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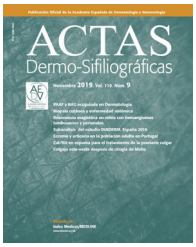

CASE FOR DIAGNOSIS

[Translated article] S100-protein–negative Mouth Lesion

Lesión de la mucosa oral negativa para la proteína S100

Medical history

An 83-year-old woman with a past medical history of atrial fibrillation and hypothyroidism presented with a 1-year history painful and bleeding lesion of the hard palate.

Physical examination

A 5cm nodular reddish lesion was found on the hard palate, with some surrounding pigmentation (Fig. 1A). No locoregional lymphadenopathies were described.

Histopathology

Histopathological examination revealed the presence of a non-pigmented, submucosal cellular proliferation of atypical characteristics consisting of large, discohesive, epithelioid and spindle cells, with pleomorphic nuclei, visible nucleoli, and multiple mitotic figures (Fig. 1B-D). Due to the absence of a specific morphological pattern, a broad differential diagnosis was considered.

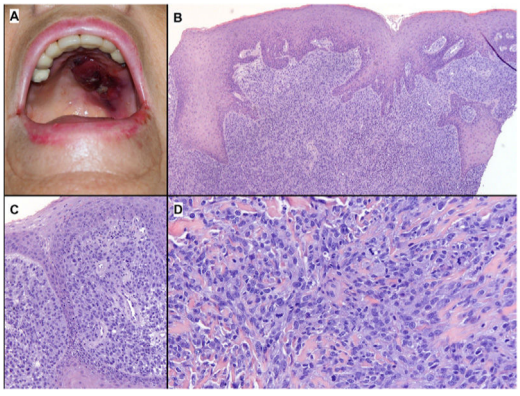

Figure 1

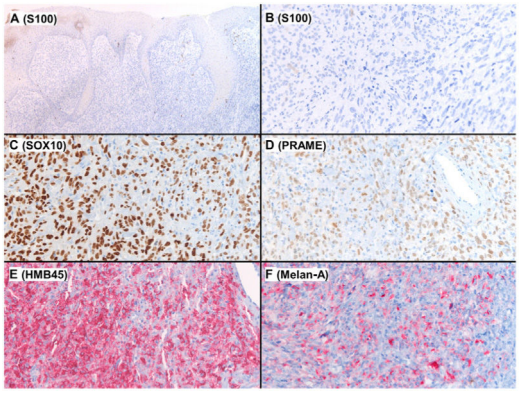

Figure 2

Other supplementary tests

The initial immunohistochemical study performed included epithelial (broad-spectrum keratins: CK AE1/AE3), hematological (CD20 and CD68), muscular (α-actin), and melanocytic markers (S100 protein). All tested negative, with appropriate positive external and/or internal controls (Fig. 2A and B). A second immunohistochemical panel conducted included EMA, p40, CK19, CD45, desmin, ERG, and SOX10. Tumor cells exhibited intense expression of SOX10 (Fig. 2C), which prompted further study, and eventually revealed the diffuse expression of PRAME and HMB45, and focal positivity for Melan-A (Fig. 2D-F).

What is your diagnosis?

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Diagnosis

The definitive histopathological diagnosis was invasive melanoma of the oral mucosa.

Course of the disease and treatment

The molecular analysis performed using the NGS Oncomine™ Focus panel (Thermo Fisher Scientific) detected gains in the KIT (4q12) and CDK4 (12q14.1) genes, without any mutations or fusions being reported in the studied DNA and RNA regions.

A PET-CT scan performed during the staging process revealed the presence of bilateral lung nodules with metabolic activity. The patient did not start cancer treatment due to rapid disease progression and died 2 months after diagnosis.

Discussion

Oral mucosal melanoma (OMM) is a rare neoplasm, representing between 0.2% and 0.5% of all oral neoplasms and 1% of melanomas.[1] The most commonly affected locations are the hard palate and the maxillary and mandibular gingiva.[2,3] Compared to its cutaneous counterpart, OMM occurs in older patients (around the 5th decade of life), and is more common in white individuals than in darker skin types, although with a lower predisposition than cutaneous melanoma.[2]

The most common clinical presentation is an asymptomatic flat or nodular lesion that may have satellite lesions too.[1,3] OMMs are often pigmented whether uniformly or heterogeneously. Nonetheless, they can also exhibit an amelanotic lesion in 10% to 30% of the patients. Ulceration and bleeding may occur, especially in later stages of the disease.[1,2]

A recent literature search revealed 2 case series, which reported on 1 case of OMM with negative immunohistochemistry for the S100 protein in each of them.[4,5] Prasad et al. reported 1 negative case of a series of 35 patients.[4] The tumor tested positive for the remaining markers (T311, A103, HMB45, and D5), with sensitivity rates of 94%, 85%, 71%, and 74%, respectively. Yu et al. reported a series of 6 cases of OMM with a tumor that tested negative for the S100 protein and Melan-A, and positive for HMB4[5]. In this study, the sensitivity rates of HMB45[5] and Melan-A were 100% and 67%, respectively.

For the molecular profile of OMM, changes in copy number and amplifications are a common finding, including amplifications of 4q12 (KIT) and 12q14 (CDK4) as seen in this case.[6]

In conclusion, the expression of the S100 protein for the diagnosis of OMM shows high sensitivity though it can be negative in up to 3% of the cases. Therefore, in the initial study of an undifferentiated malignant tumor in this region, using multiple melanocytic markers is recommended to safely exclude the diagnosis of melanoma.

Conflicts of interest

None declared.

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