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CASE REPORT

Amelanotic melanoma presented as an ulcerated, exophytic mass on the mandibular ridge

Wilson Alejandro Delgado Azañero[1], Jaime Orlando Huamaní Parra[1], Leopoldo Victor Meneses Rivadeneira[1], Claudia Gabriela Ruiz Rojas[1], Luciano Hermios Matos Valdez[1], Katman Bear Toledo Sanchez[1,2]*

Abstract:

Amelanotic melanomas are aggressive neoplasms that are exceedingly rare in the oral cavity. We report the case of a 74-year-old woman who presented with a large, ulcerated, exophytic mass on the edentulous lower alveolar ridge. Histological examination revealed two distinct cell populations: epithelioid cells arranged in an alveolar pattern and spindle-shaped cells arranged in fascicles, both exhibiting prominent nucleoli. Immunohistochemical staining was performed using S-100, SOX10, Melan-A, HMB-45, PRAME, and Ki-67. S-100 and SOX10 showed strong positivity, PRAME was focally positive, and the Ki-67 index was high. Melan-A and HMB-45 were negative. Due to the absence of clinical and histological pigmentation, amelanotic melanoma can be easily overlooked. Therefore, any rapidly growing, ulcerated mass in the oral cavity should raise suspicion for this diagnosis.

Keywords: Mucosal melanoma; Amelanotic melanoma; Oral tumor; Immunohistochemestry; Melanocytes.

INTRODUCTION

Melanoma is an aggressive malignant neoplasm originating from melanocytes, which are found in the skin, mucous membranes, choroid, and cochlea[1,2]. Of all melanomas, 91.2% occur in the skin, while only 1.3% involve the mucous membranes[3] and are classified as mucosal melanomas. Head and neck melanomas account for less than 1% of all melanoma cases[4]. Oral mucosal melanomas (OMMs) are extremely rare, comprising only 0.5% of all oral malignancies[5]. They can arise anywhere in the oral cavity; however, the hard palate and maxillary gingiva are the most commonly affected sites, while the tongue is the least frequently involved. A slight male predominance has been reported, with the age of onset typically ranging from 55 to 66 years[6].

Oral pigmented melanomas typically present clinically as macules, papules, or tumors with black, grayish-brown, or polychromatic coloration, depending on the degree of melanin production. When the tumor does not produce melanin or produces it in minimal amounts, it may appear pink, red, or white if ulcerated. These lesions are referred to as oral amelanotic melanomas (OAM)[7]. This variant is rarer than the pigmented form[8].

Statement of Clinical Significance
The significance of this case lies in the fact that an ulcerated, asymptomatic, rapidly growing lesion on the oral mucosa may represent an amelanotic melanoma. The absence of pigmentation alone does not exclude a tumor of melanocytic origin.

Diagnosis is challenging and requires histopathological evaluation supported by immunohistochemical analysis[9].

Due to the absence of pigment, the tumor can be clinically misdiagnosed as a pyogenic granuloma, reactive lesion, epithelial or mesenchymal tumor, infection, or ulceration growth, among other conditions[10,11]. These lesions are usually painless, may bleed, and can vary in size from a few millimeters to several centimeters[12]. Histologically, amelanotic melanomas may exhibit spindle cells, epithelioid cells, plasmacytoid cells, rhabdoid cells, round cells, clear cells, or a combination thereof[13,14]. The nuclei are characteristically atypical and enlarged, often with prominent nucleoli. Given the wide histological variability of this tumor, the identification of melanocytes relies on immunohistochemical staining using biomarkers such as S-100, SOX10, Melan-A, HMB-45 and PRAME[15-19].

[1]Universidad Peruana Cayetano Heredia, Faculty of Stomatology, Buccomaxillofacial, Department of Medicine and Surgery – Lima, Perú.
[2]University of Campinas, Piracicaba Dental School, Oral Diagnosis Department – Piracicaba (SP), Brazil.
***Correspondence to:** Email: katman.toledo@upch.pe
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We report a case of amelanotic melanoma presenting as an ulcerated, exophytic mass on the mandibular ridge in a 74-year-old woman. The clinical and imaging findings are described, along with the histological and immunohistochemical features that led to the definitive diagnosis.

CASE REPORT

A 74-year-old woman was referred to the Oral and Maxillofacial Medicine and Pathology Service at the Faculty of Stomatology, Universidad Peruana Cayetano Heredia, for evaluation of a firm, exophytic mass located on the alveolar ridge in the region corresponding to teeth 44–46. The surface of the tumor was ulcerated and covered by a pseudomembranous whitish layer interspersed with reddish areas, both consistent with fibrin. The lesion had a pedunculated base and extended into the mandibular bone (Figure 1A). The tumor measured approximately 5.0 × 3.5 × 2.5 cm and elicited mild tenderness on palpation.

