Oral melanotic macule and primary oral malignant melanoma: Epidemiology, location involved, and clinical implications

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Background. Oral malignant melanoma must be differentiated from melanotic macule.

Study design. Retrospective review of 2 series of oral melanotic macule (n = 52) and oral melanoma (n = 130) were conducted to investigate the epidemiology and location involved and assess their differences.

Results. The mean age of oral melanotic macule patients was 47.3 years, with female:male ratio 2.1 and the lower lip being the predominant location. The mean age of oral melanoma patients was 53.8 years, with no observed sex predilection and the main locations being palate and gingiva. Differences between the 2 cohorts in age (P = .006), gender (P = .014), and lesion site (P < .001) were noted. In this review, 1 case of oral melanotic macule was found to subsequently develop into melanoma.

Conclusions. Oral melanotic macule may possess malignant potential. Biopsy is recommended to differentiate oral melanoma from melanotic macule for male patients >60 years old with suspected melanotic macule lesion located on the palate. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;112:e21-e25)

Oral melanotic macule and primary oral malignant melanoma are 2 clinically and histologically distinctive oral pigmented lesions. Oral melanotic macule usually is a small well circumscribed and brown-to-black flat macule that occurs on the lip and mucous membranes, with an increase in melanin deposition in the basal cell layer of the epithelium. Kahn et al. described a case of benign melanotic macule developing into primary oral malignant melanoma in the follow-up period, yet oral melanotic macule is traditionally known to be a benign pigmented lesion with no malignant potential. This apparent discrepancy presents an academic and clinical challenge.

Oral malignant melanoma is a malignant neoplasm of melanocytes or of melanocyte precursors and is characterized by proliferation of atypical melanocytes at the epithelial connective tissue interface. It is exceedingly rare, representing <1% of all melanomas and only ~0.5% of oral malignancies. Oral melanoma is known to behave aggressively, often with extremely poor prognosis, e.g., a 5-year survival rate of 10%–25%. The poor clinical outcome is partly due to patients’ failure to recognize signs of early lesion and physicians’ delayed diagnoses, resulting in frequent diagnoses at advanced stage.

Oral malignant melanoma must be differentiated from other oral benign pigmented lesions. Clinically, oral melanoma is usually asymptomatic in the early stage and presents normally as a flat pigmented lesion or as a mass with a rapid growth rate. Meleti et al. reported a retrospective analysis of the presence of an oral melanocytic nevus without an increased risk of oral melanoma development. Unfortunately, there are no striking features to distinguish oral melanoma from other oral pigmented lesions. No reports comparing series of oral melanotic macule or melanoma have been found in literature from China, and information on the clinical profiles regarding these is missing. We therefore retrospectively reviewed 2 series of oral melanotic macule (n = 52) and oral malignant melanoma (n = 130) from China to investigate the epidemiologic features and locations involved and to estimate the differences of the patients of the 2 groups in a hospital-based study.

MATERIALS AND METHODS

All the medical records of patients with the clinical and pathologic diagnosis of oral melanotic macule and melanoma from 1993 to 2009 in a standard computerized database of Ninth People’s Hospital, Shanghai Jiao Tong University School of Medicine, were retrieved.
and retrospectively reviewed. Histopathologic diagnosis of oral melanotic macule and melanoma were confirmed by the oral pathologists from hematoxylin-eosin–stained slides. Diagnosis of oral melanotic macule and primary oral melanoma were made based on criteria recommended in published literature. Information regarding age, gender, and site of lesions were all documented in detail. A case-control analysis of oral melanotic macule and melanoma was performed. This study was approved by the Institutional Review Board.

The statistical differences between the melanotic macule and melanoma cohorts was assessed. Differences in age were assessed by using the Student $t$ test. Differences in age group and site of lesions were measured by using the nonparametric test. The $\chi^2$ test was used to assess the association among gender. All tests were 2 sided, and $P$ values of <.05 were considered to be statistically significant.

