximately a decade earlier in males than in females.In Japan, data suggest an equal or slight male predilection Oral melanoma reportedly occurs more commonly in the Japanese than in other groups. Among the Japanese, oral melanoma accounts for 11-14% of all cases of melanomas [18,19,20]. In Australian subcontinent, primary malignant

melanoma of the oral mucosa is rare [21]. In the East, mucosal malignant melanoma seems to be more common than the west [20]. Primary oral melanomas are extremely rare in the United States and account for less than 2% of all melanomas [21]. Jackson and Simpson concluded that primary malignant melanoma of the oral cavity represented less than 2% of all malignant melanomas [20,22,23]. However Indian studies reported the incidence of malignant melanoma involving mucosal surface was between 20.41% and 34.4% and up to 16% of these are intraoral. The oral malignant melanoma is excessively uncommon at any site in pre-pubertal children of all races [24,25]. This malignancy is a lesion of the adulthood, rarely occur under age of 20 years. Barker et al. showed that the average age of patients with mucosal melanoma was 56 years, and the age range was 22-83 years with a gender distribution of 37 male to 13 female (ratio = 2.8)[26,27]. The primary malignant melanoma involving oral cavity comprises 6.3 % of all melanomas in the head and neck region and only about 0.7 –1.6 % of all melanomas arise in the oral mucosa.The age of the patients varies between 20 and 80 years, the mean age reported in the literature ranges from 56 to 66.5 years and a modest male preponderance has been described.Only about 1% of all melanomas arise in the oral mucosa and these account for 0.5% of all oral Malignancies [4,5,12]. Pliskin reviewed the literature on oral melanoma and found that they accounted for 1.6% of over 7,500 reported melanomas [28]. Oral melanoma is slightly more common in males.Approx. 80% occur on the maxilloalveolar ridge, palate [29] and the maxillary gingiva [4]. Clinically Lopez et al [30] classified oral malignant melanoma in pigmented nodular type, non-pigmented nodular type, pigmented macular type, pigmented mixed-type and non-pigmented mixed type. Clinicaly malignant melanoma may be uniformly brown or black or may show variation of color, with black, brown, grey, purple and red shades or depigmentation [31]. It is firm on palpation and may ulcerate but does not possess a rolled, raised border. An erythematous in the mucosa often surrounds the tumor. Tumor is painless unless ulcerated, infected or both [32]. The malignant melanoma metastasize by lymphatic and hematogenous routes. There is a relationship between tumor thickness and neck metastasis. The most common nodes involved are submaxillary with upper jugular contralateral node involvement also common[33]. Clark and co-workers stated about two phases of growth in melanoma [34], first is radial growth phase- initial phase of growth of tumor during which the neoplastic growth is confined to the epidermis and second is vertical growth phase which begins when the neoplastic cells populate the underlying dermis. Radiologically contrast-enhanced CT can be used to determine the extent of the melanoma and whether local, regional, or lymph node metastasis is present.Bone scanning with a gadolinium-based agent and chest radiography can be beneficial in assessing metastasis.The magnetic resonance imaging is used to diagnose melanoma in soft tissue. The atypical intensity is correlated with the amount of intracytoplasmic melanin. On T1-weighted images, such melanomas are hypointense however T2-weighted images such melanomas are hyperintense and show increased melanin production. Positron emission tomography (PET) has poor results in distinguishing melanoma from nevi. However combined PET-CT may have diagnostic value [35]. The histological spectrum of benign melanocytic lesions of the oral mucosa is varied and includes so-called mucosal melanosis,(i.e., a junctional proliferation of melanocytes with or without cytological atypia, resulting in a macular hyperpigmentation) and a variety of melanocytic naevi. The latter comprise junctional, compound and subepithelial naevi as well as a variety of blue and combined naevi, which are proportionally more common than in the skin. The oral malignant melanoma can be histologically subclassified into a) in situ melanoma, which is limited to the epithelium and the epithelial–connective tissue interface.b) melanomas with an invasive pattern, in which the neoplasm extends into the connective tissue. c) melanomas with a combined pattern of invasive melanoma with in situ component [36]. Malignant cells of oral malignant melanoma show a wide range of shapes, including spindle, plasmocytoid, clear cell and epithelioid ones [14,36]. Usually oral malignant melanoma can be diagnosed with confidence on H&E-stained sections. If pigment is completely absent immunohistochemical stains are of significant help.Useful markers include S-100 protein, gp100 (HMB-45), Mart-1 (Melan-A) [37,38]. An excisional biopsy with a 1 to 2 mm 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. Fine needle aspiration or exfoliative cytology of primary pigmented lesions is contraindicated [35]. Treatment modalities for primary oral melanoma include surgical resection with or without neck dissection. Adjunctive modalities such as immunotherapy, chemotherapy and radiation therapy may offer a supportive but as yet non curative role. The mainstay of curative treatment is surgery, mandating complete resection of the tumor with clear margins if possible [35]. The prognosis of oral malignant melanoma is poor with a 5-year survival of about 15% [4].

