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Case Report

Oral mucosal melanoma with contrasting clinical presentations: a case series

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Abstract

Background: Oral mucosal melanoma (OMM) is a rare and aggressive malignancy accounting for approximately 0.2%–0.8% of all melanomas. Its heterogeneous clinical presentation and frequently asymptomatic early course may contribute to delayed recognition and diagnosis.

Case presentation: We report two cases of OMM with markedly contrasting clinical presentations. Case 1 involved a 67-year-old woman who presented with a painful pigmented gingival lesion noticed approximately two weeks before clinical evaluation. The lesion was relatively localized and was subsequently treated surgically. Case 2 involved a 51-year-old woman with a pigmented maxillary gingival lesion reportedly present for approximately 10 years before developing progressive nodular enlargement, pain, bleeding, and extensive involvement of the maxillary gingiva and hard palate. Both lesions received a histopathological diagnosis of microinvasive oral melanoma, despite their substantially different clinical extent and evolution.

Conclusion: These cases illustrate the considerable clinical heterogeneity of OMM and reinforce the importance of timely biopsy of suspicious oral pigmented lesions, particularly when changes in size, color, surface morphology, nodularity, ulceration, or bleeding are observed. They also highlight the need to interpret histopathological findings from incisional biopsies in conjunction with the overall clinical extent of the lesion.

Keywords: Oral mucosal melanoma; Oral melanoma; Pigmented oral lesions; Case series; Oral cancer.

Statement of Clinical Significance: This case series demonstrates the marked clinical heterogeneity of oral mucosal melanoma, showing that lesions with the same histopathological diagnostic designation may present with substantially different clinical extent and evolution. The cases reinforce the importance of careful evaluation and timely biopsy of suspicious oral pigmented lesions, particularly when changes in size, pigmentation, surface morphology, nodularity, ulceration, or bleeding are observed. They also highlight the importance of interpreting findings from incisional biopsies in conjunction with the overall clinical presentation of the lesion.

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1 Introduction

Oral mucosal melanoma (OMM) is a rare malignant neoplasm arising from melanocytes of the oral mucosa and accounts for approximately 0.2%–0.8% of all melanomas. Despite its rarity, OMM is characterized by aggressive biological behavior, a substantial propensity for local and distant spread, and unfavorable survival outcomes [1–4]. Contemporary systematic reviews and large retrospective series continue to demonstrate that OMM is frequently diagnosed at an advanced stage and is associated with poor long-term survival. [1,2,14,15]

Clinically, OMM may exhibit considerable heterogeneity. Lesions may present as macules, plaques, nodules, exophytic masses, or ulcerated lesions and may display brown, black, blue, gray, purple, or heterogeneous pigmentation. Amelanotic lesions can also occur, further complicating clinical recognition [3–5]. Early lesions may remain asymptomatic, and their resemblance to benign oral pigmentation may contribute to delayed diagnosis [4,5].

The hard palate and maxillary gingiva are consistently reported as the most frequently affected oral sites [1–4]. Clinical evolution may also vary considerably. Some lesions are detected shortly after the development of symptoms or visible changes, whereas others are associated with a history of long-standing pigmentation before enlargement, nodular development, ulceration, or bleeding becomes evident [5–10]. Importantly, however, a history of long-standing pigmentation followed by clinical progression does not, in the absence of previous histopathological evaluation, establish malignant transformation of a pre-existing benign melanocytic lesion.

Histopathological examination is essential for definitive diagnosis. OMM may demonstrate proliferation of atypical melanocytes along the epithelial–connective tissue interface, intraepithelial spread, and varying degrees of invasion into the underlying connective tissues. Immunohistochemical markers such as S100 protein, HMB-45, and Melan-A are commonly used to support melanocytic differentiation [11].

In this context, the present case series describes two oral melanomas diagnosed as microinvasive but exhibiting markedly different clinical presentations and disease trajectories, emphasizing the importance of clinicopathological correlation in the assessment of this rare malignancy.

