Concomitant endogenous and exogenous etiology for gingival pigmentation

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Abstract

Oral pigmented lesions can be physiological or pathological, exogenous or endogenous, as well as focal, multifocal, or diffuse. Among them, the oral melanotic macule (OMM) is a small, well-delimited brown-to-black macule, often affecting the lip and gingiva. Amalgam tattoo (AT) is a grey or black area of discoloration on the oral mucosa as a result of entry of dental amalgam into the soft tissues, commonly gingiva and alveolar ridge. Herein, we present a patient with gingival pigmentation with features of both OMM and AT in the same location.

Keywords: amalgam tattoo, histopathology, melanotic macule, oral mucosa, pigmentation disorders

Introduction

Intraoral pigmented lesions are common conditions, which can be of exogenous or endogenous origin [1-3]. Among exogenous origins, amalgam tattoo (AT) represents a major proportion of these lesions and is mainly caused by the accidental introduction of amalgam particles related to dental restoration or tooth extraction [2,4]. Moreover, graphite tattoo, drug-induced pigmentation, and poisoning (argyria) should also be considered in the exogenous pigmented lesion spectrum. By contrast, in endogenous origin, increased melanin production explains the pathogenicity and oral melanotic macule (OMM) is the most common condition in this category. Certain systemic conditions such as Addison disease, Peutz-Jeghers syndrome, and McCune-Albright syndrome also produce increased melanin production in the oral mucosae [3,4]. In addition, intraoral pigmented lesions can occur because of benign or malignant melanocytic proliferations, including melanocytic nevus, melanoacanthoma and melanoma [3,5]. Therefore, the clinical differential diagnosis of intraoral pigmented lesions is broad and must be carefully assessed. Herein, we present a patient with mixed gingival pigmentation showing exogenous (AT) and endogenous (OMM) origins in the same lesion, resulting in an unusual presentation.

Case Synopsis

A 33-year-old woman was referred for evaluation of an asymptomatic, pigmented gingival lesion, which was noticed by her dentist four months prior when she started chemotherapy for breast cancer (**Figure 1**). The patient reported her medications as levothyroxine and tamoxifen for hypothyroidism and breast cancer treatment, respectively. Intraoral examination revealed the presence of an asymptomatic, brown-to-black macule located on the gingiva between teeth #34 and #35. The patient denied any history of local trauma or surgery. However, she noted that she had replacement of dental amalgam by composite resin at tooth #35,

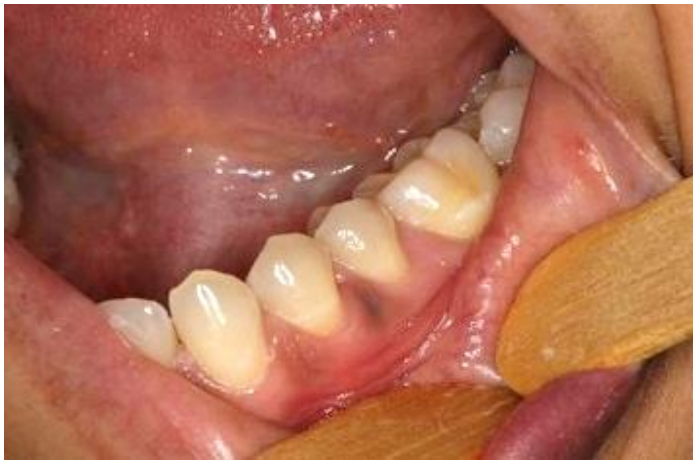

Figure 1. *Clinical aspect of the pigmented gingival lesion in the premolar region.*

which was done 2-years prior. A periapical radiography did not show alterations. The clinical differential diagnosis included AT, drug-induced pigmentation, OMM, and melanoacanthoma. An excisional biopsy was performed. Microscopical analysis revealed the presence of irregular dark fragments and numerous, fine, brown-to-black granules distributed along collagen bundles and around small blood vessels. Moreover, increased pigmentation in the epithelial basal layer cells and discreet melanin deposits in the lamina propria were also visualized. Fontana-Masson stain highlighted the melanin deposition (**Figure 2**).

Case Discussion

The color of the oral mucosa may vary depending on several factors such as degree of keratinization, vascularization, and number and activity of melanocytes [1,3]. Melanin production takes place in cytoplasmic organelles called melanosomes inside of melanocytes in the basal layer of the epithelium and melanosomes are subsequently transferred to adjacent keratinocytes [1,3,4]. The amount of melanin produced is determined genetically. However, some causes such as trauma, inflammation, hormones, and medications may result in increased production of melanin [6]. In the current case, the patient was on levothyroxine and tamoxifen medication. Although levothyroxine-induced oral pigmentation has not been reported, some skin changes related to thyroid hypofunction include dry, pale, and cold skin, palmoplantar keratoderma, keratosis pilaris, cutaneous mucinosis, and mucosal thickening with dysphonia [7]. These skin and mucosal changes were not observed in the current case. Tamoxifen is an estrogen receptor (ER)-antagonist, widely used for the treatment of breast cancer. Interestingly, one of the side effects of tamoxifen is hyperpigmentation. In fact, there are some reports showing tamoxifen-induced hair color change [8] and melasma [9], although oral pigmentation seems unusual. Moreover, by microscopy, most oral cases of drug-induced pigmentation exhibit pigment granules within the lamina propria [10]. Therefore, we believe that in the

