CASE REPORT

Primary Gingival Melanoma: An Important Entity

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Abstract Primary melanoma of the mandibular gingiva is extremely rare. It is often misinterpreted as a benign pigmented process. The prognosis of this entity is very poor. We report here the first case of primary gingival melanoma described in the Tunisian literature about a 55-year-old smoker having cerebral and pulmonary metastases from gingival melanoma at diagnosis. Our patient underwent brain radiotherapy at a dose of 18 Gy in three sessions but he died with a decline of 3 months before starting systemic therapy. Therefore, each new case should be illustrated to make clinicians aware about the importance of the early diagnosis to improve the poor diagnosis of this entity.

Keywords Primary gingival melanoma · Diagnosis · Treatment · Prognosis

Introduction

The oral cavity is a common site for pigmented lesions, most of them benign. Oral malignant melanoma is exceedingly rare. It represents 0.5 % of all malignant tumors of the oral cavity and 1 % of all melanomas [1]. It is usually diagnosed

in advanced clinical stage with 4–14 % of distant dissemination [2]. Therefore, dentists should be aware about this rare entity with poor prognosis to start treatment earlier. We report here a new case of gingival melanoma and we propose to analyze its characteristics.

Case Report

A 55-year-old smoker, without medical history, consulted for a mass of the oral cavity with heaviness in walking without weight loss. According to the patient, this gingival mass existed since 14 months and its pigmentation was progressive. Clinical examination showed a blackish pigmented and ulcerated gingival mass measuring 5 cm extended to tonsillar region with left cervical lymph node measuring 2 cm without other pigmented lesion in the skin. Neurological examination revealed left hemi paresis.

Facial computed tomography scan (CT) showed a left gingivo mandibular mass measuring 50 × 33 × 25 mm which takes the contrast. This mass extended from the mandibular region to tonsillar region (Fig. 1). Cerebral (CT) showed frontal and occipital secondary nodules measuring respectively 15 mm and 14 mm. Biopsy of the gingival mass with histopathological study concluded oral melanoma. The tumor was composed of melanocytes with large pleomorphic nuclei and eosinophilic cytoplasm. The cytoplasm of the tumor cells often contained melanin granules. Stroma was inflammatory and richly vascularized. Immunohistochemistry was positive for PS100, vimentin, Melan A and EMA (Fig. 2, 3, 4). Chest X-ray showed opacity of the left upper lobe. Chest CT scan showed bilateral pulmonary nodules.

Our patient underwent brain radiotherapy at a dose of 18 Gy in three sessions but he died with a decline of 3 months before starting systemic therapy.

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Fig. 1 Left gingivo mandibular mass in the CT

Fig. 2 The tumour is composed of melanocytes with large, pleomorphic nuclei and eosinophilic cytoplasm (*arrow*). (Hematoxylin and Eosin stain $\times 400$)

Discussion

Melanoma is a malignant tumor that usually involves the skin. Its incidence varies from 3 to 5/100,000/year in Mediterranean countries and 12–20 in Nordic countries and is still rising [3]. Mucosal melanomas account for 1.4 % of all melanomas. It may arise in the respiratory, gastrointestinal and urogenital tracts. Primary melanoma of the

Fig. 3 The cytoplasm of the tumor cells often contain melanin granules that vary in size (*arrow*). (Hematoxylin and Eosin stain $\times 400$)

Fig. 4 Note the ulcerated overlying mucosa (*star*) (Hematoxylin and Eosin stain $\times 400$)

mandibular gingiva is extremely rare [4]. It may be explained by the fact that epithelial lining of the oral mucosa contains melanocytes in its basal layer, which can evolve into melanoma as in the skin [4]. Primary gingival melanoma was described only from case reports and it is more frequent in the Japanese, Africans and Native North Americans. We report here the first case of gingival melanoma described in the Tunisian literature. It is more commonly diagnosed in older men compared with skin melanoma and is extremely rare prior to the age of 20 (median age at diagnosis, 56 years) which concord to our case [5]. The etiology of oral melanoma is unknown. Several risk factors have been proposed including human papillomavirus, denture irritation as chronic irritant, carcinogenic compounds, tobacco smoking, and chewing. However, there has been no evidence to support these risk factors. Other risk factors were described such

