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Pigmented Lesions of The Oral Cavity: Review, Differential Diagnosis

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ABSTRACT

Pigmentation is a common clinical finding of an oral cavity, but a proper diagnosis of the lesions is very challenging. Pigmentation can be focal, multifocal, associated with systemic/genetic disorder, or due to exogenous agents. Pigmented lesions are either melanocytic or nonmelanocytic. Pathologic pigmentations due to exogenous agents including drugs, tobacco smoking, amalgam tattoo, and heavy metals. Melanin, hemoglobin, hemosiderin, and carotene are endogenous pigments. Correct diagnosis is of utmost importance for proper treatment plan. Several clinical parameters, i.e., color, duration, localization, distribution, and medical history are useful for proper diagnosis.

Key Words- Pigmented lesions, exogenous agents.

INTRODUCTION

Pigmentations usually occur due to increased melanin production, increased number of melanocytes (melanocytosis), or accidental deposition of exogenous materials.[1]

Pigmentation is defined as the process of deposition of pigments in tissues. Various diseases can lead to varied colorations in the mucosa. Pigmented lesions of oral cavity are due to:[2]

- Augmentation of melanin production
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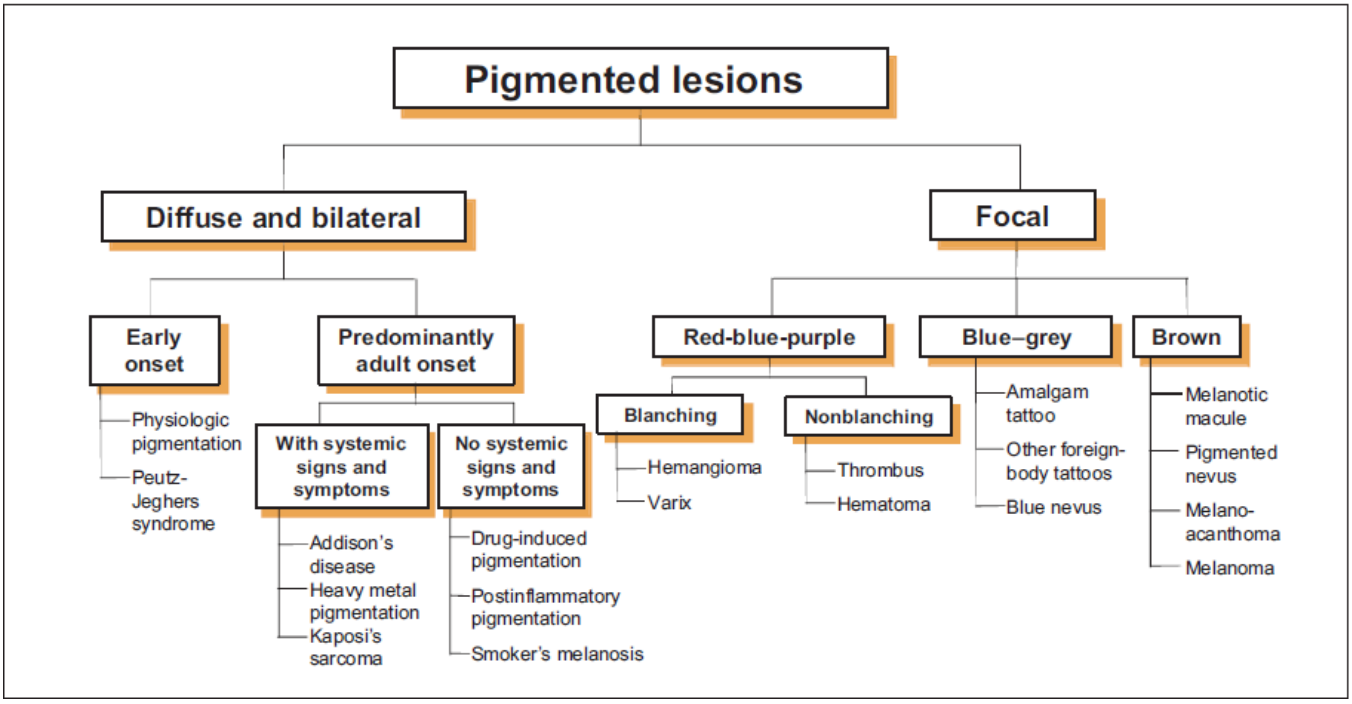
- Increased number of melanocytes (melanocytosis)

- Pathologic pigmentations due to exogenous agents including drugs, tobacco smoking, amalgam tattoo, and heavy metals. Melanin, hemoglobin, hemosiderin, and carotene are endogenous pigments.[2]