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2 Case series

Case 1

A 67-year-old woman presented to an oral medicine service with a painful gingival lesion. According to the patient, the lesion had first been noticed approximately two weeks before consultation during routine tooth brushing. She reported a burning sensation associated with the lesion, particularly during eating and oral hygiene procedures.

Intraoral examination revealed a pigmented nodular lesion involving the right maxillary gingiva in the region of FDI teeth 15 and 16. The lesion presented as an irregular, sessile, purple-gray nodule with peripheral ulceration and extension from the buccal to the palatal gingiva (Figure 1A–C). Because of its suspicious clinical appearance, the patient was referred for specialized evaluation, and an incisional biopsy was performed.

Histopathological examination of the incisional gingival biopsy revealed a malignant melanocytic neoplasm characterized by proliferation of atypical melanocytic cells arranged in sheets and nests within the connective tissue. Numerous neoplastic cells exhibited brown cytoplasmic pigment consistent with melanin (Figure 2A). Immunohistochemical analysis demonstrated positivity for S100 protein, HMB-45, and Melan-A (Figure 2B–D). Based on the clinicopathological findings, the lesion was diagnosed as microinvasive oral melanoma.

The patient subsequently underwent oncologic surgical resection of the lesion with a surgical safety margin, including removal of teeth in the involved region (Figure 1D). Rehabilitation was initiated with a temporary obturator prosthesis (Figure 1E). At the time of manuscript preparation, no chemotherapy, radiotherapy, or immunotherapy had been administered.

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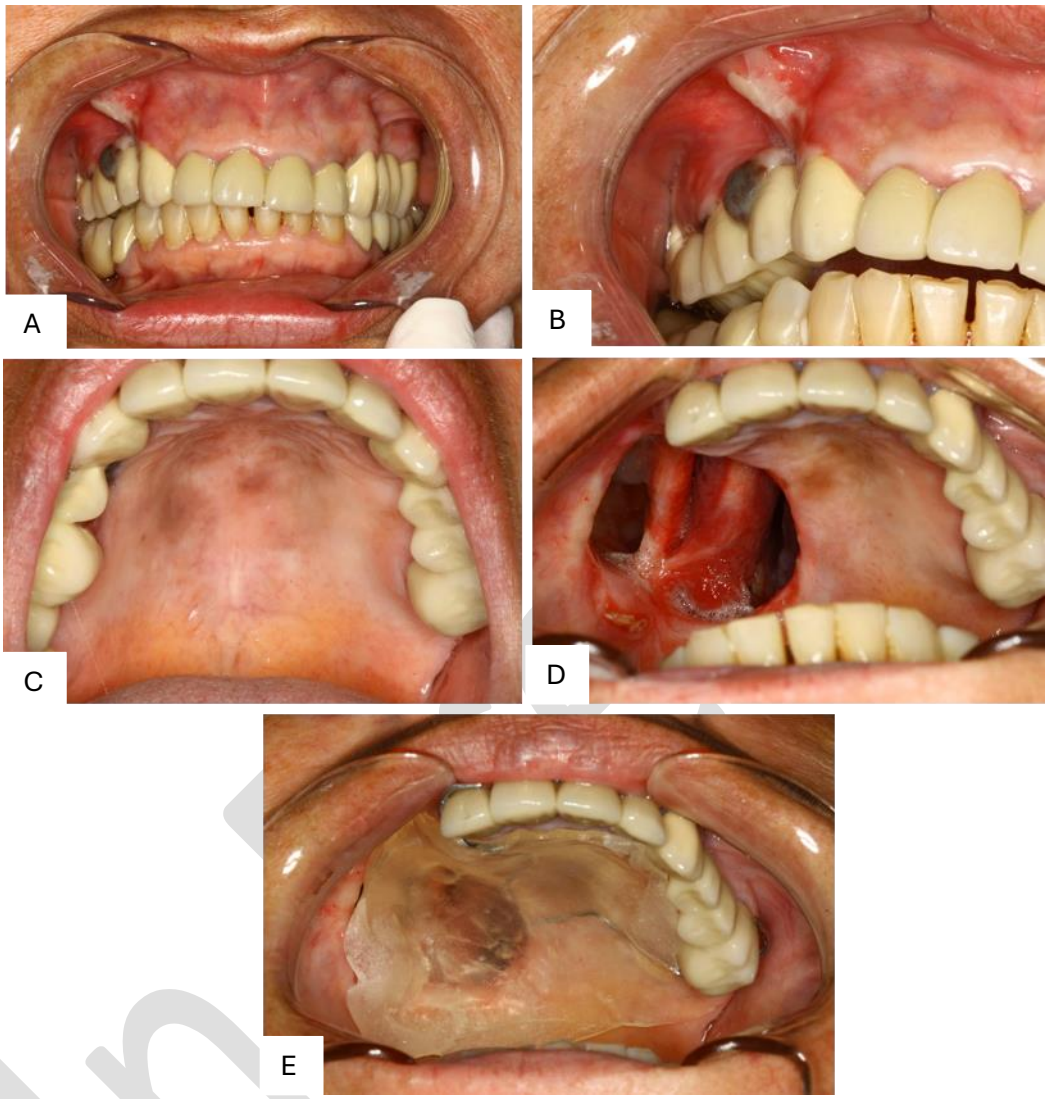


