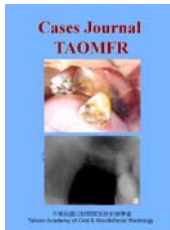


Primary Melanoma of the Oral Mucosa: Report of a Case

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Primarily oral melanoma is an aggressive neoplasm originated from the malignant transformation of melanocytes within the basal layer of oral mucosa. The prognosis of this tumor has been very poor and the reported five-year survival rate was ranged from 4.5% to 29.0% with a median survival rate of 18.5 months after initial diagnosis [1]. Primary oral melanoma can arise at any age group with the mean age of occurrence reported to be 54-year-old; and is less frequent under 30 years of age. The most common oral location is palate and maxillary gingiva but other oral regions such as mandibular gingiva, buccal mucosa, tongue, and mouth floor can also be involved. Melanoma in the oral cavity, presented as a heavily pigmented area, is usually painless in the early stages. The presence of this lesion is alerted only when either ulceration or hemorrhage occurs. Histopathologically, the tumor is consisted with dysplastic oral melanocytes featured with radial or vertical growth phases. The former pattern is characterized by the demonstration of atypical melanocytes arranged in a 'pagetoid manner' whilst the latter one is characterized by proliferation of bizarre melanocytes within the underlying connective tissue stroma [2-4].

The first reported case of primary oral melanoma was presented in 1859 by Weber [5,6]. This malignant neoplasm is rare in the oral cavity, representing for 0.2% to 8% of all melanomas [7]. The case of a 77-year-old man with primary oral melanoma occurred of the maxillary gingiva is reported.

CASE PRESENTATION

A 77-year old Taiwanese male patient referred by his family dentist presented to the Department of Oral Pathology of

our institution with the chief complaint of the black coloration in the right upper gingiva for an unknown duration. The

oral hygiene of the patient was poor with heavy gingival recession and calculus deposition. He did not chew betel-quad, but smoked cigarette and drank alcohol. The medical history of the patient was noncontributory

On clinical examination, a painless, non-tender, well-defined, asymmetric of irregular border, blackish blue lesion of approximately 2cm × 2cm in dimension was present on the right maxillary edentulous alveolus of the third molar area extending anteriorly to the buccal gingiva of the second molar (Figure 1A) and posteriorly to the tuberosity area (Figure 1B). Intraoral periapical radiograph for the edentulous alveolus of the third molar revealed surface erosion of the underlying bone (Figure 1C). There was no evidence of regional lymphadenopathy. A complete examination of the patient was done, but neither other primary site of the lesion nor regional as well as distant metastasis was found. Correlating all these clinical features, a clinical impression of

primary melanoma of the oral cavity was rendered and the patient was then referred to the Department of Oral & Maxillofacial Surgery for biopsy.

An incisional biopsy of the lesion was done under local anesthesia and the specimen was sent for histopathological examination. The hematoxylin-eosin stained section showed the connective tissue stroma was extensively infiltrated by nests of small, ovoid and/or spindle shaped dysplastic melanocytes with pleomorphic and hyperchromatic nuclei and dark brown melanin pigmentations (Figures 2A-C). Furthermore, the atypical melanocytes revealed cytoplasmic staining with HMB-45 (Figures 3A) and S-100 (Figures 3B), confirming the diagnosis of malignant melanoma. Junctional activity of the basal layer of the stratified squamous epithelium was also noted (Figures 2A & 3A). The patient was then advised to have surgical treatment but the patient's family needs further consultation due to the old age of the patient.

