FEATURE ARTICLE

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ORAL AMELANOTIC MELANOMA

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ABSTRACT

Malignant melanomas of the mucosal regions of the head and neck are extremely rare neoplasms accounting for less than 1% of all melanomas. Approximately half of all head and neck melanomas occur in the oral cavity. Less than 2% of all melanomas lack pigmentation, in the oral mucosa however, up to 75% of cases are amelanotic.

No etiologic factors or risk factors have been recognized for oral melanomas. Some authors have suggested that oral habits and self-medication may be of etiological significance. Oral melanoma is rare but it is relatively frequent in countries like Japan, Uganda, and India. It is rarely identified under the age of 20 years. In Australia where cutaneous melanomas are relatively common primary melanoma of the oral mucosa is rare.

The surface architecture of oral melanomas ranges from macular to ulcerated and nodular. The lesion is said to be asymptomatic in the early stages but may become ulcerated and painful in advanced lesions.

The diagnosis of amelanotic melanoma is more difficult than that of pigmented lesions. The neoplasm consists of spindle-shaped cells with many mitotic figures and no cytoplasmic melanin pigmentation. Immunohistochemistry using S-100, HMB-45, Melan-A and MART-1 will help in establishing the correct diagnosis.

Radical surgery with ample margins and adjuvant chemotherapy are appropriate management protocol for malignant melanoma.

Oral melanoma is associated with poor prognosis but its amelanotic variant has even worse prognosis because it exhibits a more aggressive biology and because of difficulty in diagnosis which leads to delayed treatment.

Keywords: amelanotic melanoma, oral cavity

INTRODUCTION

Malignant melanomas of the mucosal regions of the head and neck are extremely rare neoplasms accounting for less than 1% of all melanomas[1]. Approximately half of all head and neck melanomas occur in the oral cavity, followed by the nasal cavity (44%) and sinuses (8%)[2]. The most frequent sites in the oral cavity are the hard palate (more than 40%) and the gingiva[2]. Melanomas arise from the uninhibited proliferation of melanocytes found in the basal layer of the oral mucous membranes[3]. The clinical presentation of this neoplasm varies widely, from a typically pigmented macular or nodular lesion, to a non-pigmented neoplasm that may be solitary or multiple, primary or metastatic[4]. Less than 2% of all melanomas lack pigmentation, in the oral mucosa however, up to 75% of cases are amelanotic[5, 6, 7].

In contrast to cutaneous melanomas, which may present with a horizontal or vertical growth pattern, oral melanomas usually present typically with vertical growth, thus spreading to contiguous sites early[8]. The prognosis for oral melanomas is poor, with an overall 5-year survival rate of 15%[8].

Etiology

In oral mucosa, melanocytes are located along the tips and peripheries of the rete pegs. No etiologic factors have been recognized for oral melanomas. Risk factors have also remained obscure. There appears to be no geographic variations and only minor ethnic and gender differences[9]. Some oral melanomas are believed to originate from junctional nevis, others are thought to arise from pre-existing Hutchinson's malignant lentigo[10].

Some authors have suggested that oral habits and self-medication may be of etiological significance in some Indian and African groups[11]. According to Tanaka et al[12], the biological behavior of melanoma may be related to the expression of the proteins Rb, pRb2/p130, p53 and p16, which may be helpful in predicting the manifestation of this neoplasm, including the melanin content.

Epidemiology

Oral melanoma is rare but it is relatively frequent in countries like Japan, Uganda, and India[13]. Oral melanoma is a lesion of adulthood, rarely identified under the age of 20 years. In a study, the highest incidence of malignant melanoma was reported in the fifth to eight decades of life[14]. Hicks and Flaitz[8] in a review of oral malignant melanoma showed a male predilection and an age range of 22 to 83 years, with a mean age of 56 years. There is a higher incidence of melanoma of the oral mucosa among Japanese than Caucasians[15]. According to an African research, 1.7% of all melanomas in Sudan occurred in the oropharynx and 0.9% of the melanomas in Nigeria originated within the oral cavity[11]. In Australia where cutaneous melanomas are relatively common primary melanoma of the oral mucosa is rare [14].

Clinical features

The surface architecture of oral melanomas ranges from macular to ulcerated and nodular[9]. Indeed clinically, 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[16]. The lesion is said to be asymptomatic in the early stages but may become ulcerated and painful in advanced lesions[17].

Histology

The diagnosis of amelanotic melanoma is more difficult than that of pigmented lesions[18]. Histological description of a specimen by Notani *et al*[9] showed that the neoplasm consisted of spindle-shaped cells with many mitotic figures and there was no cytoplasmic melanin pigmentation. These malignant cells possess considerable pleomorphism, with large, irregular hyperchromatic nuclei and prominent nucleoli[8]. Others have reported pleomorphic epithelioid cells with bizarre nuclei, large cherry-red nucleoli, occasional nuclear pseudo-inclusions and variable amounts of dusty cytoplasmic pigment[20].

Diagnosis

Lesions that are suspected to be melanomas should be assessed both histologically and by immuno-histochemistry, which are helpful in the diagnosis of amelanotic melanoma and only slightly pigmented melanoma[21, 22]. The immunohistochemical techniques using S-100, HMB-45, Melan-A and MART-1 will help in establishing the correct diagnosis[21].

Treatment

Notani *et al*[9] suggests a combination of radical surgery with ample margins and adjuvant chemotherapy as an appropriate management protocol for malignant melanoma. Many chemotherapy agents have been used for malignant melanomas but dacarbazine was reported to have the best response rate of about 20% as a single agent[23]. The addition of the immunomodulator, OK-432, injected around the neoplasm has been advocated for treatment and prolonging survival periods in oral lesions[24].

Radiotherapy has been considered to have only a palliative role and on its own was reported to be ineffective since the lesion is not very radiosensitive[25]. On the other hand, Tanaka *et al*.[16] found radiotherapy to be more successful than surgery for oral melanoma. The treatment of amelanotic melanoma does not differ in anyway from the pigmented neoplasm.

Prognosis

Lymphatic metastasis at the time of diagnosis seems to be the best prognostic factor for oral melanoma[26]. Rogers and Gibson[22] reported that half of all patients with oral melanoma had regional lymph node metastases and 20% had disseminated melanomas at initial assessment. The prognosis of amelanotic melanoma tends to be poorer [18]. Indeed, Nandapalan *et al*.[25] in a review of 257 mucosal melanomas of the head and neck region reported that amelanotic melanomas had a 20% survival at 3 years, whereas pigmented melanoma had a 58% survival at 3 years. This has resulted in part from delays in determining a definitive diagnosis and initiating treatment. Poor prognosis may also be due to the fact that amelanotic lesions tend to exhibit vertical growth pattern while the pigmented lesion showed a more radial growth pattern. Ohashi *et al*.[21] reported that of eight oral melanomas without a radial growth pattern, only one presented as a melanotic type, whereas 18 of 27 with a radial growth patterns were melanotic. Vertical growth will lead to early involvement of contiguous structures and worsen the overall outcome. Milton also drew attention to the fact that fast-growing melanomas often have relatively less pigment than slow-growing ones [27].

CONCLUSION

Oral melanoma is a relatively rare neoplasm associated with poor prognosis but its amelanotic variant has even worse prognosis because it exhibits a more aggressive

biology and because of difficulty in diagnosis which leads to delayed treatment.

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