RESULTS

Characteristics of oral melanotic macule. The baseline characteristics of oral melanotic macule are presented in Table I. A total of 52 patients with melanotic macule were identified for this study, ranging from 20 to 75 years in age with an average age was 47.3 years at the time of diagnosis. There were 17 men and 35 women (M:F ratio 1:2.1). The peaks of age-frequency distribution were the fifth decade for women (40.0%) and after the sixth decade for men (35.3%). Lower lip (36.5%) was the main location involved.

Characteristics of oral malignant melanoma. The baseline characteristics of oral melanoma are shown in Table II. A total of 130 patients with melanoma were identified for the present study, ranging from 3 to 90 years old, with the average age at the time of diagnosis of 53.8 years. There were 69 male and 61 female patients with a male-to-female ratio of 1.1:1. There was no difference in age distribution between male and female. The highest incidence occurred in the sixth decade of life for both genders. Palate and gingiva were affected in 52 (40.0%) and 52 (40.0%) cases, respectively.

Comparative analysis of oral melanotic macule and melanoma. To define the differences of clinical parameters between oral melanotic macule and melanoma, a comparative analysis was performed (Table III). The mean age of the patients with melanotic macule was 47.3 years old compared with 53.8 years with melanoma (Student $t$ test: $P = .006$), with a difference in the age group ($<40$ years, 40-59 years, $\geq 60$ years; nonparametric test: $P = .007$). Significant differences in gender ($\chi^2$ test: $P = .014$) and site of lesion (nonparametric test: $P < .001$) were also observed between the 2 groups.

Patients with oral melanotic macule and melanoma association. We found 3 associated cases of oral melanotic macule and melanoma. Case 1 (a 60-year-old woman) was diagnosed with an oral melanotic macule at the palate by biopsy. After 1 month, diagnosis of melanoma was made at the same area of the palate (Fig. 1). Case 2 (a 60-year-old woman) was diagnosed with oral melanotic macule concomitant melanoma at the palate (Fig. 2). Case 3 (a 72-year-old man) underwent the first surgical excision with a diagnosis of oral melanoma at the lower lip. After 29 months, he had the second surgical excision and was diagnosed with a
Table III. Comparison of oral melanotic macule and melanoma

<table>
<thead>
<tr>
<th></th>
<th>Melanotic macule</th>
<th>Melanoma</th>
<th>P value</th>
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<tbody>
<tr>
<td>Patients</td>
<td>52</td>
<td>130</td>
<td></td>
</tr>
<tr>
<td>Age, y (SD)</td>
<td></td>
<td></td>
<td>.006</td>
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<tr>
<td>Mean</td>
<td>47.3 (13.9)</td>
<td>53.8 (14.4)</td>
<td></td>
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<tr>
<td>Range</td>
<td>20–75</td>
<td>3–90</td>
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<tr>
<td>Age group, y</td>
<td></td>
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<td>.007</td>
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<tr>
<td>&lt;40</td>
<td>16 (30.8)</td>
<td>21 (16.2)</td>
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<tr>
<td>40-59</td>
<td>27 (51.9)</td>
<td>65 (50.0)</td>
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<tr>
<td>≥60</td>
<td>9 (17.3)</td>
<td>44 (33.8)</td>
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<tr>
<td>Gender</td>
<td></td>
<td></td>
<td>.014</td>
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<tr>
<td>Female</td>
<td>35 (67.3)</td>
<td>61 (46.9)</td>
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</tr>
<tr>
<td>Male</td>
<td>17 (32.7)</td>
<td>69 (53.1)</td>
<td></td>
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<tr>
<td>Site</td>
<td></td>
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<td>&lt;.001</td>
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<tr>
<td>Lip</td>
<td>21 (40.4)</td>
<td>3 (2.3)</td>
<td></td>
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<tr>
<td>Gingiva</td>
<td>14 (26.9)</td>
<td>52 (40.0)</td>
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<tr>
<td>Palate</td>
<td>7 (13.5)</td>
<td>52 (40.0)</td>
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</table>

Fig. 1. Histopathology of case 1. Oral melanotic macule (A) developed into melanoma (B). Hematoxylin-eosin staining. Magnification ×100.