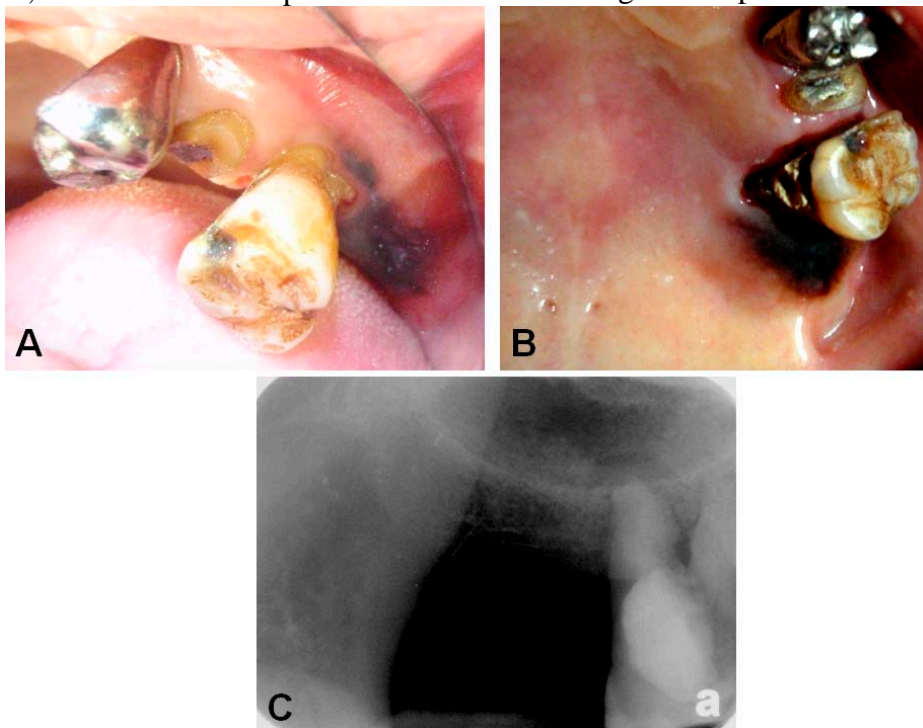


Figure 1 Buccal (A) and palatal (B) aspects of the blackish blue lesion; (C) The intraoral periapical radiograph of the region of edentulous alveolus of third molar revealed surface erosion of the underlying bone

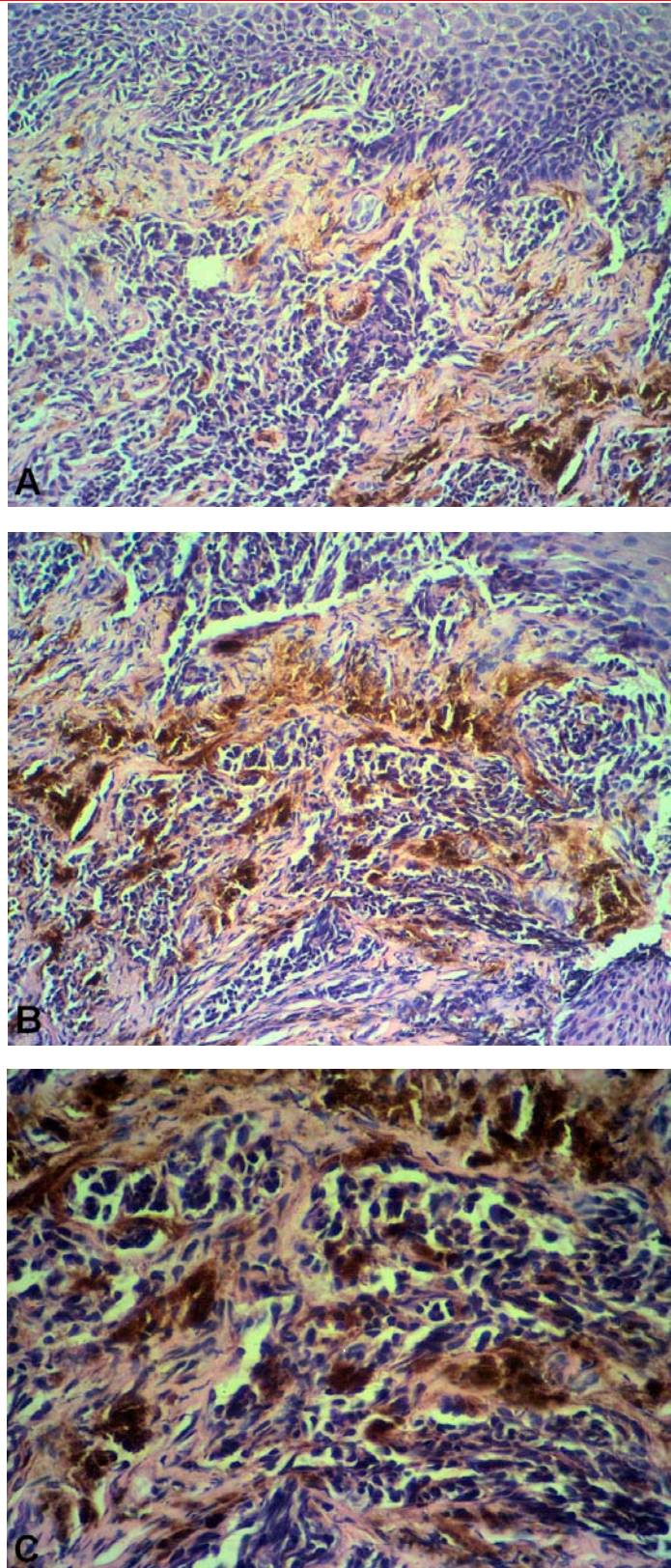


Figure 2 Histopathological examination of the lesion revealed the connective tissue stroma was extensively infiltrated by nests of dysplastic melanocytes with pleomorphic and hyperchromatic nuclei and dark brown melanin pigmentation. Junctional activity of the basal layer of the stratified squamous epithelium was also noted (Hematoxylin-eosin stain A $\times 100$, B $\times 200$, C $\times 400$)

