Primary Oral Mucosal Melanoma: a Short Review

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Abstract

Primary Oral Mucosal Melanoma (POMM) is a rare entity and is derived from malignant transformation of melanocytes from the mucosal epithelium. POMM usually presents with poor prognosis and may show a more aggressive behavior than its cutaneous counterpart [1-5].

Epidemiology

Primary oral mucosal melanoma represents 0.5% of all oral malignancies, accounting for 0.2 to 8% of all melanomas, with an incidence of 1.2 cases per 10 million per year. POMM is asymptomatic in its early stages and usually not noticed by the patients, resulting in the delay in diagnosis. Immunoreactivity of melanoma cells to antibodies against: S-100 protein; Melan-A (MART-1) and HMB-45 (gp100) can be very useful to distinguish POMM from other malignancies. Others markers may indicate variations in its biologic behavior and prognosis, such as Ki-67; P53 and P16, and maybe useful for prognostic prediction.

Clinical and Histological Features

POMM is asymptomatic in its early stages and it is usually not noticed, resulting in the delay in diagnosis [1,12,16]. The prognosis of POMM is extremely poor with a reported 5-year overall survival rate of 8%. Differential diagnosis of POMM includes: melanosis; melanotic macule; oral nevi; racial pigmentation; smoking-associated melanosis; melanoplakia; postinflammatory pigmentation; amalgam tattoo; medication melanosis; melanocacanthoma; Peutz-Jehgers syndrome; Cushing's syndrome; Addison's disease and Kaposi's sarcoma [1,10,14].

The lesions are asymmetric, irregular in outline and occasionally multiple and the surface can be macular to nodular, and it can assume white, brown, gray, black, dark blue, purple and red shades, sometimes with erythema or ulceration present [1,2,8,10-13,15]. The preferential location of melanoma in the head and neck is the nasal cavity, probably due to the more frequent findings of melanin pigmentation in oral mucosa of these races [1,8,10,13-17].

Etiopathogenesis

Sun exposure appears to play a major role in the cutaneous

Keywords: Oral; Mucosal; Melanoma; Immunohistochemistry

Introduction

Primary Oral Mucosal Melanoma (POMM) is a rare entity and it develops from malignant transformation of melanocytes from the mucosal epithelium. POMM usually unravels with poor prognosis and it may show a more aggressive behavior than its cutaneous counterpart [1-5].

Etiopathogenesis

Sun exposure appears to play a major role in the cutaneous
melanoma’s development [1]. On the other hand, mucosal melanoma of the oral cavity has no association with sun exposure, but certain factors (ethnicity; family history, syndrome and preexisting lesions) can influence the development of POMM [16].

**Immunohistochemical Features**

Immunoreactivity of melanoma cells to antibodies against: S-100 protein; Melan-A (MART-1), HMB-45 (gp100) and Tyrosinase can be very useful to distinguish POMM from other malignancies [13,19]. Others markers lead to variations in its biologic behavior and prognosis, such as Ki-67; P53, P16 and MITF [4,19,20] (Figures 1 and 2).

In 2001, Prasad et al. reported the expression of melanocytic differentiation markers in a series of Malignant Melanoma of the Oral and Sinonasal Mucosa (including: primary, recurrent and metastatic tumors), and they observed immunostaining for S100 (97%); Tyrosinase (94%); Melan-A (85%) and HMB-45 (71%) in Oral Mucosal Melanomas. Garzino-Demo et al. [7] showed S-100 protein and homotropine methylbromide (HMB-45/gp100) in 80% of all cases. In a series of primary oral and nasal melanomas, positivity for HMB-45 and S-100 protein was observed in 94% and 88% of cases, respectively [21]. Recently de-Andrade et al. [12] reported HMB-45 immunostaining in all cases of melanoma, whilst Melan-A stained 86.36% and only 50% of the cases were S100 positive.

The proliferation marker Ki-67 has been considered to be the most useful tool to assess neoplastic cell proliferation in melanomas, with some studies recognizing its prognostic value. The mean and standard deviation of Ki-67 labeling index in POMM was 15.88 ± 22.09 [4], however it was previously described by de-Andrade et al., [22] as 31.7% (range 10.3 – 52.7%).

P53 is known as a tumor suppressor gene and it can be found in half of human cancers. The mutated P53 cannot perform its natural role of protecting cell genome, consequently cell with damage DNA proliferate, resulting in the development of malignant neoplasms [4]. Hicks and Flaitz [6] found 11/17 cases expressing P53 in oral mucosal melanomas; on the other hand Tanaka et al. [23], found P53 expression in only 2/13. Ahn et al. [24] demonstrated P53 expression in 6/24 In a series of mucosal melanoma of the head and neck; later in a similar study, other group observed that P53 expression occurs in about 21% of mucosal melanomas [25]. Recently a study comparing immunohistochemical profile of oral mucosal and head and neck cutaneous melanoma, P53 was evaluated and its expression did not show a significant difference between the two locations. The exact status of the P53 gene and protein in melanoma is still unclear. Moreover data regarding its biologic; prognostic; etiologic role in this tumor are controversial, especially at mucosal sites [4].

P16 is a member of cyclin-dependent kinase (CDK/Cyclin) inhibitor protein family encode by multiple tumor suppressor gene 1 (MTS-1), thus loss of P16 expression has also been reported in a small number of oral mucosal melanomas [25]. Positive staining for P16 was found 7/13 cases of malignant melanoma of oral mucosa [23]. In 2012, p16 protein was expressed in 35% of neoplastic cell in only one case out of 13 primary oral mucosal melanoma [20], on the other hand, in our experience we observed that 50% of 35 cases were positive for P16 protein expression [26]. Lost of P16 expression was observed in 75% cases of mucosal melanoma of head and neck [25].

MITF plays a critical role in the regulatory network of transcription factors and signaling pathways that control the survival, proliferation and differentiation of melanoblasts and melanocytes, and as well as melanogenesis [27,28]. Prasad et al. [19] observed immunostaining for MITF in 27/35 Melanoma of Oral Mucosa, however, recently Alaeddini and Etemad-Moghadam [29] found MITF protein expression in 5/19 cases of Oral Mucosal Melanoma.

**Conclusion**

Primary Oral Mucosal Melanoma is very rare and it has a poor
prognostic. The POMM’s etiopathogenesis is still unclear, however immunohistochemical markers help their diagnosis. According to the literature and our experience, the first choice as a POMM marker is S100, however Melan-A, HMB-45, P53, P16, MITF or Ki-67 are good markers, thus their combination with S100 can support and validate POMM final diagnosis. Further studies, including genetic assays, are needed to draw a better understanding of this peculiar neoplasm.

References