Figure 1. Clinical presentation and management of Case 1

Figure 1: (A) Intraoral view showing a pigmented nodular lesion involving the right maxillary gingiva. **(B)** Closer view demonstrating an irregular, sessile, purple-gray nodular lesion involving the buccal gingiva between FDI teeth 15 and 16, with peripheral ulceration. **(C)** Palatal view demonstrating extension of the lesion to the palatal gingiva. **(D)** Postoperative intraoral appearance following oncologic surgical resection. **(E)** Clinical appearance during rehabilitation with a temporary obturator prosthesis.

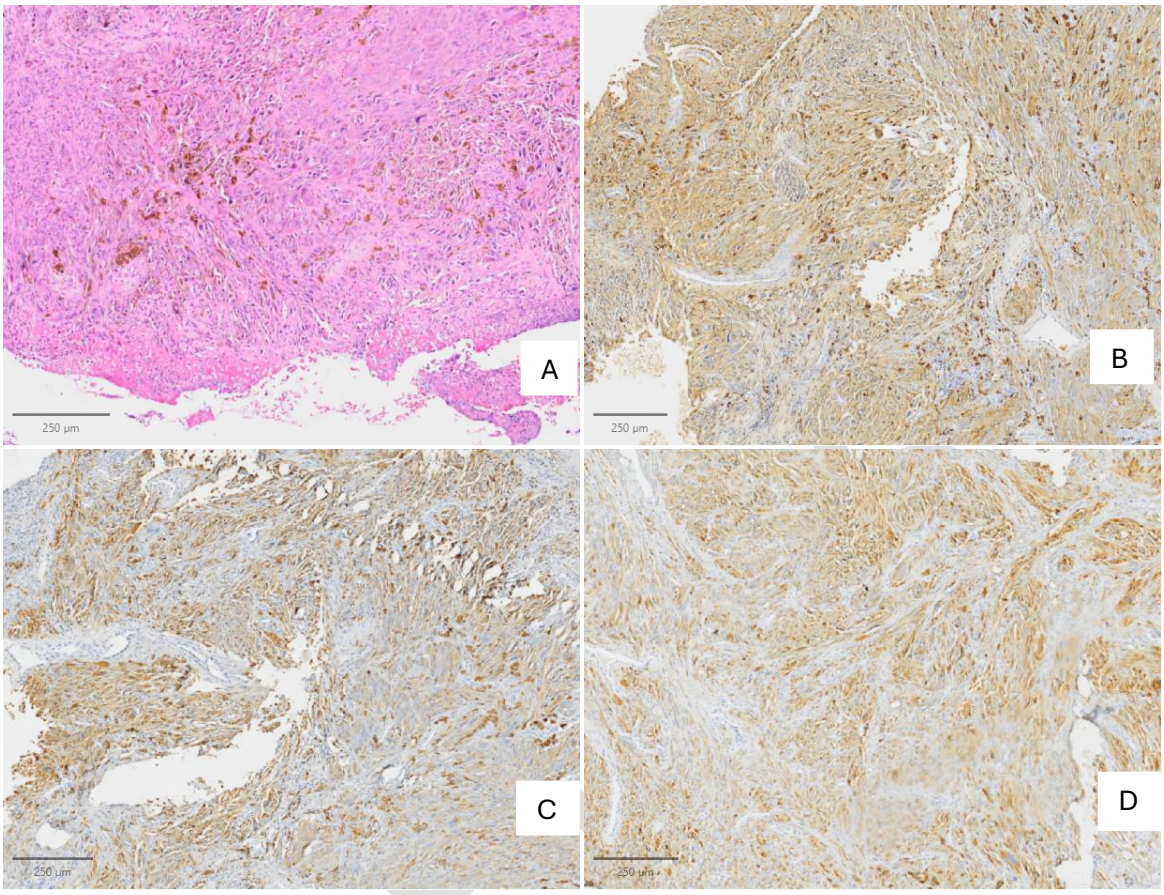


Figure 2. Histopathological and immunohistochemical findings of Case 1

Figure 2: (A) Hematoxylin and eosin-stained section of the incisional gingival biopsy showing a proliferation of atypical melanocytic cells arranged in sheets and nests within the connective tissue, with brown cytoplasmic pigment consistent with melanin (H&E; scale bar = 250 µm). Immunohistochemical staining demonstrating positivity for **(B)** S100 protein, **(C)** HMB-45, and **(D)** Melan-A (scale bars = 250 µm).

Case 2

A 51-year-old woman was referred to the oral medicine clinic because of a suspected malignant oral lesion. The patient reported a pigmented lesion involving the maxillary gingiva that had been present for approximately 10 years. According to her account, the pigmentation had remained asymptomatic and apparently stable for several years. During a previous dental evaluation, the lesion had reportedly been attributed to a previously treated tooth.

Approximately five months before presentation, however, the patient noticed progressive changes in the lesion, including the development of a nodular component and mild pain on palpation.