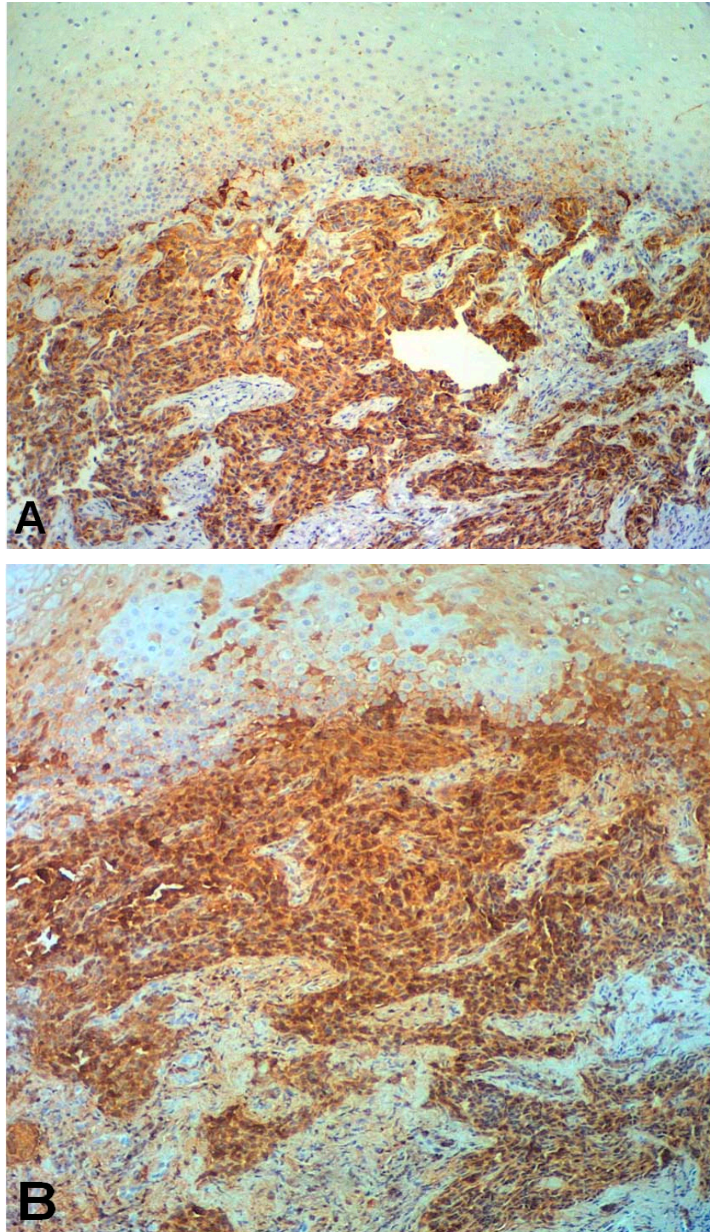


Figure 3 Immunohistochemical staining of HMB-45 (A) and S-100 (B) revealed diffuse positivity in the tumor cells. Junctional activity of the basal layer of the stratified squamous epithelium was also noted (A) (Avidin-biotin peroxidase complex staining $\times 100$)

COMMENTS

In contrast to cutaneous melanomas, no well-established etiologic or risk factors have been identified for oral melanomas. Those factors for the cutaneous melanomas are either unlikely (ultraviolet radiation) or have yet to be studied comprehensively (familial history, syndromes, cytogenetic defects) with oral counterparts [8]. Similar to

cutaneous melanoma, some primary oral melanomas are supposed to occur either from nevus, pre-existing pigmented areas or *de novo* (30% cases). Furthermore, mechanical traumas including injury from ill-fitting prostheses as well as infection to the oral mucosa have been proposed as possible factors, but all still lack direct

proof for their etiological role [9,10]. No obvious etiologic factors can be identified for our patient.

Oral cavity is not the only location of occurrence of mucosal melanoma; other mucosas may also be involved including eyes, upper respiratory tract, and vagina with the most frequent site is conjunctiva followed by upper respiratory tract and oral cavity. For the oral cavity, the common sites are gingiva and hard palate, affecting the maxilla in 80% of cases [11-13]. Our case has also been found in the maxillary gingiva extending from the second molar to the tuberosity.

