Abstract

The diagnostic procedure of pigmented lesions of the oral cavity and perioral tissues is a challenging one. Even though epidemiology may be of some help in orientating the clinician and even though some lesions may confidently be diagnosed on clinical grounds alone, such a diagnosis remains “provisional”. A definitive diagnosis usually requires histopathological evaluation. Occasionally, immunohistochemical stains such as melanocyte marker HMB-45 and macrophage marker CD68 may be required to arrive at a correct diagnosis. The so-called ABCD checklist (“Asymmetry”, “Border” irregularities, “Color” variegation and “Diameter” > 6mm) that is commonly used to aid in the identification of cutaneous melanoma may also be of some help in the clinical diagnosis of oral malignant melanoma (OMM). Rapidly growing pigmented lesions should always be biopsied. Location on the palate increases the rate of suspicion of melanoma and usually requires a biopsy or long-term follow-up.

A critical analysis of the literature on human OMM discloses a lack of thorough knowledge on the etiology and pathogenesis of this malignancy as well as a lack of evidence on the best therapeutical approach. The hypothesis that inhaled environmental carcinogens, including tobacco and formaldehyde, may have some influence in promoting an abnormal melanocytic proliferation is based on few epidemiological observations. Most of the reports do not include data on the presence or absence of exposure to carcinogenetic factors. p53 protein alterations have been identified in about two-thirds of OMM.

Surgical excision is the most frequently reported treatment for OMM. Surgery could be combined with radiotherapy, chemotherapy or immunotherapy even though the effectiveness of such therapies either as primary treatment or in association with surgical treatment is largely unknown. The Amsterdam experience with 14 patients affected by OMM confirms the extremely malignant and aggressive behaviour of this neoplasm. Five patients developed a local recurrence within a period of 4 to 72 months and 10 patients developed distant metastases within a period of 6 to 78 months. Ten patients died of their disease within an average interval of 40 months, with a range of 12 to 80 months. Of the ten patients who qualified for evaluation of the five-year survival rate, one was alive with disease and two were alive without evidence of disease, which results in a 30% five-year survival rate. However, all patients have died of their disease before the end of the ten-year follow-up period.

From the histopathological point of view it seems remarkable to report a case of OMM associated with pseudoepitheliomatous hyperplasia (PEH). The presence of both melanocytic and keratinocytic cells could lead to the misdiagnosis of a tumour with biphenotypic characteristics such as OMM associated with squamous cell carcinoma (SCC) or pigmented SCC. The presence of PEH along much of the surface epithelium, in the absence of underlying salivary gland tissue, appears to point at an origin of the PEH from the surface epithelium itself.

In another case, the presence of melanotic pigmentation of the palatal minor salivary glands was documented four years before a diagnosis of an OMM of the palate was established. Presence of melanin pigment within the epithelial cells of minor salivary glands is an exceptional finding and the biological mechanism underlying this phenomenon is unknown. The concept of “melanogenic metaplasia” as being proposed by Shivas and McLennan is an interesting one. However, until now there is no scientific evidence to support such concept. It is questionable whether melanotic pigmentation of the palatal minor salivary glands represents a potentially malignant disease.
Data from the literature show that about 30% of OMM are preceded by mucosal pigmentation for several months or even years. Some of these flat precursor lesions consist of cytologically atypical melanocytes and may in fact constitute the preinvasive macular phase of melanoma.

The apparently strong correspondence between oral subsites affected either by oral melanocytic naevi (OMNs) and OMMs (hard palate, mucobuccal fold, gingiva) may constitute an indirect argument supporting the idea that some OMNs do progress to OMM. However, the results of our own study do not confirm the hypothesis that the presence of an OMN indicates a risk of future development of OMM. In fact, None of the 119 patients with a diagnosis of OMN developed a malignant melanoma in the oral cavity in a mean follow-up period of 8.6 years.

With regard to the whole group of patients affected by head and neck mucosal melanoma (HNMM), oral malignant melanoma seems to affect patients at a younger age (mean age 58.8 years) than patients with sinonasal mucosal melanoma (SNMM) (mean age 67.1 years). The number of patients who experienced regional and/or distant metastases as well as a local failure was higher among those who did not receive postoperative radiotherapy. In particular, the percentage of neck lymph node metastases seems to be significantly decreased by the administration of radiotherapy. Surprisingly, the analysis of the overall 5-year survival rate through the Kaplan-Meier estimator, showed a better prognosis for patients treated by surgery without postoperative radiotherapy. A similar result was shown when the analysis was separately performed for patients with SNMM and patients with OMM. Because of the retrospective nature and the incompleteness of the clinical records no clear guidelines were provided with regard to the indication for postoperative radiotherapy. A bias of the present evaluation may be represented by the fact that melanomas with an apparently intrinsic worse prognosis (e.g. SNMM) are overrepresented in the group of patients receiving a combined treatment.

Unfortunately, the rarity of this neoplasm makes it rather unrealistic to perform a randomized-controlled trial for a critical evaluation of the role of postoperative radiotherapy.

The observation by Prasad et al. that the histopathological microstage for stage I disease of OMM, reflecting tumour progression within the surrounding tissues, is a predictor of survival, is not supported by the results of the present study.

The overall 5-year survival rate for the entire group of HNMM patients of the present series is 17.2%. A site specific difference was noticed with regard to survival. Patients with OMM seem to have an better disease-specific 5-year survival rate than patients with SNMM.