Fig. 2. Histopathology of case 2. This lesion exhibited the histopathologic manifestation of melanotic macule (A) concomitant with melanoma (B). Hematoxylin-eosin staining. Magnification ×100.

DISCUSSION

In this study, we attempted to investigate the clinical features of oral melanotic macule and oral melanoma, and assess the differences between the 2 groups.

Clinical features of the melanotic macule were generally similar to those found in other studies. We observed oral melanotic macule mainly occurred in the fifth decade of life, and more commonly in women (M:F ratio 1:2.1), confirming the previously reported female predilection. Lower lip and gingiva were the most common sites. Few lesions were located on the tongue, upper lip, or palate.

Studies on primary oral melanoma are scarce and mostly reports of isolated cases or small-scale case series. Sortino-Rachou et al. recently reported 28 cases of a total number of 319 patients with melanotic macule at the lower lip with no evidence of malignancy (Fig. 3).
oral melanoma in the period of 1998-2002 from Asia, using the Cancer Incidence in Five Continents Volume IX database. Here, we documented 130 new patients with oral melanoma in a hospital-based study from China, one of the largest series of primary oral melanoma. Clinical characteristics shown in our series are mostly consistent with other reports in the literature.8-12,18-23 We observed that oral melanoma mainly occurred after the fifth decade of life. Neonatal and infant cases are rare, although we identified a 3-year-old patient and Sortino-Rachou et al. reported a 4-month-old patient.14 We found no significant gender predilection (M:F ratio 1.1:1). Earlier reports also suggested no or minimal gender predilection.18,22,23 Palate and gingiva were the most common sites. Few lesions were identified on the tongue, mandible, or lip.

Overall, we found significant differences in the age, age group, gender, and site of lesions between oral melanotic macule and primary oral malignant melanoma. At present, biopsy for routine histopathologic examination is recommended to exclude melanoma from oral pigmentations. For male patients >60 years old suspected of melanotic macule with lesion on the palate, we further recommended routine biopsy to rule out oral melanoma from these patients with melanotic macule. These patients usually have a low incidence for melanotic macule but a high incidence for melanoma.

In our analysis, we noted 3 cases with apparent association between oral melanotic macule and melanoma. In the published literature, de Giorgi et al.24 reported 1 patient with oral melanotic macule who also had a previous melanoma, and Kahn et al.2 reported an oral melanotic macule developing into melanoma. Of note, our case of oral melanotic macule developed into melanoma within a 1-month time span at the same area of the palate. Given the lack of precise data on the biopsy site, we cannot rule out the possibility of sampling error. However, we also cannot confirm the benign nature of oral melanotic macule with no malignant potential. Further studies are required to assess the strength of the relationship. Although most oral melanoma arise de novo, from apparently normal mucosa, a definite precursor lesion has not yet been identified.25 Single case reports of oral premalignant melanocytic dysplasia and atypical melanocytic proliferation had been observed.17,26

In our study, a patient with diagnosis of oral melanocytic nevus was excluded. Oral melanocytic nevus is another type of benign pigmented lesions. Among 773 patients with biopsy-proven oral solitary melanocytic lesions, Buchner et al.17 reported oral melanotic macules in 86.1% of patients and oral melanocytic nevi in 11.8% of patients. Meleti et al.16 presented an analysis of 119 patients with oral melanocytic nevus, together with a review of the literature, and concluded that their evaluation did not provide concrete support for the idea that the presence of an oral melanocytic nevus indicates a risk of future melanoma transformation. Further studies are required to assess the entity of potential precursor lesions of oral melanoma.

In summary, the present paper was a retrospective epidemiologic study from 1 center of oral melanotic macule and melanoma. Significant differences in age, gender, and location of lesions were observed between the 2 groups. We observed association between oral melanotic macule and melanoma in 3 cases, and we recommend biopsy to rule out melanoma for male patients >60 years old with suspected melanotic macule lesion located on the palate.

REFERENCES


