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ORIGINAL ARTICLE

Oral squamous cell carcinoma involving a blue cell nevus in the palate

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Abstract:

Introduction: Squamous Cell Carcinoma (SCC) is the most common malignant neoplasm of the oral cavity; however, there is no report in the literature of SCC involved with blue nevus. **Case report:** We report the case of a patient, a 54-year-old woman who exhibited a brownish spot associated with whitish area, surrounded by a hyperemic area in the soft palate. After an incisional biopsy and histopathological analysis, the presence of invasive squamous cell carcinoma was shown, in addition, in other fragment, to the presence of fusiform cells disposed parallel to the epithelium, exhibiting intense brownish cytoplasmic pigments. Immunohistologically, the neoplastic epithelial cells demonstrated intense immunoexpression for the anti-pan Cytokeratin antibody, while the fusiform cells showed strong immunopositivity for the anti-S-100 and anti-Melan-A antibodies, and weak immunomarking for anti-HMB-45. Based on the microscopic findings described, the final diagnosis was Oral Squamous Cell Carcinoma (OSCC) involving a blue cell nevus. **Conclusion:** Therefore, we sought to relate the first case of involvement of OSCC and blue cell nevus, up to the present time.

Keywords: Nevus, Blue; Mouth Neoplasms; Immunohistochemistry.

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INTRODUCTION

Squamous cell carcinomas have an annual incidence of over 500 thousand cases worldwide[1], and are the most frequent malignant neoplasm in the oral cavity, accounting for approximately 95% of all the cases of malignancy in this region[1,2]. The individuals mainly affected are men between the fifth and seventh decades of life, exposed to the main risk factors, such as tobacco and alcohol consumption, with the tongue and floor of the mouth being the most frequent anatomic sites, and those that exhibit the worst prognosis[1-3].

Clinically, Oral Squamous Cell Carcinomas (OSCC) present as a tumor lesion, at time preceded by leukoplakic or erythematous lesions, exhibiting areas of ulceration and spontaneous bleeding[4]. Pigment changes in OSCC have been described in the literature, such as the pigmented variant that presents brownish or blackened areas next to the tumor[5].

The pigmented variant of OSCC is rare, and has been described in some of the few cases available in the literature, representing 0.01% to 7% of all the cases of OSCC[6], presenting the same biologic behavior as the non-pigmented variant[5,6]. The pigmentation present in the tumor results from a larger deposition of melanin in the neoplastic cells, suggesting a possible stimulus of tumor cells for the proliferation and deposition by melanocytes present in the region[7,8].

In the literature, the involvement of OSCC with other pigmented malignancies has also been related, such as oral melanoma, which is a rare malignant neoplasm arising from melanocytes present in the oral cavity[9,10]. However, there are no reports demonstrating involvement of OSCC with benign neoplasms of melanocytic origin, such as blue cell nevus, which is a benign melanocytic lesion shown mainly in women, with the palate being the most affected anatomic site in the oral cavity, exhibiting variation from a blue to blackened color[11]. Histopathologically, blue cell nevus exhibits fusiform cells disposed parallel to the epithelial tissue, exhibiting a brownish cytoplasmic pigmentation similar to that of melanin[12].

Based on this context, the aim of this report was to relate the first case of involvement of an OSCC with blue cell nevus in the palate.

CASE REPORT

The patient, a 54 year-old, black woman, sought the Stomatology Service of the Napoleão Laureano Hospital, an oncology reference in the State of Paraíba, Brazil. The patient complained of a "dark spot in the palate" that spontaneously and sporadically bleed, with a 4-year history of evolution. The patient reported no smoking and no drinking. Intraoral examination revealed an intense brown spot in the soft palate, next to right tonsil, measuring approximately 15 mm in its largest diameter. Whitish area surrounded by reddish zone, in left side to brown spot, was too observed (Fig. 1).

