

Oral mucosa pigmented lesions: an overview of the recent literature and 3 case reports

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ABSTRACT

Pigmentation in the oral mucosa may be divided in physiologic or pathologic lesion. These can be classified into exogenous (induced by drugs, tobacco, amalgam tattoo) and endogenous (caused by systemic disorders, infections, chronic irritation, reactive or neoplastic). For a correct diagnosis several features as duration, colour, localization and distribution must be investigated, and it is necessary to execute a biopsy to exclude neoplastic and traumatic pathologies. The aim of this non-

systematic review is to report the main features of these lesions based on the recent literature, and to report 3 case reports of pigmented lesions. Two of the three patients are women; two cases in the gingival/alveolar mucosa and one observed in soft palate. They refused to be undergone to the histological examination. The most common pigmented lesions are in the cheek, and amalgam tattoos are the most frequent pigmented lesions reported. The most common types of nevi found are intramucosal (40.4%) and blue nevus (23.4%). The treatment of these lesions is, in the most of cases, surgical excision, also for histological examination.

Key Words: *Oral nevus; oral pigmentation; soft palate pigmentation; gum pigmentation; oral soft tissue nevi*

Pigmentations are a heterogeneous group with several etiopathogeneses, which is usually found in the mouth (1). Oral pigmentation may be physiologic or pathologic. Pathologic pigmentations can be classified into exogenous and endogenous based upon the cause (2). Exogenous pigmentations could be induced by drugs, tobacco/smoking, amalgam tattoo or heavy metals induced, while endogenous pigmentations can be associated with endocrine disorders, syndromes, infections, chronic irritation, reactive or neoplastic (3).

For a correct diagnosis is very important to value several features as duration, color, localization, and distribution; also to investigate the family, medical and dental histories. Since for the clinician is very difficult to make a correct diagnosis of these pigmentations (4), is necessary to execute a biopsy to exclude neoplastic and traumatic pathologies (5).

REACTIVE MELANOCYTIC PIGMENTATION

Melaninic macula

The melaninic macula is caused by an accumulation of melanin produced by the melanocytes (6). The lesions are more common in female patients and they appear as solitary, well-circumscribed and small. Areas more involved are lower lip, palate, and gingiva (4). Most melanotic macules are congenital, affect Caucasian individuals, and may be single or multiple. They have a diameter varying between 0.3 cm and 3 cm, tend to grow in proportion to body growth, and are unrelated to any systemic condition (7). Some authors recommend anatomopathological examination for diagnostic confirmation, although others sustain that the diagnosis is only clinical and follow-up is necessary to investigate changes in size, shape, and color of the lesion (8). Although lingual melanotic macule is a benign condition,

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an important differential diagnosis is made with melanoma and, if necessary, the macula can be treated with surgical excision (7).

Oral melanoacanthoma

Melanoacanthoma is a rare benign mixed epithelial tumor, characterized by the mucocutaneous pigmentation (9). It appears between the third or fourth decade, in black race and women. It regresses spontaneously after incisional biopsy (6).

Smoker's melanosis

The smoker's melanosis is one of the most common causes of oral pigmentation due to the stimulation of melanocytes present in the basal layer of the oral epithelium (10). The most affected subjects are women, which presents a diffuse black-brown macule in the gingiva, buccal mucosa, lips, and hard palate (6). Diagnosis is based on clinical features, and smoking history (11,12).

CAUSES OF MELANOCYTIC PIGMENTATION

Melanocytic nevus

Melanocytic nevi are congenital or acquired benign tumors, which derive from neural crest (6,13). Rarely, they occur in the mucosa, while they are more frequent on the skin. They are small, solitary, brown or blue, well-circumscribed and asymptomatic (4). The sites affected are hard palate, buccal, labial mucosae, and gums (1).

There are four main types: intramucosal nevus, junctional nevus, compound nevus, and blue nevus. The distinction of these nevi is purely histopathological because they are all clinically similar (6). In accordance with a study by Ferreira et al., intramucosal nevi average age appearance is around 33 years old; for blue nevi is around 40 years old; for junctional, 6-12 years old, for compound types 19 to 23 years old (3).

Lesions smaller than 1.0 cm is about 80% of the cases and non-pigmented lesions account for 15-20%. The biopsy examination is essential to distinguish these lesions from melanoma or other pigmented lesions and the therapy is surgical excision (1).

Malignant melanoma

Melanoma is malignant cancer that origins from malignant melanocytes (4). Oral melanoma usually affects patients between the fifth and seventh decades of life, but a wide age range is reported. Both female and males can be affected, although some studies report a slight male or female predominance (1). The oral melanoma usually appears as an asymptomatic dark-brown to black macule on the maxillary gingiva, alveolar mucosa or palate (14). The histopathological aspects of oral melanoma can vary as well, with pigmented, epithelioid, spindle, oval, round blue cells, clear cells, or organoid patterns. Melanin is not always evident (14). No single

immunohistochemical marker is totally sensitive for oral melanoma, and a variable expression of S-100, MART-A/Melan-A, MITF, tyrosinase, and HMB-45 have been reported (6).