as a positive family history of melanoma and rarely inherited genetic mutation [6]. V600E, a protein substitution of valine for glutamic acid at position 600, is the most common BRAF mutation observed in cutaneous melanoma. Frequently, NRAS and BRAF mutations have been observed in subsets of mucosal melanoma [7]. Mutations in the c-KIT gene, along with BRAF mutations, in part, considered to be involved in the mechanism of development and progression of melanoma, have been identified in mucosal melanoma [8]. The BRAF and cKIT mutation were not tested in our case.

The intra-oral examination in our case showed pigmented and ulcerated lesion. In fact, data of the literature showed that oral melanoma vary from dark brown to blue-black, although it can be amelanotic. In 30 % of the cases, a mucosal pigmentation precedes the tumor appearance. The lesion surface can be smooth or ulcerated. The ABCDE criteria including asymmetry in the shape of the lesion, border irregularities, color variation, diameter >6 mm and evolving changes in the lesion over time may be used in the clinical diagnosis of oral melanoma [7, 8]. Physical examination with special attention to other suspicious pigmented lesions, tumor satellites, in-transit metastases, regional lymph node and systemic metastases is mandatory. In fact, cervical adenopathy can be present in 25 % of the cases as in our case. Distant metastases were pulmonary and cerebral in our case, and they represent the most common sites of secondary localization. Differential diagnosis includes oral melanotic macule, blue nevi, amalgam tattoo, smoking-associated melanosis, medication-induced melanosis (antimalarial drugs and Minocycline), and post inflammatory pigmentation and many other conditions [9]. Kaposi sarcoma and malignant melanoma should be eliminated before benign lesions. The keys for the diagnosis is biopsy with histopathological and immunohistochemistry study. In contrast to cutaneous melanoma, the mucosal melanomas usually have more frequent and aggressive growth phase. Different cell types, like spindled, plasmocytoid and epithelioid tumor cells arranged in a sheet like, organoide, alveolar, neurotropic or desmoplastic configuration may be observed. In our case, the immunohistochemistry was positive for PS100, vimentin, Melan A and EMA which concord to the literature.

The classifications that are usually used in cutaneous melanomas are hardly helpful in oral melanoma. The measurement of Breslow thickness is often difficult to use in this case [10]. Prasad et al. changed the TNM classification for the cervicofacial melanomas by proposing three stages: stage I: localized primitive tumor with no ganglion or metastasis, stage II: metastases in the regional lymph nodes and stage III: remote metastases.

The treatment of primary gingival melanoma is unclear. Surgery with complete excision with adequate negative

margins remains the preferred treatment for localized oral melanoma. Therapeutic neck dissection is indicated for lymph node metastasis in the neck. However, elective lymph node dissection in local disease is not recommended. Recently, surgical excision with a course of IL-2 as adjunctive therapy to prevent or limit recurrence has been proposed. Although melanoma is not highly radiosensitive, patients have occasionally exhibited a good response to radiation therapy, particularly in early melanomas. It reduces the rate of local recurrence without impact on overall survival [11].

Treatment modalities for advanced disease are similar to those used for cutaneous melanoma. Our patient had cerebral and pulmonary metastases. He underwent cerebral radiotherapy and was proposed to chemotherapy but he died before the systemic treatment. In fact, the treatment of metastatic oral melanoma consisted of immunotherapy and chemotherapy which exhibit a low response rate [11, 12]. Furthermore, the anti-BRAF like Vemurafenib has not been considered as a common treatment option for patients with mucosal melanoma, as BRAF mutations have been identified much less frequently in patients with mucosal melanoma [12]. The prognosis is poor, with a 5-year survival rate generally in the range of 10–25 %. The median survival is <2 years.

Conclusion

Primary oral melanoma is often misinterpreted as a benign pigmented process because of its rarity. Each new case should be illustrated to make clinicians aware about the importance of the early diagnosis to improve the poor diagnosis of this entity.

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