Intraoral examination revealed an extensive, heterogeneously pigmented lesion involving the maxillary gingiva, extending approximately from the region of FDI tooth 11 to tooth 26. The lesion displayed marked variation in pigmentation and surface morphology, areas of bleeding, and extension onto the hard palate (Figure 3A–C).

As an adjunct to the clinical examination, gentle rubbing of the lesion surface with gauze was performed. The maneuver resulted in transfer of dark pigment associated with blood onto the gauze (Figure 3D–E). A similar “rubbing with gauze” maneuver has previously been described as an adjunctive clinical finding in suspected oral melanoma; however, it is not diagnostic, and definitive diagnosis requires histopathological examination [12].

Given the extensive clinical involvement and recent changes in morphology, incisional biopsies were performed.

According to the original histopathological report, the biopsy specimens consisted of fragments of oral mucosa lined by parakeratinized stratified squamous epithelium. Melanocytic proliferation was described within the basal and suprabasal epithelial layers. Scattered melanocytic cells containing melanin pigment were also identified within the underlying lamina propria and exhibited spindle-shaped and rounded morphology. The reported histopathological diagnosis was microinvasive oral melanoma.

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The original histopathological slides from the diagnostic biopsy were not available for review by the authors; therefore, histopathological images from Case 2 could not be included in the present report.

Approximately two weeks after the incisional biopsies, further clinical changes were observed, including alterations in lesion size, pigmentation, and surface morphology (Figure 3F).

The patient subsequently underwent radical surgical excision of the lesion. At the time of manuscript preparation, further oncologic treatment planning remained under evaluation.