According to the patient, the lesion began as a small, asymptomatic growth approximately four months prior. Over the past 20 days, she reported experiencing mild paresthesia of the lower lip. As the patient was edentulous in the maxilla, she had been chewing on the mandibular lesion. In addition to the oral tumor, the patient presented with an enlarged, firm right submandibular lymph node measuring 4.5 cm in diameter, which elicited mild pain on palpation (Figure 1B). The patient stated that the lymph node enlargement began approximately two months ago.

A panoramic radiograph revealed a non-corticated, irregularly contoured, crescent-shaped radiolucent area in the region of teeth 44–46, approximately 1 cm in depth (Figure 2A). Contrast-enhanced CT scans showed a hypodense, round-shaped lesion in the mandibular body, with slight expansion of both the buccal and lingual cortical plates (Figure 2B). The enlarged submandibular lymph node appeared as a heterogeneous, round-shaped lesion on imaging (Figure 2C).

The analysis of the clinical and imaging findings, along with the presence of an enlarged submandibular lymph node without signs of inflammation, led to the consideration of the following differential diagnoses: squamous cell carcinoma, malignant mesenchymal neoplasm, malignant odontogenic tumor, and metastatic tumor.

Histopathological examination of two biopsies obtained from the vestibular and lingual aspects of the lesion revealed an ulcerated tumor covered by a fibrin layer containing numerous polymorphonuclear cells (Figure 3A). The tumor exhibited two distinct cellular populations. One consisted of epithelioid cells of varying sizes, arranged in an alveolar pattern. These cells were ovoid to polygonal in shape, with clear cytoplasm in some, and all displayed prominent nucleoli (Figure 3B). The stroma was inconspicuous. In other areas,

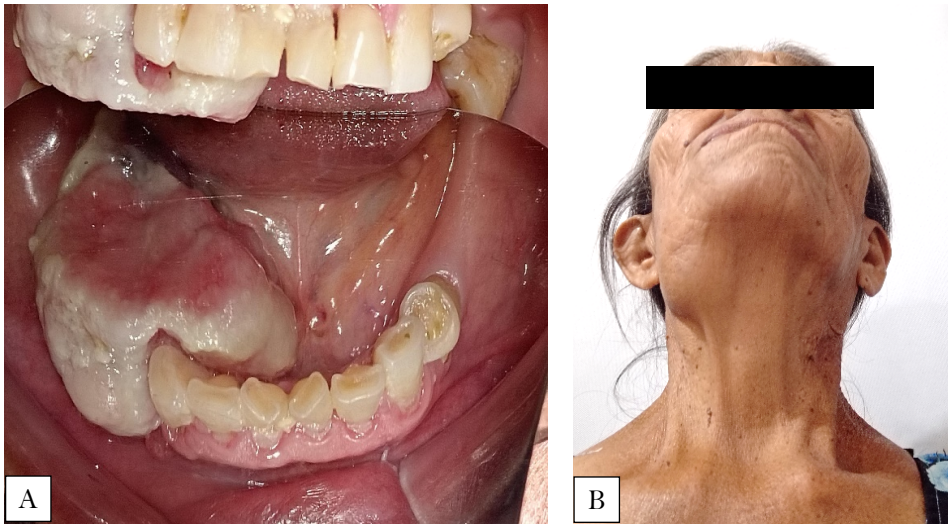

Figure 1. (A) A 74-year-old woman presenting with an exophytic lesion on the alveolar ridge in the region of teeth 44–46, characterized by whitish lateral surfaces, a reddish superior surface, and a pedunculated base extending into the mandibular bone. **(B)** An enlarged, firm right submandibular lymph node.

a different growth pattern was observed, characterized by spindle-shaped cells with elongated nuclei arranged in parallel fascicles (Figure 3C). Additionally, blood vessels surrounded by proliferating tumor cells were identified.

Considering the frequency of malignant tumors of the oral mucosa, the microscopic differential diagnoses included poorly differentiated squamous cell carcinoma, spindle cell carcinoma, poorly differentiated sarcoma, and amelanotic melanoma. Although the cellular morphology was highly suggestive of melanoma, careful examination of multiple hematoxylin and eosin (H&E)-stained sections did not reveal the presence of melanin pigment. Nevertheless, given the possibility of amelanotic melanoma, immunohistochemical staining was performed using S-100, SOX10, Melan-A, HMB-45, and PRAME. Ki-67 was used to evaluate the proliferative index.