Conclusion

Oral malignant melanoma is an extremely rare malignancy which is potentially very aggressive and a rapidly invasive tumor. Clinically these tumors are very silent and asymptomatic in their appearance leading to delayed diagnosis until symptoms such as swelling, ulceration, and bleeding occur. As an early diagnosis is very important for better survival and prognosis in oral melanoma, all oral pigmented lesions that are not clinically diagnostic should be biopsied. Dental and medical practitioners who treat oral lesions should include malignant melanoma in the differential diagnosis of pigmented lesions.

References

1. Van der Waal RIF, Snow GB, Karim AB and van der Waal I. Primary malignant melanoma of the oral cavity: a review of eight cases. Br Dent J. 1994; 176: 185–188.
2. Kumar A., Bindal R., Shetty D. C., Singh H. P. Primary oral malignant melanoma: clinicopathological series of four cases. Dental Research Journal. 2012; 9(3): 33–44.
3. Gupta M., Gupta M., Aggarwal A., Ahuja R., Pachauri A., Kumar P. Significance of early detection of oral malignant melanoma: some reasonable facts. Clinical Cancer Investigation Journal. 2013; 2(3): 178–180.
4. Hicks MJ and Flaitz CM. Oral mucosal melanoma: epidemiology and pathobiology. Oral Oncol. 2000; 36: 152–169.
5. Rapini RP, Golitz LE, Greer RO Jr, Krekorian EA and Poulson T. Primary malignant melanoma of the oral cavity. A review of 177 cases. Cancer. 1985; 55: 1543–1551.
6. Chaudhry AP, Hampel A and Gorlin RJ. Primary malignant melanoma of the oral cavity: a review of 105 cases. Cancer. 1958; 11: 923–928.
7. Martinez EA, Alonso FC, Siles MS. Melanoma of the oral mucosa with cerebral metastasis: A clinical case. Oral Oncol Extra. 2005; 41: 30–3.
8. Dimitrakopoulos I., Lazaridis N., Skordalaki A. Primary malignant melanoma of the oral cavity. Report of an unusual case. Australian Dental Journal. 1998; 43(6): 379–381.
9. Patton LL, Brahim JS, Baker AR. Metastatic malignant melanoma of the oral cavity. A retrospective study. Oral Surg Oral Med Oral Pathol. 1994; 78: 51-6.
10. Strauss JE, Strauss SI. Oral malignant melanoma: a case report and review of literature. J Oral Maxillofac Surg. 1994; 52: 972-6.
11. Medina JE, Ferlito A, Pellitteri PK, Shaha AR, Khafif A and Devaney KO et al. Current management of mucosal melanoma of the head and neck. J SurgOncol. 2003; 83: 116–122.
12. Gu GM, Epstein JB and Morton TH Jr, Intraoral melanoma: long-term follow-up and implication for dental clinicians. A case report and literature review. Oral Surg Oral Med Oral Pathol Oral RadiolEndod. 2003; 96: 404–413.
13. Prasad ML, Jungbluth AA, Patel SG, Iversen K, Hoshaw-Woodard S and Busam KJ. Expression and significance of cancer testis antigens in primary mucosal melanoma of the head and neck. Head Neck. 2004; 26: 1053–1057.
14. Woenckhaus C, Fenic I, Giebel J, Hauser S, Failing K, Woenckhaus J et al. Loss of heterozygosity at 12p13 and loss of p27KIP1 protein expression contribute to melanoma progression. Virchows Arch. 2004; 445: 491–49.
15. Korabiowska M, Brinck U, Hoenig JF, Bartkowski SB, Kellner S, Marx D et al. Significance of P-53 antigen in malignant melanomas and naevi of the head and neck area. Anticancer Res. 1995; 15: 885–889.
16. Farnedi A, Magrini E, Betts CM, Cocchi R, Pession A and Foschini MP. Cytogenetic analysis of oral malignant melanoma. Oral Surg Oral Med Oral Pathol Oral RadiolEndod. 2005; 99: 655–656.
17. Sedghizadeh PP, Williams JO, Allen CM and Prasad ML. MSG-1 expression in benign and malignant melanocytic lesions of cutaneous and mucosal epithelium. Med Sci Monitor. 2005; 11: 189–194.
18. Greenberg MS, Glic KM. Burket's oral medicine. 9th ed. BC Decker: Hamilton. 2003; p. 131-2,214-5.
19. Neville BW, Damm D, Allenc R, Bouquot JE. Oral and maxillofacial pathology. 2 nd ed. W.B Saunders: Philadelphia. 2002; p. 334: 376-80.
20. Reddy CR, Ramachandra T, Ramulu C. Primary malignant melanoma of the hard palate. J Oral Surg. 1976; 34: 937-9.
21. D'Silva NJ, Kurago Z, Polverini PJ, Hanks CT, Paulino AF. Malignant melanoma of the oral mucosa in a 17-year-old adolescent girl. Arch Pathol lab Med. 2002; 126: 1110-3.
22. Jackson D, Simpson HE. Primary malignant melanoma of the oral cavity. Oral Surg Oral Med Oral Pathol. 1975; 39: 553-9.
23. Robertson GR, Defiebre BK, Firtell DN. Primary malignant melanoma of the mouth. J Oral Surg. 1979; 37: 349-52.
24. Goubran GF, Adekeye EO, Edwards MB. Melanoma of the face and mouth in Nigeria: A review and comment on three cases. Int J Oral Surg. 1978; 7: 453-62.
25. Shah JP. Cancer of head and neck. BC Decker Inc: Hamilton. 2001; p. 40-2,79-80.
26. Barker BF, Carpenter WM, Daniels TE, Kahn MA, Leider AS, Lozada-Nur F, et al. Oral mucasal