DIFFERENTIAL DIAGNOSIS OF ORAL PIGMENTED LESIONS

The history should include the onset and duration of the lesion, the presence of associated skin hyperpigmentation, the presence of systemic signs and symptoms (e.g., malaise, fatigue, weight loss), use of prescription and non-prescription medications, and smoking habits. Pigmented lesions on the face, perioral skin and lips should be noted. [1] In general, benign pigmented lesions show regular borders and are small, symmetric and uniform in colour. They may be either flat or slightly elevated.In contrast, irregular borders, colour variation, and surface ulceration suggest malignancy[3]



DIFFUSE AND BILATERAL PIGMENTATION *PHYSIOLOGIC (RACIAL) PIGMENTATION*

The colour ranges from light to dark brown. The attached gingiva is the most common intraoral site of such pigmentation, where it appears as a bilateral, well-demarcated, ribbon-like, dark brown band that usually spares the marginal gingiva.The pigmentation is asymptomatic, and no treatment is required.[2]Color, location, distribution, and duration as well as drugs use, family history, and change in pattern are important for the differential diagnosis.[3]

PEUTZ-JEGHERS SYNDROME

Peutz-Jeghers syndrome is a rare genetic disorder associated with mutation of the *LKB1* gene on chromosome.[4] The Peutz-Jeghers syndrome (PJS) consists of mucocutaneous macules, intestinal hamartomatous polyposis, and increased risk of carcinomas of the gastrointestinal tract, pancreas, breast, and thyroid. Black-to-brown spots of less than 1 mm in size are typically localized on the lower lip and in the perioral area .Intraoral, intranasal, conjunctival, and rectal pigmented lesions as well as spots localized on the acral surfaces may also be present.[5] Mucocutaneous melanin pigmentation occurs in more than 90% of patients. Intraoral sites include buccal and labial mucosa, hard palate, gingivae, and very rarely on the tongue. Extraoral sites include facial skin around mouth, lips, nose, eyes, hands, feet, and genital region. They fade from third decade onward, whereas intraoral lesions persist. They are not affected by solar exposure.These macules are benign and no malignant transformation has been described. Nails can demonstrate longitudinal melanonychia.[4]

ADDISON'S DISEASE

Addison´s disease, is characterized by deficient production of hormones of the adrenal cortex, leading to increased production of adrenocorticotropic hormone (ACTH). This may result in a diffuse dark pigmentation of the skin and the oral mucosa.[5]

Addison's disease is rare endocrinal disorder that affects 1 in 100,000 people. It is seen in all age groups and affects male and female equally. This disease is named after Thomas Addison, who first described patients affected by this disorder in 1855, in the book titled "On the constitutional and local effects of the disease of supra renal capsule.The pigmentation may involve skin, oral cavity, conjunctiva, and genitalia.[7]

The symptom of Addison's disease begins gradually, chronic worsening fatigue, loss of appetite, generalized weakness, hypotension, and weight loss. The clinical features of hypoadrenocorticism do not actually begin to appear until at least 90% of the glandular tissue has been destroyed. Generalized hyperpigmentation of skin is seen, which is classically described as "bronzing" the hyperpigmentation is generally more prominent on sun-exposed skin and over pressure points, such as the elbows and knees which are caused by increased levels of beta-lipotropin or Adrenocorticotropic hormone, each of which can stimulate melanocyte production. Hyperpigmentation of the mucous membrane and skin usually proceeds over other symptoms by month to year.[8]

HEAVY METAL PIGMENTATION

- Heavy metals such as lead, arsenic, bismuth, gold, silver, mercury, and platinum are capable of producing oral pigmentation due to an increased level in blood.
- The pigmentation usually involves the marginal gingiva and lips as blue-black lesion.[8]
- The lead pigmentation on the gingival margin is usually characterized by "lead lines," while gold, bismuth, and mercury cause slate-gray appearance of the gingiva. Silver product deposition may appear on the hard palate as permanent diffuse bluish-gray pigmentation. Identification of heavy-metal pigmentation is important to avoid severe systemic toxic effects.[9]

KAPOSI'S SARCOMA

Kaposi's Sarcoma (KS), being first described in 1872, is an unusual vascular neoplasm that most likely arises from endothelial cells, with some evidence of lymphatic origin. Current evidence suggests that KS is caused by human herpes virus 8 (HHV-8). The course of the disease is strongly influenced by the immune status of the patient.[10]Clinically KS strongly resembles certain vascular lesions that include ecchymosis or a deeply located low grade mucoepidermoid carcinoma (at initial stages); or these appear more like hemangiomas, lymphangiomas and arteriovenous hemangiomas (at papular or nodular stage). Even though uncommon, bacillary angiomatosis may appear as multifocal KS lesions. [11]Kaposi sarcoma is estimated that of all patients with AIDS who develop KS, up to 71% develop oral lesions concurrently with skin and visceral lesions. In an additional 22% of patients, the disease initially presents in the mouth and in some instances remains restricted to the oral cavity. Oral classic KS could present initially as well-demarcated, painless, brownish red to violaceous macule or papule. It could appear as a single or multiple lesions with dimensions varying from a few millimeters to centimeters, increasing slowly in size, forming nodules or tumors with or without ulceration. Classic KS could invade bone and create tooth mobility. The most frequent locations are the hard palate and gingiva, whereas appearance on the buccal mucosa and tongue are rarer. Morbidity may be associated with pain, bleeding, and functional interferences caused by the tumor.[12]

