Multifocal amelanotic and melanotic melanomas of the oral cavity

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DESCRIPTION

A healthy woman in her 60s presented to her general dentist for a routine check-up. Examination of the oral cavity revealed a small non-pigmented tumour at the gingival margin of the right maxilla, unknown to the patient (figure 1A). The vascularised tumour measured 5×6 mm and was slightly elevated from the underlying tissue. The lesion was excised with a margin of 1 mm. Histological examination showed a broad-based, epithelium-lined outgrowth, with ulceration in the most prominent region. The epithelium was atrophic, but with some elongated rete pegs with keratin pearls, compatible with pseudoepithelial hyperplasia. The diagnosis of malignant melanoma was confirmed with HMB-45, S100, SOX-10 and Melan A staining (figure 2). Ki-67 staining showed high mitotic activity. Staining with Schmorl was negative, confirming an absence of melanin pigmentation. In the connective tissue, there was a dense infiltrate of tumour cells, with relatively large, mainly spindle-shaped cells, partly organised in nests. Malignant cells were also invading epithelium (figure 3). Next, the patient was referred to a regional university hospital where clinical examination of the oral cavity revealed an additional non-pigmented ulcer of the hard palate (figure 1B), as well as diffuse pigmentation of the soft palate (figure 1C). Incisional biopsies were performed, and histological diagnoses of malignant melanoma were confirmed for both lesions. Further investigation included positron emission tomography-CT and MRI, where no other primary tumours or metastases could be detected. The final diagnosis was set to be multifocal malignant melanoma isolated to the oral cavity. Due to the multifocal location of the tumours, immunotherapy was initiated. However, the patient developed autoimmune toxicity following treatment, and the immunotherapy had to be discontinued. The patient was treated with high-dose corticosteroids and surgical treatment with a hemimaxillectomy and reconstruction with a radial forearm flap. She has no signs of recurrency 1 year after surgery and 18 months after the initial diagnosis.

This report describes an unusual case of multifocal malignant melanoma isolated to the oral cavity, with both amelanotic and melanotic

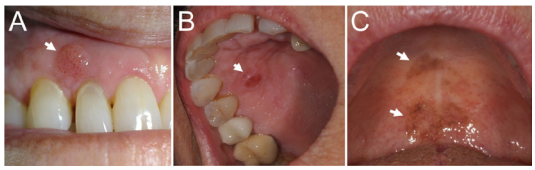

Figure 1 Clinical photos: (A) amelanotic melanoma of the gingiva (arrow); (B) amelanotic melanoma of the hard palate (arrow); (C) multifocal melanotic melanoma of the soft palate (arrows).

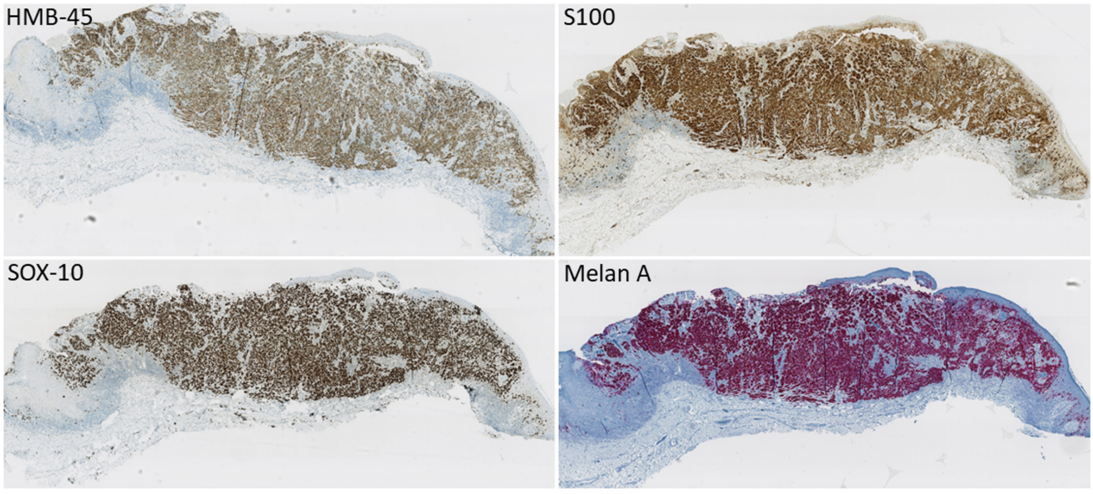

Figure 2 Histology. Immunohistochemical staining of the non-pigmented tumour presented in figure 1A, showing partly ulcerated tissue infiltrated with tumour cells in stroma stained with four different antibodies (HMB-45, S100, SOX-10 and Melan A), all confirming malignant melanoma.

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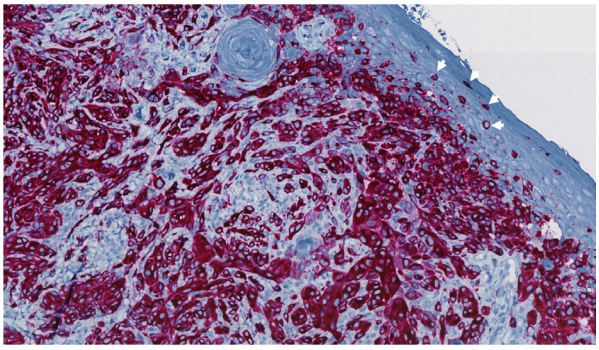

Figure 3 Melan A staining of amelanotic melanoma. A dense infiltrate of tumour cells in the connective tissue was found, with relatively large, mainly spindle-shaped cells, partly organised in nests. Malignant cells were also invading the epithelium (arrows).

lesions. The innocuous clinical presentation of the case illustrates the importance of biopsy of tumours and ulcerative lesions of the oral mucosa, regardless of size. Mucosal oral malignant melanoma is a rare form of melanoma, accounting for only 1%–3% of the cases.[1] Distinct molecular features including a lower incidence of BRAF oncogene mutations, but a higher incidence of KIT oncogene mutations, suggest divergent genetic aetiologies.[2] Surgery is considered the primary treatment option, followed by adjuvant radiotherapy. However, such treatment is often challenging, especially in cases of multifocal primary tumours, due to adjacent anatomical structures and often delayed diagnosis.[3] Treatment with targeted therapies and immunotherapies with checkpoint inhibitors is increasingly investigated, but the evidence is limited to a low volume of cases, and the majority of data are obtained from case reports and treatment of cutaneous melanomas. To date, there is no consensus or international guidelines regarding use of immune checkpoint inhibitors (ICIs) in treating non-cutaneous melanomas. Autoimmune toxicities are commonly reported including high-grade toxicity in up to a half of patients and fatal toxicities in 0.4%–1.2%, depending on the administered ICI regimen.[4]

Patient's perspective

My general condition has improved after discontinuing immunotherapy, which I found very demanding. Surgical treatment was extensive, but I am now feeling better and looking forward to the future.

Learning points

- Multifocal malignant melanoma of the oral cavity can present as both amelanotic and melanotic lesions.
- Treatment can include both immunotherapy and surgical resection.
- Immunotherapy is commonly associated with autoimmune toxicity.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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