melanomas: The WESTOP Banff workshop preceedings: Western Society of Teachers of Oral Pathology. Oral Surg Oral Med Oral Pathol Oral RadiolEndod. 1977; 83: 672-9.

27. Hashemipour MA, Zarei MR, Chamani G. Epidemiological aspects of non- squamous cell malignant tumors of the oral cavity in Kerman province (1991-2002). Doctorate Thesis. School of dentistry. Kerman university of medical science. 2004 July.
28. Pliskin ME, Melignant melanoma of the oral cavity: in WH Clark, Jr LI Goldman, MJ Mastrangelo, Human malignant melanoma. Grune and Stratton, New York 1979.
29. Taylor CO, Lewis JS: Histologically documented transformation of benign oral melanosis into malignant melanoma: a case report, J Oral and Maxillofac Surg. 1990; 48: 732-734.
30. Lopez-Graniel CM, Ochoa-Carrilo FJ, Menese-Garcia A. Malignant melanoma of the oral cavity: Diagnosis and treatment experience in a Mexican population. Oral Oncol. 1999; 35: 425–30.
31. Mendenhall WM, Amdur RJ, Hinerman RW, Werning JW, Villaret DB and NP Mendenhall. Head and neck mucosal melanoma. Am J ClinOncol. 2005; 28: 626–630.
32. Wood NK, Goaz PW ,Differential diagnosis of Oral and Maxillofacial lesions, 5th ed, Pg 199, Mosby 1997.
33. Umeda M, Shimada K: Primary malignant melanoma of the oral cavity: its histological classification and treatment, Br J Oral MaxillofacSurg. 1994; 32: 39-47.
34. Clark WH, Jr Ainsworth AM, Bernardino EA, Yang CH et al. The developmental biology of primary human malignant melanomas. SeminOncol. 1975; 2: 83.
35. M. N. Younes and J. N. Myers, "Melanoma of the head and neck: current concepts in staging, diagnosis, and management," Surgical Oncology Clinics of North America. 2004; 13(1): 201–229.
36. Barker BF, Carpenter WM, Daniels TE, Kahn MA, Leider AS, Lozada-Nur F et al. Oral mucosal melanomas: the WESTOP Banff workshop proceedings. Western Society of Teachers of Oral Pathology. Oral Surg Oral Med Oral Pathol Oral RadiolEndod. 1997; 83: 672–679.
37. Lengyel E, Gilde K, Remenar E and Esik O, Malignant mucosal melanoma of the head and neck. PatholOncol Res. 2003; 9: 7–12.
38. Scolyer RA, Thompson JF, Stretch JR, Sharma R and McCarthy SW. Pathology of melanocytic lesions: new, controversial, and clinically important issues, J SurgOncol. 2004; 86: 200–211.