DIFFUSE ORAL MUCOSAL PIGMENTATION

The systemic condition can lead to a multifocal or diffuse oral mucosal pigmentation, such as Cushing disease, Peutz-Jeghers syndrome, and Laugier-Hunziker pigmentation (4). It is necessary to execute a medical history, physical examination and laboratory tests for a correct diagnosis (15).

Diagnosis of pigmentations of the oral mucosa requires a clinical examination, as some entities show similar histopathological aspects (racial pigmentation, smoker's melanosis, melanotic macule, and Addison's disease), so a proper report to the pathologist is basic for a correct histopathological diagnosis (1).

CASE REPORTS

We would like to document three cases of oral pigmentations, presented to our attention in the last 2 years.

The first case was a 65 years old female patient, who presented a gum pigmented lesion similar to a nevus, in the area of the tooth 43. The anamnesis reported previous breast cancer and chemotherapy treatment 10 years earlier (Figure 1). Patient referred us that she had never seen the lesion before our examination and she was totally asymptomatic. She refused to be undergone to histological examination and we performed a follow up every 4-6 months. The lesion after 2 years was the same.

The second case was a female patient, aged 78, who presented a gum pigmented lesion similar to a nevus in the edentulous area of 34-35. The anamnesis was positive for atopic dermatitis. No other problems have been reported (Figure 2). Patient referred us that she had never seen the pigmented lesion and she was asymptomatic. She had not reported the presence of amalgam restoration in this area when the teeth were present. An x-ray in the region did not reveal radiolucency that could be associated with amalgam pigmentations. She refused to be undergone to histological examination. We have seen after 4 months the lesion showed the same clinical features and size.

The third case was a healthy 48 years old male patient, who presented around well- a circumscribed pigmented lesion of 3 mm of diameter on the soft palate (Figure 3). The patient did not report the traumatic event in the area and was asymptomatic. He referred us that he has seen the lesion when he was 20 years old and he refused the incisional biopsy for histological examination. We visited the patient

after 6 months and the lesion was the same in size and clinical features.

Patients were informed of the importance of the histological examination, but they choose to refuse this diagnostic examination. We, therefore, could not make a definite diagnosis of pigmented lesions.



Figure 1) An oral pigmented lesion in a 65 years old female patient



Figure 2) A gum pigmented lesion in a 78 years old female patient



Figure 3) A soft palate pigmented lesion in a male patient

DISCUSSION

The pigmentation is given by the deposition of pigments in tissues, which can derive from intrinsic or extrinsic factors that could be physiological or pathological (15). These lesions' clinical features may be blue, purple, brown, gray, or black and they can be focal, multifocal or diffuse (4). The most common lesions are amalgam tattoos, melanotic macules, and nevi.

Tavares T.S. et al, find that the cheek mucosa is the most frequent oral localization (21.0%). Other frequent sites involved are alveolar

mucosa (16.6%), gingiva (11.8%) and hard palate (10.0%) (1). There are different histological subtypes of oral nevi: intramucosal (40.4%), blue nevus (23.4%), compound (21.3%), junctional (2.1%) and nevus not specified (12.8%) (1). Amalgam tattoo are the most common pigmented lesion found in this work (46.3%), followed by melanotic macule (22.9%) and nevus (20.5%). The most common types of nevi found are intramucosal (40.4%) and blue nevus (23.4%) (1). These lesions are more frequent in the females than in males, between the third and seventh decades of life. In the melanocytic nevi frequently you can find oncogenic serine/threonine-protein kinase B-Raf (BRAF) but rarely neuroblastoma RAS viral oncogene homolog (NRAS) mutations (16).

The hyperproliferation can be caused by oncogenic mutations, which lead the formation of the nevi with subsequent cellular senescence by oncogenic-induced, which it might arrest further growth (16). Although the clinical aspects of pigmented lesions are sufficient in establishing the diagnosis, it is necessary to execute a biopsy to exclude melanoma, particularly if the lesion is localized on the palate (1).

In according to a study of Tavares et al., a proper report to the pathologist is essential for an accurate histopathological diagnosis. In this study, accuracy between the clinical and histopathological diagnoses is found in less of 45% (1). In according to a study of Ferreira et al., the clinical diagnosis includes nevi in only 30% of the 100 oral nevi reported, so, the continuous information of the dental practitioners is important to reach the correct diagnosis (3). The treatment of these lesions is, in the most of cases, surgical excision.

CONCLUSION

In order to formulate a correct diagnosis of pigmented lesions, an histopathological confirmation is recommended especially because the differential diagnosis includes malignant melanoma (16). However, medical history and laboratory studies are important in order to establish a definitive diagnosis (4). It is also essential to execute follow-ups of patients to exclude recurrence of oral nevi.

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