

Oral Pigmentation

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Rec date: December 22, 2015; Acc date: January 23, 2016; Pub date: January 28, 2016

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Abstract

Diagnosis of pigmented lesions of the oral cavity is challenging. Oral pigmentation can be physiological or pathological, melanin-associated or non-melanin-associated, and endogenous or exogenous. Evaluation of a patient with oral pigmentation requires a systemic approach. This review presents diagnosis, differential diagnosis and management of pigmentary findings in the oral cavity.

Keywords: Pigmentation; Melanoma; Drugs

Introduction

Oral pigmentation is fairly common, and its differential diagnosis is broad. A distinction can be made between melanin-associated and non-melanin associated pigmentation. The pigmentation can result from endogenous or exogenous factors, and may include both benign and malignant etiologies. The color, location, distribution, duration, and appearance of the pigmentation may be of diagnostic importance. The investigation of medical, dental, family and social histories and the presence of cutaneous pigmentation or other systemic signs and symptoms may be helpful in making the differential diagnosis. Pigmentation that cannot be identified by history may necessitate a biopsy to exclude malignancy.

Melanin – Associated Pigmented Lesions of the Oral Cavity

Physiologic pigmentation

Physiologic pigmentation of oral mucosa is the most common cause of oral pigmentation, and it is symmetrically distributed, especially on the gingiva in dark-skinned individuals. It can be seen anywhere in the oral cavity, including the buccal mucosa, hard palate, lips and tongue [1]. The pigmentation arises from increased melanocyte activity rather than increased melanocyte number [2]. Physiological pigmentation increases with age, smoking, hormones, and medications. The diagnosis can be made clinically, and no treatment is required.

Ephelides and lentiginos

Ephelides are common, uniform, small, light brown macules localized on sun-exposed areas of skin, including the perioral skin and lips. They occur most frequently in childhood. Histological examination shows increased melanin pigmentation of the basal layer without an increased number of melanocytes.³

Solar lentiginos are ultraviolet (UV) induced pigmented lesions and may be seen in the perioral region. They are more common in older individuals. Histopathological examination shows hyperplasia of basal melanocytes with elongation of the rete ridges [3,4]. Non-sun-induced

multiple labial lentiginos may be seen as a part of some lentiginos syndromes, which will be discussed later.

Oral melanotic macule

The oral melanotic macule, also known as focal melanosis, is a benign, solitary, well-demarcated, dark brown macule, most commonly located on the vermilion border of the lower lip followed by the palate, gingiva, and buccal mucosa [5]. It is presents in up to 3% of the normal population. The female to male ratio is almost 2:1 and the mean age of onset is 30 years [1,6]. Histopathologic examination shows increased basal pigmentation, especially at the tips of the rete ridges and the number of melanocytes is normal [7-9]. There is a mild perivascular infiltration and pigmentary incontinance in the upper dermis [8,10]. In contrast to nevi and melanomas, melanotic macules are HMB-45 negative. Lesions have no malignant potential, therefore no treatment is require.

Melanocytic nevi

Oral melanocytic nevi are uncommon lesions most frequently occur in female gender and in the third and fourth decades of life [1,3]. It may be a variety of colors including brown, blue, and gray [11,12]. The most common site for occurrence of oral nevi is the hard palate, followed by the buccal mucosa, gingiva or vermilion border [13]. Intramucosal nevi are the most common type, followed by the blue, compound, and junctional nevi [3]. Histologically, melanocytic nevi are identical to cutaneous nevi, demonstrating junctional or intramucosal nests of nevus cells [3]. Malignant transformation has rarely been documented. However oral nevi cannot be clinically differentiated from early melanoma, thus excision of all lesions is advisable.

Melanoacanthoma

Melanoacanthoma is a rare, benign, solitary, well-demarcated, flat or slightly raised hyperpigmented lesion [1,13]. Lesions typically develop after trauma, most commonly on the buccal mucosa and are more frequently unilateral. The majority of cases reported so far have occurred in young black females. Histological examination shows acanthosis, basal layer hyperpigmentation, and many dendritic melanocytes distributed through all layers of the epithelium without

atypia [14]. Many lesions regress spontaneously after removal of traumatic irritants or following incisional biopsy [4]. Histological confirmation is always required for differentiated melanoma.