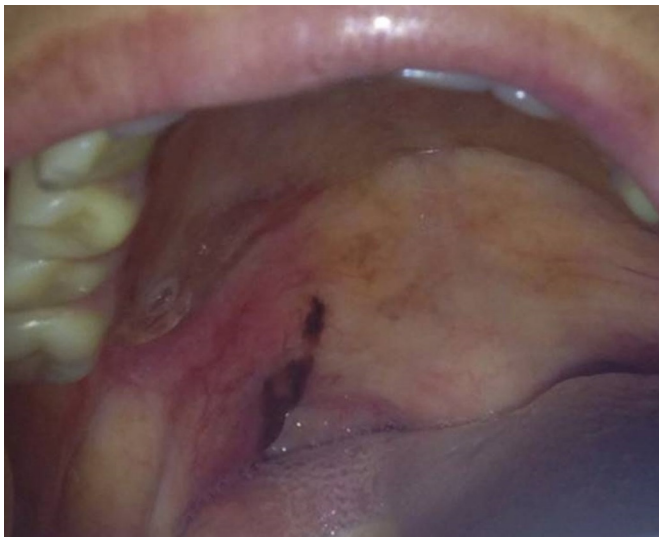

Figure 1. Intraoral clinical aspect of brown spot in the soft palate, next to right tonsil, and whitish area surrounded by reddish zone.

Neck lymph nodes were not painful on palpation. No radiographic changes were observed. Based on clinical findings, the diagnostic hypothesis was oral melanoma. An incisional biopsy and histopathological exam were performed, with use of the routine hematoxylin and eosin staining technique showed proliferation of atypical epidermal cells in groups of nests and islands in a stroma made up of dense fibrous connective tissue. Individually, atypical cells showed hyperchromatic nuclei, nuclear pleomorphism and increase in the nucleus/cytoplasm (Fig. 2A).

In an underlying zone of dysplastic epithelium, spindle-shaped cells were shown, distributed parallel to the epithelium within an intense brown cytoplasmic pigment, compatible with melanin (Fig. 2B). The findings were consistent with invasive oral squamous cell carcinoma well differentiated. However, additional immunohistochemical analysis (pan Cytokeratins, S-100, Melan-A and HMB-45) was requested to clarify the phenotype of the pigmented cells in the stroma (Figs. 2C, D, E and F, respectively).