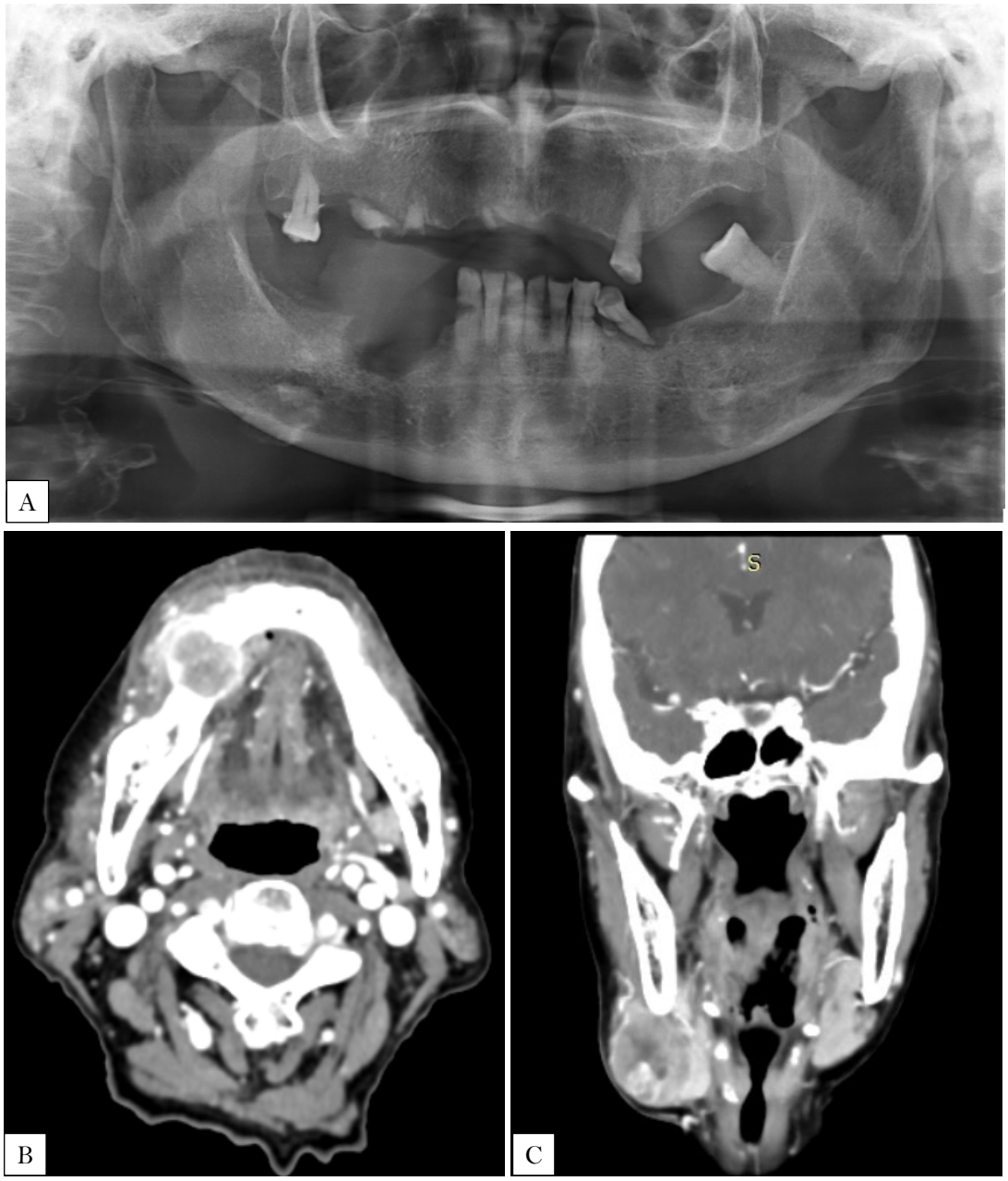

Figure 2. (A) Panoramic radiograph showing a non-corticated, irregularly contoured, crescent-shaped radiolucency. **(B)** Contrast-enhanced CT scans, revealing a hypodense, round-shaped lesion in the mandibular body that expands both cortical bones. **(C)** Enlarged submandibular lymph node showing a heterogeneous, round-shaped image.

Immunohistochemical analysis revealed strong positivity for S-100 (Figures 3D, 3E) and SOX10 (Figure 3F) in all tumor cells, while PRAME showed focal positivity (Figure 3G). Melan-A and HMB-45 (Figures 3H, 3I) were negative. Ki-67 demonstrated a high proliferative index (Figure 3J). Based on these findings, a diagnosis of amelanotic melanoma was established.