Smoker's melanosis

Smoker's melanosis characterized by pigmentation, predominantly on the anterior attached mandibular gingiva and interdental papillae [4,5]. This pigmentation is thought to be caused by increased melanin production in response to tobacco smoke. Females are most commonly affected, suggesting that estrogen may play a role [1,15]. Histologic findings are non-specific. There is abundant melanin within the basal layer with melanin incontinence. Smoker's melanosis does not require treatment and disappearance has been reported after cessation of the habit.

Malignant melanoma

Oral malignant melanoma is extremely rare make up less than 1% of all melanomas. The most frequently affected oral sites include the hard palate and maxillary gingiva [16]. It presents most commonly as dark brown or black pigmented patches or plaques with asymmetric and irregular borders. However 5% to 15% of oral melanomas are amelanotic. These cancers typically occur in persons after the age of 50 years, and a male:female ratio of 2.5-3:1 is noted [1,9]. Oral melanoma may represent a metastatic lesion rather than a primary lesion. They develop most frequently on the tongue and buccal mucosa [1,3]. Nodal metastases at the time of diagnosis have been reported in more than 50% of oral melanoma cases. The most common growth patterns determined are acral lentiginous and/or nodular patterns [3-5]. The depth of invasion (Breslow depth) proven to be the most important prognostic factor for oral melanomas [16,17]. The prognosis in mucosal melanoma is worse than in cutaneous melanoma with five-year survival of about 5%. Histologically, oral melanoma is identical to cutaneous melanomas and exhibits epitheloid or spindle nuclei. Treatment of oral melanomas is primarily by radical surgery. Chemotherapy and immunotherapy may be used as an adjunct.

Systemic Disorders – Associated Pigmented Lesions of the Oral Cavity

Endocrine disease

Primary adrenocortical insufficiency, also referred to as Addison's disease, is characterized by deficient production of hormones of the adrenal cortex, leading to increased production of adrenocorticotropic hormone (ACTH) and melanocyte-stimulating hormone (MSH) [1,5,9]. This may result in a diffuse dark pigmentation of the skin and the oral mucosa. In one-third of cases, the pigmentation is the initial sign of the disease. Other manifestations of the disease include anorexia, nausea, malaise, abdominal pain, and postural hypotension [4,8]. Cutaneous pigmentation is commonly seen in areas of friction or pressure such as the palms and soles and flexures.

Similar patterns of pigmentation can find in Cushing's disease, Nelson's syndrome, hyperthyroidism, McCune-Albright syndrome, and acromegaly [1,9].

Haemochromatosis is an autosomal recessive disease with increased iron absorption, resulting in cirrhosis, hyperpigmentation, diabetes, and cardiac failure [7,9]. Oral findings are present in 25% of patients and consist of bluish-gray pigmentation of the hard palate and

attached gingiva. Generalized bronze or slate gray discoloration of the skin is present in 70% of cases.

Lentiginosis syndromes

Peutz-Jeghers syndrome is inherited with an autosomal dominant trait, characterized by mucocutaneous hyperpigmentation, gastrointestinal hamartomatous polyposis and the increased risk of carcinomas of the gastrointestinal tract, pancreas, thyroid and breast [1,4,5,7]. Classically, hyperpigmentation is found on the buccal mucosa and in a perioral distribution. Black-to-brown spots are typically localized on the lower lip, buccal mucosa and in the perioral area. Buccal pigmentation is commonly seen at birth and in early infancy [5,7]. Perioral and peripheral pigmentation often fades in early adult life while buccal mucosal pigmentation usually persists.

Bandler syndrome is a rare genodermatosis that presents with hyperpigmented macules in the lips, hands, nails, perioral area, and oral mucosa during infancy, as well as intestinal vascular malformation that can cause significant gastrointestinal bleeding [7].

The Carney complex, is an autosomal dominant disorder characterized by multiple myxomas, spotty mucocutaneous pigmentation, schwannomas, and endocrine overactivity [18]. The spotty skin pigmentation includes lentiginos, blue nevi, ephelides and junctional and compound nevi. The lentiginos are widespread and typically involve the centofacial area, including the vermilion border of the lips and conjunctiva [7,18]. One or more intraoral pigmented spots are seen occasionally. Endocrine overactivity includes Cushing's syndrome, acromegaly and sexual precocity.