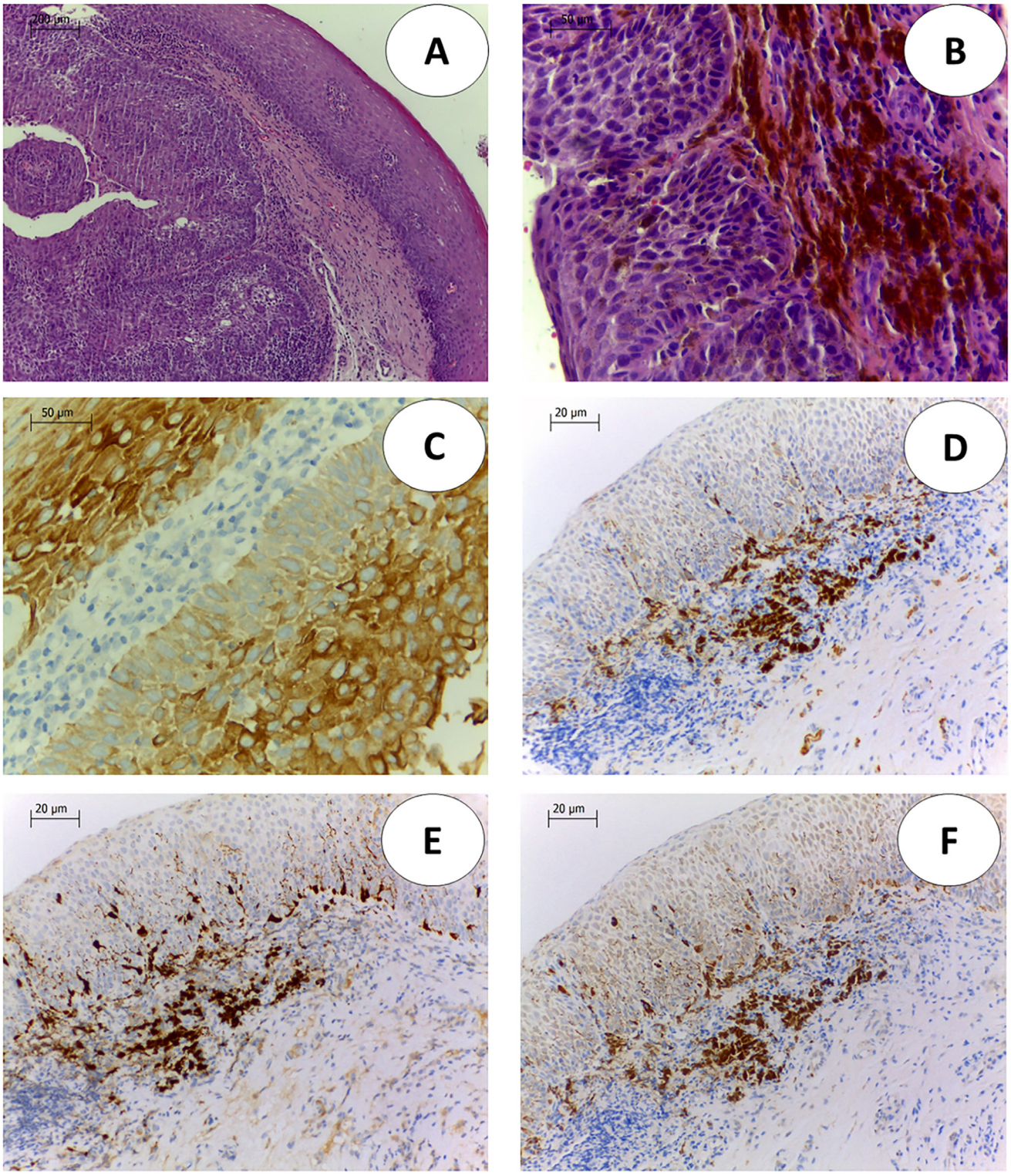

Figure 2. (A) Photomicrograph showed invasive oral squamous cell carcinoma with a solid invasion pattern (HE, x40). (B) Photomicrograph showed atypical cells with hyperchromatic and pleomorphic nucleus, and loss of epithelial stratification. In the adjacent lamina propria ovoid and spindle-shaped cells were observed, with brown cytoplasmic pigment, compatible with melanin (HE, x100). (C) Strong cytoplasmic staining in cytoplasm of keratinocyte for pan Cytokeratins, AE1/AE3 (Advanced, x100). (D) Strong staining for pigmented cells for antibody S-100 (Advanced, x100). (E) Immunoexpression for anti-Melan-A (Advanced, x100). (F) Weak expression of pigmented cells for HMB-45 (Advanced, x100).

Immunohistochemical exam showed strong expression of epithelium cells for pan Cytokeratins AE1/AE3, while pigmented cells showed strong expression of antibodies S-100 and Melan-A, and weak expression of HMB-45. Based on these findings, final diagnosis was OSCC involving with blue cell nevus.

According to the Union for International Cancer Control (UICC) classification of malignant tumors, described in 2002, the clinical stage of the lesion was classified as T1N0M0. It was performed adequacy of oral environment and the patient was referred to the head and neck surgery service and for radiotherapy. At 8-months of follow-up after treatment, no signs of local recurrence or metastasis were seen.

DISCUSSION

The oral cavity is among the main sites affected by squamous cell carcinoma in the head and neck region, in the majority of cases affecting men who are non-smokers and non-drinkers, over the age of 50 years. The most frequent localization is the tongue that presents the worst prognosis[1-3]. This differed from our case, in which the patient was a woman who did not report the habit of smoking or drinking. In spite of OSCC being more prevalent in men, over the last few years, an increase in the incidence in women could be noted, believed to be associated with factors such as hormonal questions, genetic predisposition and increase in the exposure of women to the classical risk factors of smoking and alcoholism, although these risk factors were not associated in our case[3,13].

Clinically, OSCC may present as a tumor lesion with vegetative growth, or presence of ulcerations and irregularities on the oral mucosa surface[4]. In our case reported, we only observed a little ulceration with an erythematous halo, also exhibiting the presence of a blackened area diverging from the classical presentation of OSCC, thus alerting the authors of the possibility of being an oral melanoma.

