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Primary Invasive Intraoral Malignant Melanoma of the Mandibular Mucosa

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Primary oral malignant melanoma is an exceptionally rare neoplasm, comprising approximately 0.2-8% of all melanomas, with even fewer cases originating from mandibular mucosa. It is characterised by an aggressive clinical progression, rapid local invasion, early metastases and poor prognosis. Unlike cutaneous melanomas, oral melanomas often present asymptomatically, which significantly delays diagnosis and limits treatment options. This report presents a case of a 78-year-old female patient with an asymptomatic, pigmented lesion located in the left mandibular region. Radiological imaging revealed an infiltrative heterodense mass with underlying bone destruction. The histopathological analysis showed solid tumour nests with marked atypia and brown pigmentation. Immunohistochemical staining demonstrated strong positivity for S-100 and Melan-A, confirming the diagnosis of primary invasive mucosal melanoma. This case underscores the diagnostic challenges posed by mucosal melanomas, particularly in atypical locations such as the mandible, and emphasizes the critical role of early biopsy and immunohistochemistry in establishing a definitive diagnosis.

Key words: melanoma, oral, mucosa, mandible, primary

Introduction

Melanomas are malignant neoplasms arising from melanocytes, which are neural crest-derived cells [3, 5, 7, 8]. The first description of oral mucosal melanoma was provided by Weber in 1859, and in 1869, Lucke coined the term "melanotic sarcoma" [2, 4 ,8]. Most melanomas develop on the skin, originating from melanocytes in the basal layer of the epidermis.

Mucosal melanomas constitute approximately 1.4% of all melanomas across all races, and 0.8-3.7% among Caucasians. Some sources report a higher incidence in Asians (particularly Japanese), Indians, Hispanics and individuals of African descent [5, 9] – possibly due to the greater prevalence of oral mucosal pigmentation – whereas

others suggest a higher incidence in Caucasians. Mucosal melanomas have been documented in various anatomical sites, including the rectum, anal canal, vagina, cervix, larynx, esophagus, and head and neck regions. Within the head and neck, the oral cavity is the least frequently affected site [4, 9].

Primary intraoral malignant melanoma is a rare and aggressive subtype with a greater propensity for rapid metastasis and often presents asymptomatically. Consequently, it is frequently diagnosed at an advanced stage, contributing to its poor prognosis and low survival rate [2, 9]. An important fact to note is that tumour thickness, ulceration and level of invasion are not of any prognostic value [9].

Case Report

We report the case of a 78-year-old female patient who presented with an asymptomatic lesion located in the upper ridge of the left mandibular region. The lesion exhibited infiltrative behavior and destruction of the surrounding bone. A CT scan revealed a heterodense mass measuring 31 × 48 mm, involving adjacent tissues. Clinically, the lesion appeared darker in colour. No relevant clinical history was provided. A biopsy sample was submitted to our department for histopathological evaluation.

Materials and Methods

Tissue specimens were fixed in 10% neutral buffered formalin and embedded in paraffin. Sections of 4 μm thickness were obtained for histological analysis. Further immunohistochemical testing was performed to confirm the diagnosis using the following antibodies – **S-100, Melan-A, p63, CK AE1/AE3, CK34βE12**. All the antibodies are supplied by Dako and are ready-to-use (pre-diluted). The staining protocols are validated by Dako.

Results

Hematoxylin and eosin (H&E) staining revealed fragmented material covered with multilayered squamous epithelium. Underlying infiltration of solid tumour nests exhibiting marked cellular atypia and the presence of brown pigment, with focal ulceration of the overlying mucosa. The most likely diagnosis is primary invasive melanoma of the oral mucosa (**Fig. 1).**

Immunohistochemical analysis supported this diagnosis: S-100 and Melan-A **- strong positive (+++) in tumour cells;** p63**,** CK AE1/AE3**,** CK34βE12 - negative in tumour cells and positive in squamous epithelium (internal control); CD79a - negative in tumour cells (**Fig. 2, Fig. 3).**

The comprehensive immunohistochemical panel confirmed the final diagnosis of primary invasive malignant melanoma of the mandibular mucosa, as supported by the images below:

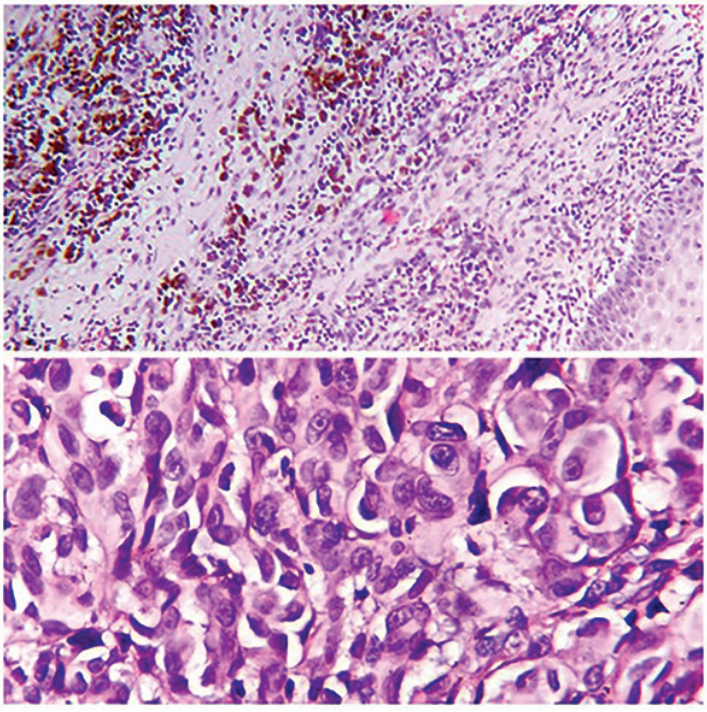

Fig. 1. Solid nests of polygonal atypical cells filled with intracytoplasmic brown pigment H-E (Upper picture x 200) and an achromatic area with scarse pigment granules H-E (lower picture ×400).