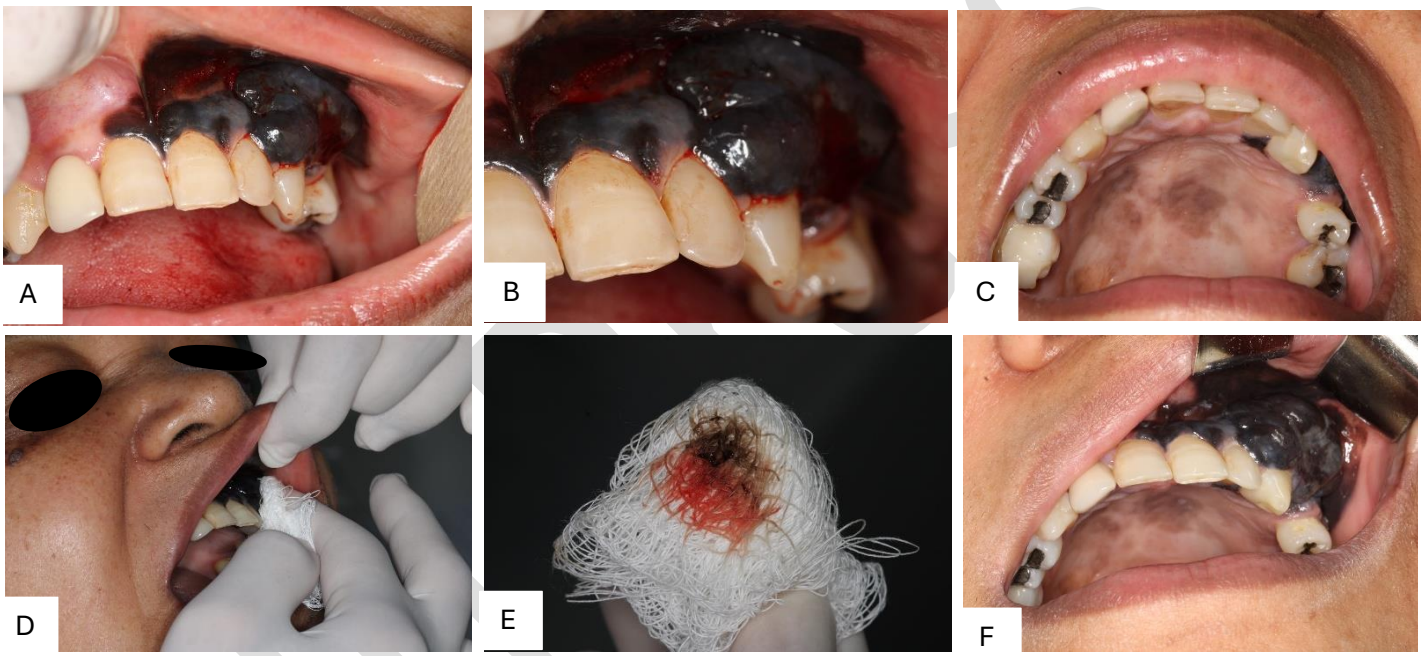


Figure 3. Clinical presentation, adjunctive gauze-rubbing maneuver, and short-term evolution of Case 2

Figure 3: (A–B) Intraoral views showing an extensive, heterogeneously pigmented lesion involving the maxillary gingiva, extending approximately from the region of FDI tooth 11 to tooth 26, with irregular surface morphology and areas of bleeding. **(C)** Palatal view demonstrating extension of the lesion onto the hard palate. **(D)** Gentle rubbing of the lesion surface with gauze. **(E)** Gauze showing transfer of dark pigment associated with blood following the maneuver. **(F)** Clinical appearance approximately two weeks after the incisional biopsies, showing interval changes in lesion size, pigmentation, and surface morphology.

3 Discussion

OMM is an uncommon but highly aggressive malignancy whose rarity and heterogeneous clinical appearance continue to represent substantial diagnostic challenges. Systematic reviews and contemporary multicenter studies indicate that many patients are diagnosed with locally advanced or metastatic disease and that long-term survival remains unfavorable [1,2,4]. A recent meta-analysis including 1,151 patients estimated a pooled 5-year survival of 34%, whereas another meta-analysis involving 3,767 patients reported a 5-year overall survival of 29% [14,15].