Laugier-Hunziker syndrome

Laugier-Hunziker syndrome is a rare, benign, acquired disorder characterized by diffuse hyperpigmentation of the oral mucosa and longitudinal melanonychia in adults [1,19]. There are no systemic findings. It occurs predominantly among middle-aged adults and more prevalent in women.

Aspergillus and mucor infection

Aspergillosis and zygomycosis are fungal infections. If untreated, these infections lead to necrotic palatal perforation that is seen as a black ulcer, especially immunocompromised patients [4].

Human Immunodeficiency Virus (HIV) infection

HIV infection has been associated with multiple, oral, well-circumscribed melanotic macules on the lips, gingiva, palate, and buccal mucosa [4,20]. Pigmentation may become generalized mimicking adrenal insufficiency in some cases. In some individuals the appearance of these melanotic macules can pre-date the diagnosis of HIV.

Exogenous Etiologies-associated Pigmented Lesions of the Oral Cavity

Drug-induced oral pigmentation

Many drugs induce pigmentary changes in the oral mucosa. Some of these drugs are listed in Table 1. Usually drug-induced oral pigmentation is not directly related to dose or duration of medication. Most agents produce a diffuse melanosis but some drugs may be

localized to one mucosal region [1,4,21]. The causative mechanisms could include direct deposition of pigmented drug particles or drug metabolites, accumulation of drug by-products after systemic absorption, and increased synthesis of melanin [8,9]. Systemic drugs commonly causing oral pigmentation, that presents as a well demarcated, diffuse, bluish-gray discoloration of the hard palate and gingiva, include minocycline, antimalarials, amiodarone, and clofazimine [1,5,8]. Drug-induced oral pigmentation generally resolves within weeks to months when the offending drug is withdrawn, although sometimes it is permanent.

Nicotine
Heroin
Tetracyclines
Minocycline
Busulfan
Doxorubicin
5-fluorouracil
Bleomycin
Cyclophosphamide
Nitrogen mustard
Amiodarone
Quinidine
Antimalarials
Phenothiazines
Zidovudine
Ketoconazole
Clofazimine
Premarin
Oral contraceptives
Chlorhexidine
Carotene
Gold
Tacrolimus
Imatinib mesylate

Table 1: Drugs causing oral pigmentation.

Amalgam tattoo

Amalgam tattoo is the most common cause of exogenous pigmentation of the oral mucosa. It is iatrogenic lesions that traumatic soft tissue implantation of dental amalgam particles [4,22]. Lesions can be solitary or multiple, displaying a gray, blue or black hue depending upon the depth of tissue in which the amalgam particles lodge. Most lesions are located on the gingiva and alveolar mucosa, but can also be seen on the hard palate, buccal mucosa, and floor of the mouth [9,15].

Radiographic features may show localized radiopacities [5]. No treatment is required, however it must be distinguished from a melanoma and sometimes histological examination is necessary to confirm the diagnosis.

Heavy metal exposure

Heavy metals capable of producing oral pigmentation include arsenic, bismuth, lead, mercury, silver, gold, and platinum. It usually appears as blue-black discoloration on the lips and gingival margins [1,21]. Lead produces characteristic generalized cutaneous “lead hue” and “lead lines” on the gingiva; mercury, gold and bismuth can cause slate-gray gingival hyperpigmentation; silver can produce a permanent diffuse bluish-gray pigmentation, most frequently of the hard palate [9,12]. Systemic symptoms and signs associated with chronic exposure may occur, depending on the type of metal implicated.

Hairy tongue

A brown or black discoloration of the tongue may be caused by poor oral hygiene, general debilitation, radiation therapy, tobacco smoking, oxidizing mouthwashes or antacids, fungal or bacterial organisms or broad-spectrum antibiotic usage [4,9]. Hypertrophy of the filiform papillae with accumulation of bacteria and yeast occurs with discoloration and furring of the tongue [4]. Treatment consist of stopping any predisposing factors, and good oral hygiene should be encouraged. Retin-A gel may be applied to the tongue.

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