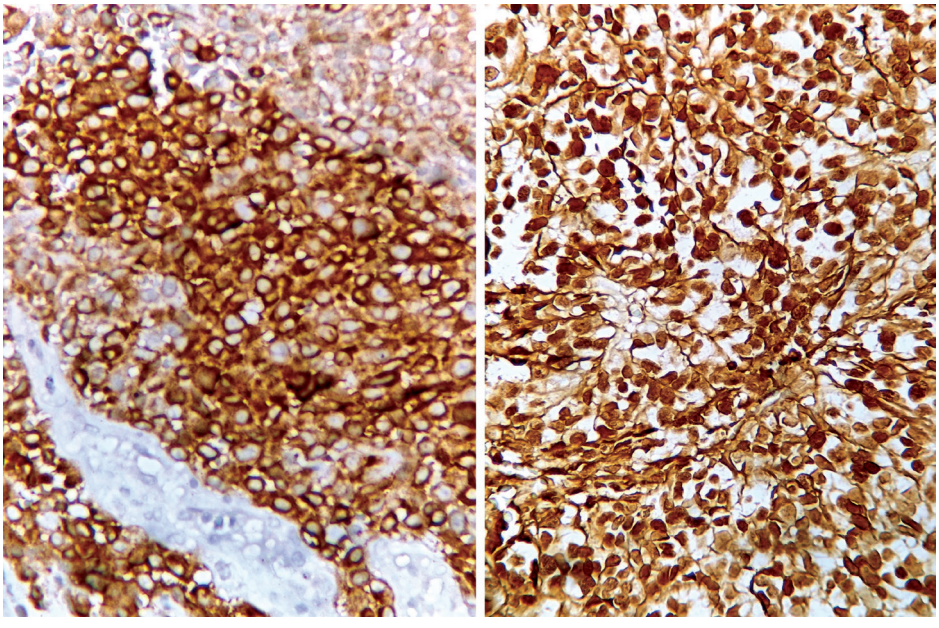

Fig. 2. Strong positive reaction in the tumour cells with Melan-A (left x400) and S-100 (right ×400)

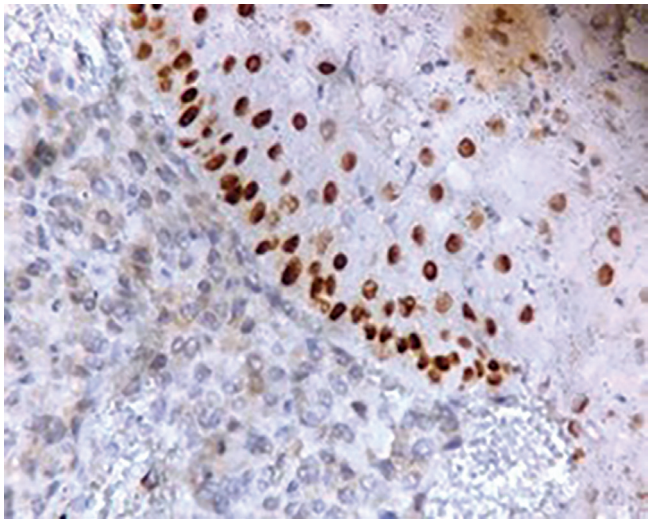

Fig. 3. Negative reaction in the tumour cells, with a positive internal control in the epithelial cells with p63 (×400)

Discussion

Primary mucosal malignant melanoma of the mandible is an exceptionally rare tumour, with mandibular localization being particularly uncommon. While the etiology remains unclear, some reported contributing factors may include smoking, denture use, and exposure to carcinogens such as tobacco and formaldehyde [3, 4]. Genetic mutations such as NRAS**,** BRAF**, and c-**KIT **have been implicated [7, 8]. Although the lesion can occur at any age, the average age of diagnosis is around 56 years [4]. The condition is reported to be two to three times more common in males than females [2, 3, 4, 8].**

Within the head and neck region, the most frequent sites of mucosal melanoma include the nasal cavity/septum and maxillary sinus, followed by the paranasal sinuses and, less commonly, the oral cavity. When present in the oral cavity, lesions most frequently involve the palate and maxillary gingiva (in 80–90% of cases) [1, 2, 3, 4, 6, 7, 8].

The differential diagnosis of oral melanoma includes [4, 6, 7]:

- Amalgam tattoo
- Melanotic macule
- Melanotic nevus
- Melanoacanthoma
- Post-traumatic or racial pigmentation
- Systemic conditions (e.g., Peutz–Jeghers syndrome, Addison‘s disease)
- Drug-induced pigmentation
- Vascular malformations
- Epulis, pyogenic granuloma, irritation fibroma
- Peripheral giant cell granuloma, peripheral ossifying fibroma
- Kaposi sarcoma
- Metastatic non-pigmented lesions

The reported five-year survival rate is approximately 7% [7], underscoring the aggressive nature and diagnostic challenges of this malignancy.

Conclusion

This case underlines the importance of considering primary mucosal melanoma in the differential diagnosis of pigmented oral lesions, especially in older patients – even in the absence of symptoms. Early biopsy and histopathological evaluation, supported by immunohistochemistry, remain critical tools for accurate diagnosis. Given the aggressive behaviour and poor prognosis associated with oral melanomas, raising clinical awareness and promoting routine oral examinations may aid in earlier detection and potentially improve patient outcomes.

Patient consent

The authors certify to obtaining the patient's consent for using of the information, age and gender, as well as pictures of the microscopic slides.

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