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# A case of oral mucosal melanoma. Clinical and dermoscopic correlation.

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## Abstract

**Background:** Most patients with oral mucosal melanoma have had a mucosal hyper pigmented area for months or even years before the diagnosis, it is important to consider the differential diagnosis of mucosal melanoma, which in many cases is a difficult diagnosis and because of the aggressive biological behavior of mucosal melanoma it is important to do a quick diagnosis.

**Main observation:** A 40-year-old Mexican male patient, presented with a lesion on the lower right half of the lip covering almost the entire vermillion border, 1 mm below the white roll. The lesion was a 1.5 x 4 cm pigmented macule with asymmetric and irregular borders and colors. Dermoscopy showed a multi component pattern. An incision biopsy was performed under the impression of mucosal melanoma. The pathologic report described a Clark I vermillion edge mucosal melanoma in situ.

**Conclusions:** This case had confounding clinical signs that could have misguided the clinician. But dermoscopy proved to be useful when suspecting a malignant lesion, which prompted a biopsy and a correct diagnosis. (*J Dermatol Case Rep*. 2012; 6(1): 1-4)

## Introduction

There are many lesions that present with an increase in oral mucosal pigmentation, with an intrinsic and extrinsic origin. Since most patients with oral mucosal melanoma have had a mucosal hyper pigmented area for months or even years before the diagnosis, it is important to consider the differential diagnosis of mucosal melanoma.

## Case Report

A 40-year-old Mexican male patient, Fitzpatrick's skin type III, presented with a lesion on the lower right half of the lip covering almost the entire vermillion border, 1 mm below the white roll. The lesion was a 1.5 x 4 cm pigmented macule with asymmetric and irregular borders and colors. The white roll had an infiltrated area that was slightly elevated and deformed with grouped vesicles and erythema (Fig. 1).

According to the patient, the lesion had always been present, and was confident the elevation and erythema were

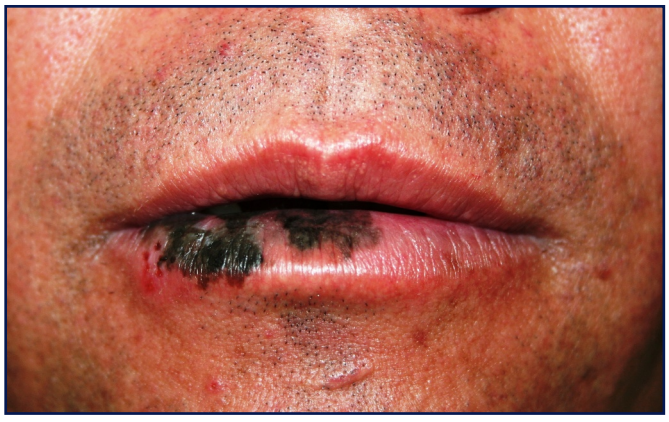

**Figure 1**

*40-year-old male patient with a lesion on the right half of the lower lip involving almost the entire vermillion border up to 1 mm below the white roll. A 1.5 x 4 cm pigmented macule with asymmetric and irregular borders and colors. The white roll had infiltratration, causing a slight elevation and deformation of the area.*

due to a recurrent herpes virus infection given no significant change had occurred.

Dermoscopy showed a multi component pattern with 7 colors, a central blue-white veil, regression structures, dots and globules with irregular shape, size & distribution, and irregular vessels. The periphery showed radial streaks (Fig. 2).

Based on the clinical dermoscopic correlation, an incision biopsy was performed under the impression of mucosal melanoma. The pathologic report described a Clark I vermillion edge mucosal melanoma in situ. The patient was referred to the National Institute of Oncology where the lesion was excised and reconstructed.