Mucosal melanomas may be primary or metastatic from other area in the body [2]. Metastases occur via lymphatic or vascular route. Therefore, investigation of regional and distant lymph nodes as well as other organs is very important. It is also essential to differentiate the possibility of the primary melanoma elsewhere in the oral cavity. For any microscopic diagnosed oral melanoma, it is necessary to have a thorough investigation to evaluate the infiltration of the tumor and potential of distant metastasis due to its predilection for pulmonary, hepatic, brain and bone involvements [1]. For the present case, neither oral metastasis from other sites nor metastasis to the other organs has been confirmed.

Most oral melanomas are asymptomatic for a long duration and, hence, most oral lesions are usually large at presentation and the diagnosis is often delayed until symptoms of ulceration or bleeding is noted. As a result, the prognosis of oral melanoma is very poor [14]. Undoubtedly, early detection of the oral melanoma is important to a probable cure. The first symptom for the patient with oral melanoma is the occurrence of a pigmented, elevated mass on the mucosa (85% of cases) [15] or for other

situations, the initial symptom is pain (15% of cases) [16]. In our case, the patient did not aware for the presence a pigmented lesion, perhaps due to the fact that the lesion is painless, and in addition, it is neither ulcerated nor hemorrhages. This asymptomatic pigmented lesion is discovered by his family dentist on oral examination.

The differential diagnosis should include other melanotic diseases (melanocytic nevi, melanoacanthoma), physiological pigmentations, those related with systemic diseases such as Cushing's syndrome as well as Peutz-Jeghers syndrome, and chemical or physical pigmentations (amalgam tattoo) [13,17]. However, for many cases, the final diagnosis is solely depended on biopsy which must be done in the darkest and thickest area of the lesion. The histological diagnosis of melanoma, especially for amelanotic melanomas, can be confirmed by positive immunohistochemical staining for S-100 and HMB-45, as reported in the present case. Involvement of jawbone by oral melanoma is very rare. However, if it involves the jawbone, an ill-defined radiolucency with invasive border and floating teeth appearance may be evidenced [1]. For the present reported case, poorly defined radiolucency was demonstrated in the edentulous ridge.

In accordance to Rapidis et al [3], a primary oral melanoma should be confirmed for (a) clinical and histological demonstration that it is an oral melanoma, (b) presence of junctional activity in the lesion, and (c) the inability to demonstrate another primary tumor. All these three criteria have been fulfilled for the present case.

The recommended treatment for oral melanoma is wide surgical excision with adequate negative margins with or without neck dissection [13,18], if the neoplasm is found to be resectable, as

originally planned for the case presented here. Radiotherapy and chemotherapy is used as adjunctive treatment modalities. For cases where distant metastasis has been confirmed, and/or where there are recurrences, the lesions are regarded as typically incurable, surgery being used exclusively for palliative treatment.

Melanomas of the skin can be classified by Clark levels or Breslow tumor thickness grading system. The former classification evaluates the invasion depth, whilst Breslow's system determines the tumor thickness from the top of the epidermis to the maximum depth of the tumor. The possibility for developing metastatic lesions from primary melanomas of the skin increases with tumor thickness. However, both the Breslow and Clark grading systems have not been validated as prognostic predictors for melanomas of the oral cavity, perhaps due to the infrequency and peculiarity of oral lesion [19]. Furthermore, as aforementioned, in contrast to skin lesions, most oral melanomas are greater than 4 mm at the time of first presentation. This factor, in addition to insufficient resection of margins and higher stage at initial diagnosis, may lead to the difference in patients' 5-year survival rates between melanoma of skin and oral cavity [20]. In the case reported here, the patient was kept under follow-up.

Marco et al [21] proposed a TNM (T, primary tumor size; N, regional lymph node metastasis; M, distant metastasis) clinical staging system for oral melanoma. Then, according to this classification, oral melanoma is categorized as: Stage I: Presence of primary tumor only ($T_{any} N_0 M_0$), Level I: Pure in situ melanoma without evidence of invasion or in situ melanoma with microinvasion, Level II: Invasion up to the lamina propria, Level III: Deep skeletal tissue invasion into

muscle, bone or cartilage; Stage II: Tumor metastatic to regional lymph nodes ($T_{any} N_1 M_0$); Stage III: Tumor metastatic to distant sites ($T_{any} N_{any} M_1$). The patient presented here belonged to the classification of Stage I, Level II. On the other hand, the so-called ABCDE checklist (asymmetry, border, irregularities, color variegations, diameter greater than 6 mm, and elevation, a raised surface) is employed to identify cutaneous melanoma, could also claim to have some benefit in the identification of oral counterpart [22].

CONCLUSION

An uncommon case of primary oral melanoma has been reported. In addition, we emphasize that the general practice dentist, as shown in this report, should be alerted for the intraoral pigmented lesions which do not have apparent connection to physical or chemical factors and these pigmented lesions should be subjected to biopsy. ■

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