Primary mucosal melanoma of the oral cavity: current therapy and future directions

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Background. Primary mucosal melanoma of the oral cavity is a highly aggressive malignancy of melanocytic origin. The aim of this study is to report a case series of oral mucosal melanomas (OMMs) and provide a review of the literature with regard to treatment guidelines for and prognosis of this pathologic entity.

Study Design. We report three cases of OMMs treated in our institutions and the results of a literature review, in which the words "oral" and "mucosal melanoma" were used as the main keywords.

Results. Surgical resection of the primary tumor with wide resection margins appears to be the recommended primary treatment modality with the aim to achieve tumor-free margins. Elective neck dissection and adjuvant radiotherapy have been advocated for locoregional control. Chemotherapy has not been shown to improve survival and is mainly used for palliative purposes. Immunotherapy and biochemotherapy seem to significantly improve survival and could open new therapeutic horizons.

Conclusions. The prognosis of OMMs remains poor despite treatment. Early diagnosis and aggressive surgical resection followed by adjuvant therapies could be the key to improving survival. Multicenter randomized clinical trials, which may be difficult to conduct because of the rarity to the lesion, would aid in the development of new strategies. (Oral Surg Oral Med Oral Pathol Oral Radiol 2016;122:17-27)

Primary mucosal melanoma of the head and neck region is a rare, aggressive malignancy of melanocytic origin.[1] It is often associated with early distant dissemination and high rates of treatment failure.[2] According to the US National Cancer Database, only 611 (.7%) of the 84,836 melanoma cases were found to be of head and neck mucosal origin.[3] Almost 50% of mucosal melanomas are located in the oral cavity, representing .5% of all oral malignancies and less than .01% of all oral biopsies.[1,4] The palate (47%) and the gingiva (27.6%) are the most commonly encountered anatomic sites of origin, followed by the retromolar region and the buccal mucosa.[5] Typically, they present after the fifth decade of life (median age at diagnosis 65−69 years), with a slight male predilection (1.2:1) according to the Cancer Incidence in Five Continents (CI5-IX) database.[5]

In addition to the significantly lower incidence, oral mucosal melanomas (OMMs) also differ in invasion progress, exposure profiles, clinical behavior, and treatment response from their cutaneous counterparts.[6-9] In contrast to cutaneous melanomas, mucosal melanomas have not been adequately studied because of their low prevalence and the lack of long-term follow-up to allow for prospective randomized clinical trials to be conducted. The aim of this report is to present a case series of four OMMs treated in two institutions by the Oral and Maxillofacial Surgery service and review the available English language literature with regard to available treatment guidelines and outcomes. In addition, we provide a review on the available data on the pathogenesis, histopathologic features, and classification of OMMs, as well as diagnosis and staging.

MATERIALS AND METHODS

Two cases of OMM treated at the "G. Papanikolaou" General Hospital/Aristotle University of Thessaloniki (AUTh) and one case of OMM treated at the University of Illinois at Chicago (UIC), in their respective Departments of Oral and Maxillofacial Surgery (OMFS) between 2010 and 2013 (UIC case: 2011 and 2014) were identified and are presented here. The report of this case series meets the criteria of exemption from the Institutional Review Board for the protection of Human Patients from UIC and the "G. Papanikolaou" General Hospital. All patients treated in both institutions had consented to clinical photos being obtained by the treating doctors. In addition, we conducted a review of

Statement of Clinical Relevance

Primary oral mucosal melanoma is one of the most aggressive malignancies in the head and neck region. The prognosis is very poor. Early diagnosis is the key, and aggressive treatment is required.

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Figure 1. Intraoral presentation of oral mucosal melanoma in the anterior maxilla (Case #1).

the relevant English language literature using the Medline database from April 1982 to the present. "Oral melanoma" and "mucosal melanoma" were used as the main keywords; "head and neck," "diagnosis," "staging," "outcomes," "surgery," "radiotherapy," "chemotherapy," and "immunotherapy" were used in conjunction with the main keywords.

RESULTS

Case 1

A 53-year-old Hispanic male presented to the OMFS at UIC for evaluation of a lesion in the anterior maxillary gingiva in the area of teeth #6–#9 extending into the vestibule and the palatal gingiva (Figure 1). His medical history and social history were noncontributory. His surgical history was significant for removal of a similar lesion in the same location by his dentist 2 to 3 months earlier in Mexico. The excised lesion was never submitted for histopathologic examination as it was thought, per the patient's report, to represent reactive tissue from the newly fabricated prosthetic work that was done by the same dentist few months earlier. The patient denied pain, numbness, or loosening of teeth in the area, but he did state that the area bled while performing oral hygiene. He further denied constitutional symptoms, weight loss, or fatigue.

On clinical examination, the lesion appeared to be a broad-based, well-defined, bluish-purple soft tissue mass that did not blanch on palpation. Radiographic examination, with periapical X-rays and panoramic radiography, did not demonstrate significant bone loss

Figure 2. Resection specimen-composite anterior maxillectomy- of oral mucosal melanoma (Case #1).

around the teeth in the location corresponding to the lesion. No other lesions were identified in the oral cavity or elsewhere in the body. Bilateral level I, freely movable lymph nodes were palpated. An incisional biopsy of the primary lesion was performed, and the diagnosis of oral mucosal melanoma of the spindle type was confirmed. Further workup included contrast-enhanced computed tomography (CT) of the head and neck, chest, abdomen, and pelvis and a complete blood laboratory workup, including liver function enzymes. CT of the head and neck revealed a nonenhancing mass measuring roughly 4.4 cm in transverse diameter × 2.0 cm in anteroposterior diameter × 1.7 cm in superoinferior diameter in the anterior maxilla, with no evidence of underlying bone loss or reactive bilateral cervical lymphadenopathy at level I. Based on radiographic criteria, none of the lymph nodes was suspicious for a metastatic process. No other pathologic findings were identified. The patient's disease was staged as T4 aN0 M0. Following discussion at the institutional multidisciplinary head and neck tumor board, the decision was made to perform a composite anterior maxillectomy that included the upper lip (Figure 2). Reconstruction was done with local flaps and fabrication of an obturator. Neck dissection was discussed as well, but the patient refused to undergo bilateral neck dissections, which was our recommendation. Clear