Recent regional evidence provides additional context for OMM in Latin America. A 2024 systematic review of primary oral and sinonasal mucosal melanomas identified 33 Latin American studies comprising 1,212 cases; 19 studies specifically reported oral melanoma, while the overall cohort had a mean age of 58 years and an almost balanced sex distribution [21]. More recently, de Arruda et al. described 21 primary oral melanomas diagnosed between 2003 and 2025 across centers in Argentina, Venezuela, Colombia, and Brazil. The mean age was 63 years, 52.4% of patients were women, 78.3% were asymptomatic at diagnosis, and 66.7% involved the palate/maxillary gingiva. Surgical resection was performed in 85.7% of cases, and 52.6% of patients died during follow-up [22]. These contemporary regional data reinforce the marked clinical heterogeneity and unfavorable prognosis of OMM while also highlighting the relative scarcity of South American epidemiological data.

The two cases presented here are particularly illustrative because both received the histopathological diagnostic designation of microinvasive oral melanoma despite strikingly different clinical presentations. Case 1 presented as a relatively localized gingival lesion identified shortly after the patient became aware of symptoms. By contrast, Case 2 demonstrated extensive maxillary involvement following a history of pigmentation reportedly spanning approximately 10 years and several months of progressive morphological change.

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The clinical history of Case 2 requires cautious interpretation. Although the patient reported long-standing pigmentation followed by nodular enlargement and rapid progression, it cannot be concluded that a benign pigmented lesion underwent malignant transformation because no histopathological evaluation of the original pigmentation was available. Nevertheless, changes in size, color, surface morphology, nodularity, ulceration, and bleeding are recognized warning features that warrant prompt diagnostic investigation of oral pigmented lesions [5,7–10].

The distinction between the histopathological term microinvasive and the overall clinical extent of disease is particularly important in the present cases. Prasad et al. proposed a histopathological microstaging system for mucosal melanoma in which Level I includes melanoma in situ with or without microinvasion, defined as individual invasive cells or small clusters of fewer than 10 atypical melanocytes near the epithelial–subepithelial junction; Level II corresponds to invasion into the lamina propria, and Level III to invasion of deeper structures such as skeletal muscle, bone, or cartilage [13]. Subsequent studies of oral melanoma have applied similar histopathological concepts [11].

This histopathological concept should not be regarded as synonymous with limited clinical disease or with a low TNM category. Contemporary staging of head and neck mucosal melanoma is based principally on anatomical extent, and histopathological microstaging and clinical TNM staging provide different types of information [13,18].

This distinction is particularly relevant to Case 2. Although the diagnostic biopsy was reported as microinvasive, the lesion was clinically extensive. An incisional biopsy samples only a limited portion of a potentially heterogeneous tumor and may not represent the area of greatest invasion or the full anatomical extent of disease. Accordingly, findings from an incisional specimen should be interpreted in conjunction with clinical examination, imaging when available, and pathological assessment of the definitive surgical specimen.

The absence of the original histopathological slides from Case 2 represents a limitation of the present report. Although the original pathology report documented the diagnosis and microscopic findings, lack of access to the slides precluded independent histopathological reassessment by the authors and prevented direct comparison of the microscopic pattern and depth of invasion

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between the two cases. For this reason, the histopathological description of Case 2 in this report is explicitly based on the original diagnostic report.

The histopathological features observed in Case 1 are consistent with established descriptions of OMM. Primary oral melanomas may exhibit epithelioid, spindle-shaped, plasmacytoid, or mixed tumor cell morphologies and may form sheets, nests, or other architectural patterns. Melanin pigmentation is variable, and amelanotic cases are well documented [11]. Immunohistochemistry is therefore important in supporting melanocytic differentiation, particularly in poorly pigmented or morphologically challenging lesions. In a Latin American series of 22 primary oral melanomas, S100 and HMB-45 were expressed in all cases, whereas Melan-A expression was somewhat less consistent [11].

The gauze-rubbing maneuver performed in Case 2 has also been previously described in the literature. Delgado-Azañero and Mosqueda-Taylor evaluated this maneuver in 13 clinically suspected oral melanomas and reported dark staining of the gauze in 11 cases. Importantly, the authors emphasized that the maneuver is only an adjunct to clinical examination and that definitive diagnosis must be established histopathologically or immunohistochemically [12]. Thus, the pigment transferred to the gauze in the present case should not itself be interpreted as diagnostic of melanoma.