Oral melanoma accounts for approximately 0.5% of malignant neoplasms that affect the oral cavity. They mainly affect men over the age of 40 years, with etiology linked to local trauma, smoking or alcoholism, with the palate and gingiva being the anatomic sites most affected[14]. However, in our case reported, the microscopic findings were compatible with OSCC, in addition to observing the presence of fusiform cells with brownish pigment in its cytoplasm, disposed in the lamina propria subjacent and parallel to the epithelial tissue, thus allowing the hypothesis of isolated oral melanoma to be discarded.

Nakahara et al.[9] related a clinical case of simultaneous OSCC and oral melanoma oral in a 74-year-old woman. The melanoma was localized in the anterior region of the maxilla, clinically shown as a tumor lesion presenting blackened color, while the OSCC was found in the molar region of the maxilla on the right side, shown as an ulcerated lesion.

The association of lesions has also been described by Rodríguez et al.[10] when relating the first case of co-existence of an OSCC with a metastatic melanoma, found in the oral cavity of a dog. To elucidate the case, the authors performed an immunohistochemical panel, in which strong immunoexpression was shown of epithelial neoplastic cells for anti-pan Cytokeratins; and strong immunomarking for anti-S100 and anti-Melan-A for the melanocytic component.

Our other clinical hypothesis suggested was that of Pigmented Squamous Cell Carcinoma, which is a variant of OSCC that has been related in the literature, which clinically presents with blackened areas associated with the tumor. These neoplastic epithelial cells are believed to stimulate greater proliferation and release of melanin by the local melanocytes[7,8].

Morphologically, Pigmented Squamous Cell Carcinoma is characterized by the presence of neoplastic cells of epithelial origin, and the presence of blackened pigmentation present in the cytoplasm of dendritic cells disposed in the tumoral parenchyma and stroma[5,8]. Immunohistochemically, this variant exhibits intense immunoexpression of neoplastic epithelial cells for the cytokeratins AE1/AE3, and strong immunoexpression of the cells of melanocytic origin for the anti-S100 and anti-HMB45[7] antibodies.

In our reported case, in addition to the S-100, pan cytokeratin and HMB-45, we also used Melan-A, in which we observed that the malignant neoplastic epithelial cells demonstrated intense immunoexpression for the cytokeratins AE1 and AE3, and negativity for the anti-S100, anti-Melan-A and anti-HMB-45 antibodies, thus confirming the diagnosis of invasive carcinoma.

However, the fusiform cells with brownish cytoplasmic pigmentation demonstrated intense immunoexpression for the anti-S100 and anti-Melan-A antibodies, and weak immunoexpression for the Anti-HMB-45 antibody. The anti-S-100 antibody is immunoexpressed by cells of neural crest origin, such as melanocytes and nevus cells, while the anti-Melan-A

or anti-MART-1, are antigens responsible for the recognition of melanocytes by the T lymphocytes. In turn, the anti-HMB-45 (Human Melanoma Black-45) antibody is a specific marker for the protein of melanoma[7,15].

Immunohistochemically, the neoplastic cells in melanoma present strong immunoexpression for the anti-S-100, anti-HMB-45 and anti-Melan-A antibodies[14], while the nevus cells exhibit strong immunoexpression for the anti-S-100 and anti-Melan-A antibodies, and weak immunoexpression for the anti-HMB-45 antibody[15].

Based on the findings described, our case was diagnosed as OSCC involving with blue cell nevus. Therefore, this is the first case related in the literature of an OSCC co-existent, coincidentally, with a benign melanocytic lesion. Blue cell nevus, characterized as a rare benign melanocytic lesion, is ranked the second most common type of lesion, with an incidence between 19 and 36%, and clinically presents as a flat or elevated lesion with a blue to blackish color[16].

The clinical characteristics of the lesion were shown to be similar to those of oral melanoma, which emphasizes the importance of an early, correct conduct and careful diagnosis, seeing that the microscopic characteristics led to the authors discarding the clinical hypothesis.

The rare involvement of OSCC with benign pigmented lesions makes the clinical diagnosis difficult, and raises the possibility of a differential clinical diagnosis with other changes in pigment, such as oral melanoma, and Pigmented Squamous Cell Carcinoma. Knowledge of the cell phenotype associated with immunohistochemistry is fundamental for conclusion of the case.

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