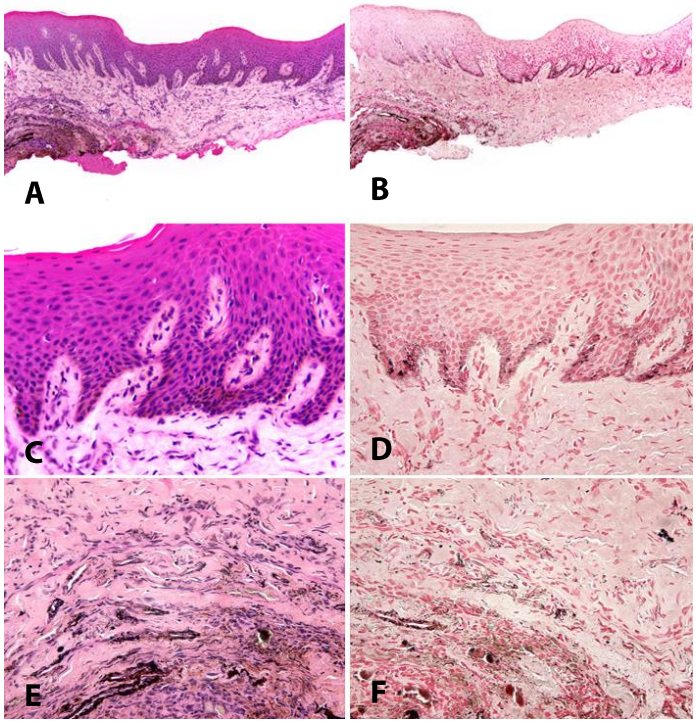

Figure 2. ***A)*** *Increased melanin deposition within the basal-cell layer and scarce melanin granules in subepithelial location. Moreover, notice the scattered large and small fragments of dark material distributed in the lamina propria at left bottom. H&E, 100×.* ***B)*** *Melanin deposition in the basal-cell layer and subepithelial location highlighted by Fontana-Masson stain, 100×.* ***C)*** *In high-power view, notice the epithelium with parakeratinization and pigmented basal-cell layer. H&E, 400×.* ***D)*** *The basal-cell layer showing deposition of melanin granules evidenced by Fontana-Masson stain, 400×.* ***E)*** *The lamina propria containing deposits of amalgam interspersed among collagen bundles and around small blood vessels. H&E, 400×.* ***F)*** *The amalgam deposits were not highlighted by Fontana-Masson stain, 400×.*

current case the gingival pigmentation is endogenous in nature.

Oral melanotic macule is characterized clinically as a solitary macule with black, blue, or brown color, usually with a diameter of less than 10mm. The main sites of involvement are the lower lip and gingiva. Oral melanotic macule is noted mostly in patients over 40 years of age, but can be observed in a wide age range of ages (from four to 98 years). The microscopic analysis shows melanin deposition in the basal-cell layer and lamina propria [4]. Oral melanotic macule should be differentiated from melanocytic nevus, melanoacanthoma, and melanoma, through strict clinicopathological correlation [5]. After an extensive review of the literature, we have neither found a study showing the simultaneous presence of these melanocytic lesions in the same area nor an association with AT. Therefore, it seems that the present case is the first report to show such characteristics.

The AT is the most common oral pigmentation of exogenous origin. Dental amalgams contain silver (67-74%), tin (25%), and copper (6%), mercury (3%), and zinc (2%), [11]. Studies have shown that although copper and zinc are rapidly lost from AT areas, mercury and tin are lost more slowly. In addition, silver remains permanently in AT [11,12]. To the best of our knowledge, there is a single report of cutaneous AT to date [6], which although rare, should also be included in the differential diagnosis when assessing pigmented skin lesions, especially in dental service workers. Amalgam tattoo is caused by traumatic implantation of amalgam fragments into the oral mucosa, which clinically presents as a bluish-to-black macule. Amalgam tattoo is usually discovered during routine dental treatment, such as in the current case. A radiograph can show the presence of metallic particles, but its absence does not rule out the possibility. In fact, we did not observe any changes when assessing periapical radiography in our patient. Microscopically, AT shows aggregates of black granules, coarse and/or fine, among collagen fibers and surrounding small blood vessels and nerves. Some cases show a foreign-body granulomatous reaction [2,6]. The clinical differential diagnosis of AT includes OMM, melanocytic nevus, melanoacanthoma, and melanoma [1-3]. It is relevant to mention that localized argyria with cutaneous involvement is uncommon, with most cases related to trauma, acupuncture, topical medication, and use of earrings [6].

Conclusion

We present a patient with gingival pigmentation as a result of simultaneously presence of OMM and AT in the same location, an unusual finding. To the best of our knowledge, the current case is the first report showing such characteristics. Although rare, AT can also involve cutaneous tissue [6]. These findings expand the clinicopathological spectrum of pigmented lesions affecting the skin and oral mucosa.

Potential conflicts of interest

The authors declare no conflicts of interest.

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