From a therapeutic perspective, complete surgical resection remains the main treatment for localized and resectable OMM [1,4,6,16]. Contemporary retrospective data indicate that depth of invasion, bone involvement, resection margin status, higher T classification, and systemic metastases may influence prognosis [16]. Because OMM is rare, however, high-quality prospective evidence defining optimal surgical margins and management of the clinically negative neck remains limited.

Radiotherapy may be considered in selected patients, particularly in the adjuvant setting. Evidence is derived predominantly from head and neck mucosal melanoma rather than exclusively oral disease. A systematic review and meta-analysis found improved local control with surgery followed by radiotherapy compared with surgery alone and suggested a modest survival benefit, although radiotherapy did not reduce distant metastasis [17]. Therefore, treatment decisions should consider anatomical extent, surgical margins, nodal disease,

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expected morbidity, and multidisciplinary assessment rather than relying solely on the histopathological descriptor of invasion.

Systemic treatment has evolved considerably with the introduction of immune checkpoint inhibitors. Nevertheless, evidence specifically addressing OMM remains substantially more limited than that available for cutaneous melanoma. A 2026 systematic review devoted specifically to immune checkpoint inhibitors in OMM identified 14 case reports and only two cohorts, comprising 124 patients in the cohort studies, demonstrating the current limitations of the evidence base [19]. A contemporary review likewise emphasized that most therapeutic evidence remains derived from pooled mucosal melanoma cohorts or individual oral melanoma cases rather than prospective OMM-specific clinical trials [20].

OMM also exhibits a molecular profile distinct from that of conventional cutaneous melanoma. In the systematic review by Thuaire et al., reported mutations included KIT in 14.6%, BRAF in 7%, and NRAS in 5.6% of evaluated cases. These differences may have implications for molecular testing and targeted therapeutic strategies, although oral melanoma-specific evidence remains limited [1,3].

The substantial difference in management between the two patients reported here should therefore not be attributed solely to the microscopic term “microinvasive.” Oncologic management depends on the complete clinical context, including anatomical extent, resectability, surgical margins, regional and distant disease, histopathological findings, patient-related factors, and multidisciplinary assessment.

Finally, these cases reinforce the important role of oral health professionals in recognizing potentially malignant pigmentation. Because benign pigmented oral lesions are considerably more common than melanoma, not every pigmented lesion warrants identical management. Nevertheless, unexplained lesions demonstrating recent or progressive alterations in size, color, symmetry, surface architecture, nodularity, ulceration, or bleeding should prompt careful evaluation and, when clinically indicated, timely biopsy [5]. Early recognition remains particularly important given the consistently unfavorable prognosis associated with OMM.

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4 Conclusion

Oral mucosal melanoma is a rare and aggressive malignancy characterized by considerable clinical heterogeneity. The cases presented here demonstrate that lesions receiving a similar histopathological diagnostic designation may exhibit markedly different clinical extent and evolution.

Suspicious oral pigmented lesions, particularly those showing recent changes in size, pigmentation, morphology, nodularity, ulceration, or bleeding, should be investigated promptly. Furthermore, histopathological findings obtained from an incisional biopsy should be interpreted in conjunction with the overall clinical extent of the lesion. Careful clinicopathological correlation and multidisciplinary oncologic management are essential in patients with OMM.

Contribution of all authors: **EASF:** Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. **ARGJ:** Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. **PSP:** Investigation, Data curation, Visualization, Writing – review & editing. **SCO:** Investigation, Data curation, Visualization, Writing – review & editing. **CBG:** Investigation, Writing – review & editing. **FAA:** Investigation, Writing – review & editing. **CAL:** Investigation, Writing – review & editing. **CVE:** Investigation, Writing – review & editing.

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Ethical considerations: Written informed consent was obtained from both patients for publication of the clinical information and accompanying images included in this case series.

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Originality statement: We affirm that this study is original, has not been published previously, and is not currently under consideration for publication elsewhere.

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