Primary Melanoma of the Oral Mucosa: A Case Report and Review of Literature

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Abstract

Primary oral melanoma is a rare neoplasm accounting for 0.5% of all oral malignancies. It has an aggressive behavior with a tendency of local invasion and distant metastases more readily than other malignant tumors of the oral cavity. Due to its rarity data on epidemiology, tumor behavior, treatment, follow up and survival of patients are mainly based on single case reports. Here we present a case of 85 years old female who presented with a hard palate blackish lesion and bilateral neck nodes enlargement, biopsy positive for malignant melanoma. With no evidence of extra oral primary melanoma evidence.

Keywords: Primary; Oral melanoma; Tumor; Biopsy

Introduction

Oral melanoma is an extremely rare tumor arising from uncontrolled growth of melanocytes found in the basal layer of the oral mucosa. Its incidence varies from 0.2% to 8% of all melanomas [1]. With an age range between 30 and 90 years, with a higher incidence in the 6th decade, and a mean age of 56 years [2]. It has a higher prevalence in yellows, blacks, Japanese, and Indians of Asia due to more melanin pigmentation in the oral mucosa in these races. Green et al. described criteria for diagnosis of primary oral melanoma which includes demonstration of melanoma in the oral mucosa, presence of junctional activity, inability to demonstrate extra oral primary melanoma [3].

A total of 80% to 90% of oral malignant melanomas arises in the mucosa of the maxilla with a majority occurring in the keratinized mucosa of the hard palate and gingiva. The other sites are mandibular gingiva, buccal mucosa, and floor of the mouth [4]. Clinically, it is easy to notice them as they usually present as pigmented lesions. They are mostly asymptomatic at presentation. The delayed detection is an important cause of poor prognosis [4].

Case Report

This is a case of an 85-year-old housewife. With ECOG performance status of 3 and no significant comorbidities. She reported to the dental hospital, with a black hard palate macular lesion 4 × 5 cm with intact surface, and bilateral upper cervical lymph nodes enlargement, 6 × 5 × 4 cm firm and fixed, (Figure 1), bad oral hygiene with extensive dental caries and loss of many teeth. Complete clinical examination was done and no other abnormality was detected. Correlating all the clinical features, a provisional diagnosis of primary malignant melanoma of the palate was made and the patient was referred for further investigations. CT of the chest, abdomen, and pelvis and bone scan, were all normal excluding any other primary sites or evidence of distant metastasis.

CT scan of the neck showed soft tissue mass at the right side of the oropharynx not separable from the mucosa, filling and obliterating the right para pharyngeal space, measuring about 4.5 × 3.2 × 3.1 cm, with multiple lytic lesions associated with enhancing soft tissue masses components noted in the left maxilla protruding from the hard palate, multiple bilateral enlarged lymph nodes at levels 2 and 3, the largest at the left posterior triangle infiltrating the sternocleidomastoid about 6.2 × 5.8 cm. CBC, Urea and electrolytes and LFT were all normal. An incisional biopsy was taken from the palate lesion under local anesthesia, and macroscopic features showed fragmented blackish soft tissue biopsy measuring in aggregate 1.2 × 1.2 × 0.4 cm, microscopic features showed malignant infiltrative tumor of atypical epithelioid cells exhibiting pleomorphism and cytoplasmic melanin granules, the malignant cells spread along the epithelial connective tissue junction with focal vertical growth consistent with malignant melanoma. In the superficial layers of the tissue, pigmented junctional nevus was found. The diagnosis of an invasive melanoma arising most likely from a pre-existing junctional nevus was made and the patient was seen at a multidisciplinary meeting. Our patient falls into class 2 because adjacent lymph nodes were involved (stage I clinically localized disease, stage II regional lymph nodes involvement, and stage III distant disease) [5]. The possibility of surgery was excluded due to the locally advanced disease and her low performance status, patient was given two phases of external irradiation using 2 lateral opposed wedged fields, two phases, a total dose of 5500 c Gy/20 fractions/4 weeks by Co 60 was given, off cord at the second phase (Figures 2 and 3).

Discussion

We reported a case of 85 years old female with primary malignant melanoma of the hard palate. The incidence of mucosal melanomas