The patient was informed of her diagnosis, the available treatment options, and the potential for distant metastatic dissemination, pending completion of a full physical examination, including imaging studies such as a chest CT scan and a PET scan. After receiving this information, she chose to return to her hometown and declined further treatment.

DISCUSSION

Amelanotic melanomas are non-pigmented melanocytic neoplasms[1,3]. Within the oral cavity, they may arise at various sites; however, similar to their pigmented counterparts, they exhibit a predilection for the hard palate and maxillary gingiva[4,5]. Most cases have been reported in patients in their seventh decade of life, although some studies indicate a mean age of 54 years[6,7]. A slight male predominance has also been noted. In contrast to these trends, our case involved a 74-year-old female patient with a lesion affecting the edentulous mandibular alveolar ridge in the region of teeth 44–46, a less common site for this type of neoplasm.

In this report, the amelanotic melanoma presented as a large exophytic mass with whitish lateral surfaces and a reddish superior surface, indicative of ulceration with vascular congestion (Figure 1A). Without taking imaging findings and the enlarged lymph node into account, the lesion clinically resembled pyogenic granuloma, peripheral giant cell granuloma, ulcerated squamous cell carcinoma, and mesenchymal neoplasms. These differential diagnoses are consistent with those proposed in the literature[2,8,11].

As has been mention in the case presentation, bone destruction was observed as an osteolytic area underlying the tumor. The possibility of primary intraosseous origin was not considered, as melanocytes have not been