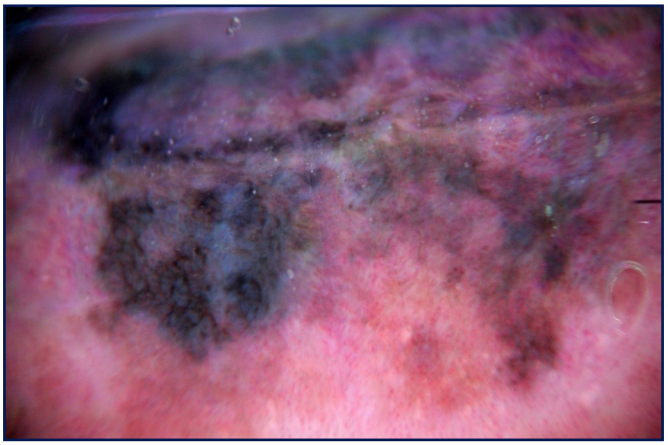

**Figure 2**

*Dermoscopy of melanoma of the lip showing multicomponent pattern.*

## Discussion

Skin cancer is the second most frequent cancer in Mexico.[1] Melanoma represents 2% of all malignant neoplasm; and 11% of all malignant skin tumors,[2] however, it is responsible for more than 80% skin cancer deaths.[3] Oral mucosal melanomas are rare, with a 1.2 to 10 million people ratio per year.[4]

In the international literature, oral mucosal melanoma is most often found in the Japanese population accounting for 11- to 12% of all melanomas.[8] There is a greater incidence in males, showing a 2:1 male:female ratio. It is frequently found in people over 40, and seldom found in those under 20. The average age is between 51 to 60 in males and 61-70 in females.

A study by Hicks and Flaitz[5] found that most melanomas affect the skin (91.2%), 5.3% affect the eyes, 2.2% are an unknown primary tumors, and only 1.3% are mucosal. Mucosal melanomas are most commonly present in head and neck areas. The nasal cavity (31.9%) is the primary location, closely followed by oral mucosa (23.9%), esophagus (6.3%) and lips (2.8%). Within the oral cavity, the hard palate and maxillary gum are the most usual sites for these lesions to be present.[6] Lourenço, Martin Sangueza *et al*. recently reported 35 oral mucosal melanoma cases, within the Latin American population. Most cases (25; 71.42%) were found in the hard palate and upper alveolar ridge. Jaw, retromolar, trigone, and floor of the mouth were involved in 3 cases (8.57%); 3 melanomas (8.57%) were detected in the labial mucosa and 2 (5.71%) on buccal/vestibular mucosa. Only 1 case (2.86%) was diagnosed on the lateral border of tongue, and in 1 case (2.86%), they could not identify the site of the lesion.[7]

The biological behavior of mucosal melanoma notoriously differs from the one shown in case of skin melanomas. Likely reasons are late diagnosis and treatment; anatomic differences in location, a greater blood and lymphatic flow in mucosa, easing its spread and differences in its genetic profile. For the above, in general, it has a bad prognosis with a 5-year survival rate in 10 to 25% of cases, with a survival average of 2 years. If lymphatic glands have been affected prognosis drops even further. Prognosis improves with early detection and total removal lesion before it spreads.

Although it is widely known that UV radiation plays a vital role in the physiopathology of cutaneous melanomas, oral mucosal melanomas usually appear in areas protected from UV radiation. These melanomas have significant differences from those present in areas exposed to sunlight. Risk factors relative to the development of mucosal melanomas are unknown. Apparently there is no correlation to chemical, thermal, or physical events, and according to a study performed at the Dr. Manuel Gea Gonzalez Hospital (by Aguilar A. *et al*.) no relationship was found to VPH infections. The current belief is that most oral cavity melanomas emerge *de novo*.

Oral mucosal melanomas are indolent and asymptomatic until the condition worsens. Most people do not inspect their oral mucosa properly until swelling, dental mobility, or bleeding occurs. Early lesions appear as a variable size pigmented macules. However long lasting lesions can be nodular or pediculated, pigments vary from dark brown to blue or black. Nevertheless, it is common to find white or red macules, especially in swollen lesions.

Since these lesions are asymptomatic during the early stages, they can be confused with an important number of benign conditions such as Addison disease, blue nevus, lentigines, Kaposi sarcoma, oral nevus, amalgam tattoos, mucosal melanotic macule, Peutz-Jeghers syndrome, smoker's melanosis and physiological pigmentation.