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of the head and neck varies from 0.2% to 8% of all melanomas [5,6]. They affect adults mainly, with an average age of about 55, but with a uniform age distribution between 20 to 80 years [7]. Very rare cases have been reported in children. In most case reports, there is a male predominance, with a ratio of about 3:1. [8]. There are no known etiological factors associated with oral melanoma, but exposure to ultraviolet B light, sunburn, tobacco consumption, alcohol and chronic irritation from unstable dentures were all postulated [9]. To our knowledge this case is the second similar case reported from Sudan, Elneel et al. reported a case of a 47-year-old female diagnosed as oral malignant melanoma of the mandible with an unusual pattern of growth and clinical presentation [10]. From the UAE, Fatemeh et al. reported an aggressive case of oral melanoma in a 71-year-old male presenting with blackish gingival lesion, paresthesia, and denture ill-fitting [11]. Kai-Yuan Hsiao et al. from Taiwan in 2015, reported a case of a 70-year-old male who presented with a painless ulcerated mass at the right upper posterior gingiva. Pathology revealed a malignant melanoma, characterized by proliferative epithelioid cells with marked cytological atypia, frequent mitoses (more than 15 per 10 high power field), and dense lymphoid aggregation [12]. Kumar et al. reported a case in India of a 42-year-old woman with primary malignant melanoma at the left retromolar region a rare site, involving the left side of the mandible, up to level IV with ipsilateral cervical lymph nodes involvement. The patient was treated with left hemimandibulectomy, and radical neck dissection, and was followed up for two years and 3 months without any local recurrence or distant metastasis [13]. Masahiro Umed et al. reported a patient with malignant melanoma of the oral cavity who lived for a long period despite developing liver metastasis, an 81-year-old female who presented with a pigmented tumor of the lower gingiva. She had bilateral functional neck dissection and partial mandibulectomy. Pathology confirmed a malignant melanoma with regional lymph node metastasis. In spite of loco-regional control, liver metastasis developed 7 months after the surgery [14]. The initial symptoms and signs of oral melanoma is often a pigmented growth or swelling. The surface may be smooth, intact or ulcerated. Satellite foci may surround the primary tumor. The color may be uniformly brown or black or may show variation of color, with black, brown, grey, purple, and red shades, or hypo pigmented [15]. In a melanotic melanomas, pigmentation is absent [16]. Oral melanoma has an initial phase characterized by radial growth followed by a phase of invasion of the underlying tissues the so-called, vertical growth phase. Regional lymph nodes involvement denotes a poor prognosis [17]. Clinically, oral melanomas are classified into five types: pigmented nodular, non-pigmented nodular, pigmented macular, pigmented mixed, and non-pigmented mixed [18]. Distant metastasis usually to the lungs, brain, liver, and bones are frequently observed [19].

Usually oral malignant melanoma can be diagnosed with confidence on hematoxylin and eosin–stained sections. If pigment is completely absent [a melanotic melanoma], immune-histochemical stains are helpful. Useful markers include S-100 protein, gp 100 (HMB-45), and Mart-1 (Melan A) [20].

Treatment of OM is still controversial. There are no randomized trials studying treatment modalities such as surgery, radiotherapy, or chemo-/immunotherapy for oral melanomas. Surgical resection remains the treatment of choice and can result in cure in early cases [21-23]. Excision of the primary lesion with at least a margin of 1.5-cm of healthy tissue, is recommended [24]. Patients with primary OM present with lymph node metastasis in 25% of cases [25]. Neck dissection should be reserved for cases with preoperatively confirmed lymph node metastases and the choice of the neck dissection modality should be guided by the extent and the level of the nodes [25]. Prophylactic lymph node dissection has no overall survival benefit as was observed in systematic review and meta-analysis of randomized controlled trials [26,27]. The role of adjuvant therapy was not studied in randomized trials because of rarity of the disease [28]. Most authors recommend adjuvant radiation to the primary sites and lymph node regions [29]. Although interferon-a2b is frequently offered to mucosal melanoma patients as systemic adjuvant therapy, it has not been formally studied in this patient population [30]. Marked tumor regression was reported in one study in patients with metastatic mucosal melanoma who were treated with single agent Imatinib [30]. Although OM is regarded as radio resistant, postoperative external radiotherapy is recommended if poor prognostic pathologic features are present, such as multiple positive nodes, or extra capsular spread. Intraoral mould (60 Co, 192Ir, or 198Au), as well as intraoral electron beam and interstitial brachytherapy were used with no survival outcome [30]. Different combinations of the following cytotoxic drugs dacarbazine, platinum analogs, nitrosoureas, micro tubular toxins, dimethyl triazeno imidazol carboxamide, mustine hydrochloride, or vincristine were used without any significant improvement in overall survival [31]. Iplimunumab (CTLA-4) antibody was approved in 2014 in treatment of melanoma and was the first agent to be associated with an improvement in overall survival 3.4 months in patients with metastatic melanoma [32,33], and when added to dacarbazine. Overall survival was significantly increased by 2.1 months, [34].

It was reported in ASCO 2016, that PD-1 inhibitor pembrolizumab provides long-term survival benefit for patients with advanced melanoma, 40% of patients were alive 3 years after using the drug.

15% of patients in this study experienced complete remissions, 89% remain in remission [35]. Two Additional studies confirmed the survival benefit of pembrolizumab in patients with advanced melanoma,
compared with chemotherapy or ipilimumab [36]. These data add to the evidence supporting the durability of long-term survival in ipilimumab-treated patients with advanced melanoma median OS was 11.4. [37]. In 5 February 2016 (Australia) New research shows long-term survival in group of advanced melanoma patients treated with BRAF inhibitors dabrafenib and trametinib, (62%) were still alive 3 years after starting treatment. This is a great improvement over the survival rates, only 5 years it was less than 10%. We presented a rare case of palate melanoma. Prognosis of this malignancy is poor and it's both chemo resistant and radio resistant, treatment with immune-checkpoint inhibitors PD-1/ PD-L1 and CTLA4 inhibitors in the coming future may give hope for both patient and oncologist. The stage of the tumor at time of diagnosis impact the survival of patients, medical doctors and dentists should keep the possibility of malignant melanoma in mind during any differential diagnosis of suspicious oral lesions.

References