DRUG-INDUCED PIGMENTATION

Pathogenesis of drug-induced pigmentation varies, depending on the causative drug.[3]

- Antimalarials: quinacrine, chloroquine, hydroxychloroquine
- Quinidine
- Zidovudine (AZT)
- Tetracycline
- Minocycline
- Chlorpromazine
- Oral contraceptives
- Clofazimine
- Ketoconazole
- Amiodarone
- Busulfan
- Doxorubicin
- Bleomycin
- Cyclophosphamide

- It can involve accumulation of melanin, deposits of the drug or one of its metabolites, synthesis of pigments under the influencen of the drug or deposition of iron after damage to the dermal vessels.Mucosal discolouration associated with this group of drugs is described as blue–grey or blue–black, and in most cases only the hard palate is involved.Long-standing inflammatory mucosal diseases, particularly lichen planus, can cause mucosal pigmentation.[12]There is increased production of melanin, which may provide a biologic defence against the noxious agents present in tobacco smoke.Smoker's melanosis occurs in up to 21.5% of smokers.[3]
- The brown–black lesions most often involve the anterior labial gingiva followed by the buccal mucosa.It has no malignant potentiality.[5]

AMALGAM TATTOO*(FOCAL ARGYROSIS) *AND OTHER FOREIGN-BODY PIGMENTATION

- The most common cause of intraoral pigmentation by an exogenous agent is amalgam tattoo.[14].
  The common site of occurrence includes the gingival and alveolar mucosa. Sometimes, it is also sited on the buccal mucosa, hard palate, and floor of the mouth. Radiographically, localized radiopacities can be noted.[9]

  Reasons for amalgam tattoo are:[1]

  (1) Previous areas of mucosal abrasion can be contaminated by amalgam dust within the oral fluids

(2) broken amalgam pieces can fall into extraction sites

(3) if dental floss becomes contaminated with amalgam particles of a recently placed restoration, linear areas of pigmentation can be created in the gingival tissue as a result of hygiene procedures

(4) amalgam from the endodontic retrofill procedures can be left within the soft tissue at the surgical site

(5) fine metal particles can be driven through the oral mucosa from the pressure of high-speed air turbine drills.

MELANOTIC MACULES

Oral melanotic macules (brown, black, blue, or gray) are well-circumscribed, flat lesions. The common site of occurrence is the vermillion border of lip, palate, gingival, and buccal mucosa, and females are more affected than male.[9] The labial melanotic macule is a benign pigmented lesion that is common on the lower lip.Melanotic macules are usually smaller than 1 cm in diameter and show a well-demarcated smooth border.Pigmented nevi are rare causes of focal oral pigmentation.[16] They occur due to increased melanin production by the melanocyte rather than an increased number of melanocytes.[9]Histologically, nevi are composed of an accumulation of nevus cells in the basal epithelial layers, the connective tissue or both.Blue nevi are characterized by proliferation of dermal melanocytes within the deep connective tissue at some distance from the surface epithelium, which accounts for the blue colour.Blue nevus is the second most common type, occurring most commonly in the palate.[16]

ORAL MELANOACANTHOMAThe term melanoacanthoma refers to a lesion exhibiting a proliferation of dendritic melanocytes throughout the surface epithelium. Cutaneous melanoacanthoma is also known as pigmented seborrheic keratosis .Oral melanoacanthoma is a benign, reactive process and is unrelated to cutaneous [16]Oralmelanoacanthomas show a female predilection, with a male to female ratio of 2:1 The etiology has been largely attributed to local irritation or even mild trauma The intra-oral site most commonly affected is the buccal mucosa but involvement of other sites such as the mucosa of the lip, palate, gingiva and alveolar mucosa has also been reported. Clinically, the lesion is a flat or slightly raised black or brown macule and may rapidly increase in size, ranging from a few millimeters to several centimeters .[17]Superficial spreading melanoma, nodular melanoma, lentigomaligna melanoma, and acral lentiginous melanoma are four clinicopathological types of melanoma.[18]Histopathologically, malignant melanocytes proliferate at the epithelial and connective tissue junction, and they can also invade into the connective tissue stroma.[19]

CONCLUSION

- The diagnosis of oral pigmentation is difficult.
- Thus, biopsy is indeed essential for each and every lesion, so that histopathological evaluation confirms the diagnosis.
- Biopsy help the clinicians establish a better approach towards the patients with pigmented oral lesions and to provide thorough knowledge regarding such lesions for patient reassurance , early definitive diagnosis and prompt treatment.

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