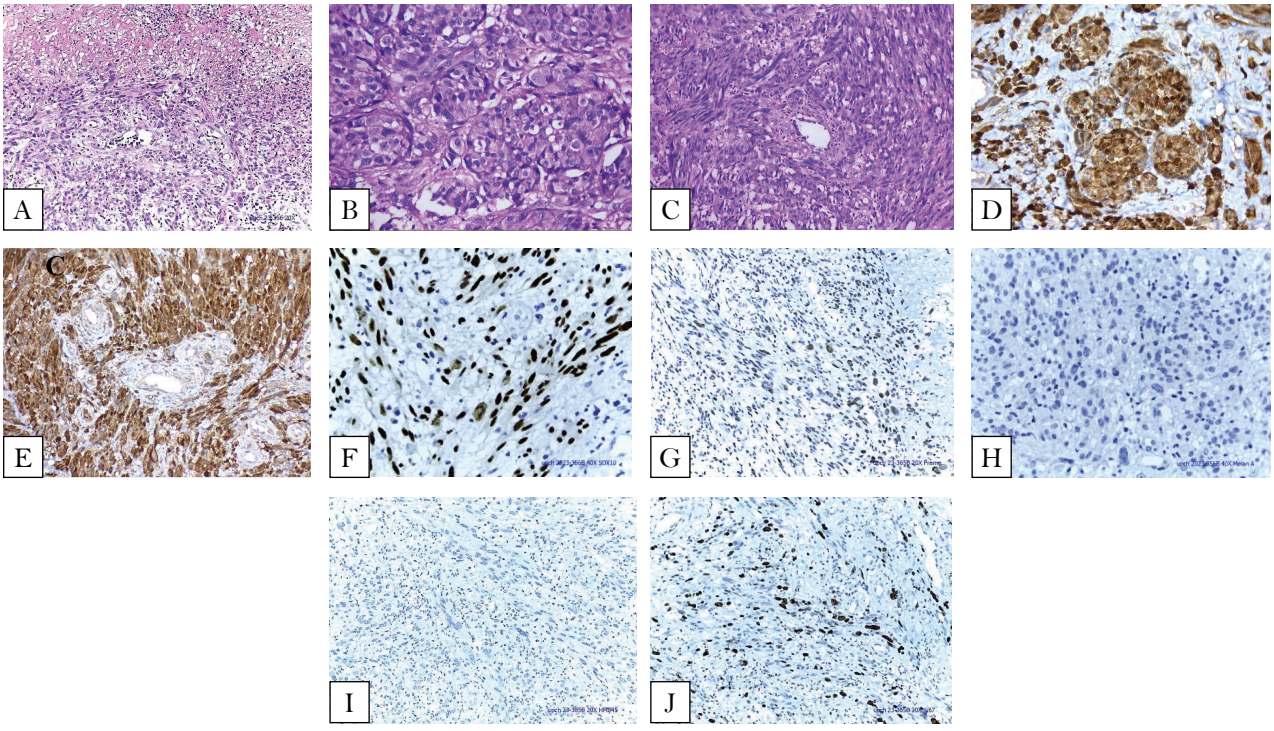

Figure 3. (A) The surface of the tumor shows ulceration covered by a fibrin layer infiltrated by tumor cells. (★). **(B)** The tumor exhibited an alveolar pattern composed of ovoid to polygonal epithelioid cells, some with clear cytoplasm and prominent nucleoli, within an inconspicuous stroma **(C)** The spindle cell component of the tumor was arranged in parallel bundles with elongated nuclei. **(D, E)** S-100 positivity was strong in both alveolar and spindle cell patterns. **(F)** SOX10 immunoreactivity was positive in the nuclei of all tumor cells. **(G)** PRAME demonstrated focal positivity within the tumor. **(H, I)** Melan-A and HMB-45 were negative. **(J)** Ki-67 demonstrated a high proliferative index.

identified within the jawbones[2,14]. Conversely, metastatic melanoma was also considered unlikely, as the patient had no history of melanoma elsewhere in the body.

It is noteworthy that, despite the tumor's considerable size, the patient reported only mild pain. Paresthesia developed only within the last twenty days, even though significant mandibular bone destruction was evident on imaging (Figures 2A-C). This observation suggests that neurological symptoms in amelanotic melanomas may not present early[10,12]. According to the literature, the average size of reported amelanotic melanomas ranges from 0.15 to 70 mm[3,16,20-22]. with only four cases exceeding 5 cm. This case likely represents the fifth.

Microscopic examination revealed a morphologically complex neoplasm with features variably consistent with poorly differentiated squamous cell carcinoma, spindle cell carcinoma, poorly differentiated sarcoma, and amelanotic melanoma. These entities are well-documented in the literature as important differential diagnoses to consider when evaluating a potential case of amelanotic melanoma[6,8,13,14].

According to the literature, no single marker is consistently positive across all melanoma subtypes. The findings in our case support this observation and confirm that S-100 is the most reliable marker, having been reported as positive in 93–100% of all melanoma subtypes[19], and in 97–100% of cases in other reports[6,8,17]. SOX10 was also positive in our case, consistent with reports indicating 97–100% positivity in both primary and metastatic melanomas[6,8,19]. Although PRAME has been proposed as an essential marker for the identification of mucosal melanomas of the head and neck region, it was only focally expressed in our case. It is noteworthy that this marker has been reported as negative in lesions of the hard and soft palate, and positive in tongue melanomas[18]. Both Melan-A and HMB-45 were negative.

The negative results for Melan-A and HMB-45, along with the focal expression of PRAME, underscore the variability in marker expression among melanoma subtypes and highlight the importance of using a comprehensive immunohistochemical panel that must include S-100 and SOX10[15,16,23]. It appears that the tumor's site of development within the oral cavity is associated with variations in immunohistochemical reactivity[6,8,18]. Finally, Ki-67 demonstrated strong positivity, indicating a high proliferative index (Figure 3J).

As previously stated, the patient declined all proposed treatments following disclosure of her diagnosis. Consequently, this decision precluded further assessment for potential metastatic dissemination to other anatomical sites.

CONCLUSION

Amelanotic melanoma of the oral cavity is an extremely rare and aggressive neoplasm of melanocytic origin that presents significant diagnostic challenges due to its lack of pigmentation and variable histological features. In this case, immunohistochemical analysis was essential for diagnosis, with strong positivity for S-100 and SOX10, despite negative results for Melan-A and HMB-45, and only focal expression of PRAME. This case highlights the importance of considering amelanotic melanoma in the differential diagnosis of rapidly growing, ulcerated oral lesions, and highlights the need for a comprehensive immunohistochemical panel to achieve accurate identification.

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AUTHORS' CONTRIBUTIONS

WADA: investigation, methodology, supervision, validation, visualization, writing – original draft, writing – review & editing. JOHP: conceptualization, validation, visualization. LVMR: supervision, validation. CGRR: methodology, resources. LHMV: data curation, formal analysis. KBTS: conceptualization, funding acquisition, investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing – original draft, writing – review & editing.

CONFLICT OF INTEREST STATEMENT

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Ethics approval: The patient passed away before informed consent could be obtained. Contact with relatives or legal representatives was not possible. All data were fully anonymized. The Ethics Committee of the Oral and Maxillofacial Medicine and Pathology Service, Faculty of Stomatology, Universidad Peruana Cayetano Heredia, approved the publication in accordance with the Declaration of Helsinki and ICMJE guidelines.

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