The use of dermoscopy has proven to improve diagnostic accuracy of pigmented skin lesions on hairy skin. However, little is known about the role of dermoscopy in pigmented mucosal lesions. Mucosal malignant melanomas, in particular flat lesions, often pose diagnostic challenges, because at times they share some features with benign mucosal melanotic macule. In a study by Lin *et al*. malignant pigmented lesion of the mucosa presented the multicomponent pattern (6 of 8, 75%) and the homogeneous pattern (2 of 8, 25%). The most common mucosal melanoma features as opposed to benign mucosal pigmented lesions were: asymmetry of structure (8 of 8, 100%), multiple colours (8 of 8, 100%), blue-white veil (6 of 8, 75%), irregular dots or globules (5 of 8, 62%), regression structure (3 of 8, 38%), blotches (2 of 8, 25%), irregular vessels (2 of 8, 25%) and an irregular pigment network (3 of 8, 38%).[10]

This case had confounding clinical signs of a long standing inflamed lesion due to infection that could have misguided the clinician. But dermoscopy proved to be useful when suspecting a malignant lesion, which prompted a biopsy and a correct diagnosis.

Due to mistaken signs of mucosal lesions, definite diagnosis must be performed through an histopathologic study.

The most important histopathologic finding is an ephitheloid or fusiform (sarcomatose) or neural, melanocitic proliferation in asymmetric shape nest arrays. In the dermal-epidermis junction there is a predominance of individual cells with an abundant eosinophilic, clear cytoplasm, and melanin granules in its interior. They can have a large nucleolus, with prominent eosinophilic nucleoli and nuclear pseudo inclusions are found due to nuclear membrane irregularities. Necrosis and ulcerations are not unusual.[6] The histopathology differential diagnosis is extensive; therefore, in some occasions, immune-staining is required. Cells are positive for S-100, HMB-45, Melan-A, tirosinase and Microphtalmic-associated Transcription factor (MITF).

The biological behavior of mucosal melanoma notoriously differs from the one shown in case of skin melanomas. The growth of mucosal melanoma closely resembles the nodular pattern of its cutaneous counterpart. This characteristic, in part, explains the poor prognosis of these lesions, and several studies have corroborating data linking survival most closely to tumor thickness. Patients with lesions under 2 mm in thickness have an important survival rate, over those with lesions with thickness over 2 mm.[11] Likely reasons are late diagnosis and treatment; anatomic differences in location, a greater blood and lymphatic flow in mucosa, easing its spread and differences in its genetic profile. For the above, in general, it has a bad prognosis with a 5-year survival rate in 10 to 25% of cases, with a survival average of 2 years. If lymphatic glands have been affected prognosis drops even further. Prognosis improves with early detection and total removal lesion before it spreads.

Imaging studies such as the contrast computed tomography can be very useful to determine the extension of the condition, and if local or regional lymphatic nodes have also been compromised.

In mucosal melanoma tumor staging with negative lymph nodes were proposed by Prasad *et al*.[12] and by Patel *et al*.[13] Stage I is melanoma in situ (none invasive), Stage II is the one invading the lamina propia and Stage III is the one invading deeper tissues. Survival average drops as stages progress.

The American Joint Committee on Cancer has not yet published Clinical guidelines for the of oral mucosal melanoma staging. However the most widely accepted classification is the following: Stage I: localized condition, Stage II: metastasis to regional lymphatic nodes, Stage III: remote metastasis. Metastasis are not unusually found when lesions are under 0.75 mm according to Breslow's scale.

Surgical removal is the treatment of choice, by totally removing the tumor with histological verification of free margins. Eighty percent (80%) of patients with oral mucosal melanoma have a local disease, 5-10% of cases have neck and/or subclavian lymphatic node involvement. After complete removal 10-20% regional relapses have been reported, with a 10-25% 5 year survival rate.

In spite of the fact that radiation has limited benefits, it has been observed that when used as adjuvant treatment with high and fractioned doses, it can be useful to achieve patient's survival without relapses.[14]

Given the propensity for mucosal melanoma to disseminate and to exclude metastatic melanoma from a cutaneous primary, a basic metastatic workup should be considered. This workup includes serum lactate dehydrogenase, chest radiograph, and combined positron emission tomography/computed tomography scanning of the chest, abdomen, and pelvis.[11] These can be very useful to determine the extent of the disorder, local or regional affection of lymphatic nodes can be determined.

Sentinel-node biopsy or lymphoscintigraphy, beneficial in cutaneous melanoma staging, is less valuable in staging or treating oral melanoma, given they do not predict the tumor's lymphatic drainage due to the existing anatomical ambiguity and as a result the erratic drainage does not allow for a consistent evaluation of how this method is used. Prophylactic lymph node dissection also does not impact outcomes and is reserved for patients with clinically evident nodal involvement.[11]

The adjuvant medical treatment used for skin melanoma has not shown the same benefits in case of oral mucosal melanoma.

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