Oral pigmented lesions

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Associations with Melanin Pigmentation of Oral Mucosa

Physiologic or syndromic associations
- Racial or physiologic pigmentation
- Peutz-Jeghers syndrome
- McCune-Albright syndrome
- Dyskeratosis congenita
- Endocrine candidiasis syndrome
- Xeroderma pigmentosum
- Addison’s disease
- Neurofibromatosis type I

Chronic or irritation or environmental
- Chronic mucosal trauma or irritation (chronic cheek bite)
- Chronic autoimmune disease (erosive lichen planus)
- Smoker’s melanosis

Systemic medications
- Chloroquine and other quinine derivatives
- Estrogen
- AIDS-related medications

▼ BROWN MELANOTIC LESIONS

Ephelis and Oral Melanotic Macule
The common cutaneous freckle, or ephelis, represents an increase in melanin pigment synthesis by basal-layer melanocytes, without an increase in the number of melanocytes. On the skin, this increased melanogenesis can be attributed to actinic exposure.

- The vermilion of lower lip is the most common site, followed by buccal mucosa.
- The lesion is Oval brown or even black macul and ranges from being quite small to over a centimeter in diameter that do not tend to enlarge further.
- Lip ephelides are asymptomatic.

The differential diagnosis includes:
- Nevus.
- Early superficial spreading melanoma.
- Amalgam tattoo.
- Focal ecchymosis. If such pigmented ephelis

**Blue nevus:**

A benign pigmented lesion (dark blue, dome shaped or flat macule on the skin or mucosa most commonly on the hard palate.

Nevi are due to benign proliferations of melanocytes. They are found most frequently on the palate and gingiva but may also be encountered in the buccal mucosa and on the lip. Lesions tend to persist unchanged throughout life.

Clinically benign. Because of their large size, biopsy and excision tend to be performed. Two clinically recognized variants of blue nevus exist: the common blue nevus and the cellular blue nevus.

Rare cases of malignant melanoma have been reported to arise in cellular blue nevi. Any change in these lesions is an indication for biopsy or excision.

Once a blue nevus appears, it tends to remain unchanged throughout life. Occasionally, Blue nevi are usually smooth-surfaced, dome-shaped papules that slowly develop from a macule to a papule. Common blue nevi tend to be smaller than 1 cm, and cellular blue nevi tend to be larger than 1 cm.

**Differential diagnosis**

1- Dermatofibroma
2- Malignant Melanoma
3- Tattoo Reactions
4- Nevi and, Melanocytic
Malignant Melanoma:

On the facial skin, the malar region is a common site for melanoma because this area of the face is subject to significant solar exposure.

- Facial cutaneous melanomas may appear macular or nodular, and the coloration can be quite varied, ranging from brown to black to blue, with zones of depigmentation.
- Melanomas show jagged irregular margins.
- Lentigo maligna melanoma has been applied to these facial skin lesions that exhibit atypical melanocytic hyperplasia or melanoma in situ. The melanocytic tumor cells spread laterally and therefore superficially. These lesions have a good prognosis if they are detected and treated before the appearance of nodular lesions, which indicates invasion into the deeper connective tissue (ie, a vertical growth phase).
- Melanomas arising in the oral mucosa are extremely rare and tend to occur on the anterior labial gingiva and the anterior aspect of the hard palate. Excision with wide margins is the treatment of choice; once nodularity has evolved, however, the lesion has probably already metastasized.

The development of melanoma is multifactorial and appears to be related to multiple risk factors.

1- Fair complexion (A fair-skin phenotype) (blue/green eyes, blond or red hair.
2- Tendency to sun burn and or blistering sunburn or history of painful sun burn.
3- Large number of common nevi or Large (giant) congenital nevi.
4- Changing mole (most important clinical warning sign).
5- Melanoma in first-degree relative.
6- Age older than 50 years.
7- Presence of xeroderma pigmentosum.
8- Ultraviolet light radiation (UVR).
9- Genetics.

Treatment:
A variety of chemo- and immunotherapeutic strategies can be used once metastases have been identified.

Drug-Induced Melanosis
A variety of drugs can induce oral mucosal pigmentation. These pigmentations can be large yet localized, usually to the hard palate, or they can be multifocal, throughout the mouth. The lesions are flat and without any evidence of nodularity or swelling.

The chief drugs implicated are the quinoline, hydroxyquinoline, antimalarials. These medications have also been used in the treatment of autoimmune diseases.

Minocycline, used in the treatment of acne, can also produce oral pigmentation. The pigment is not confined to oral mucosa and is also encountered in the nail bed and on the skin.

Oral contraceptives. Estrogen and pregnancy are occasionally associated with hyperpigmentation of the facial skin, particularly in the periorbital and perioral regions (Figure 6-7). This condition is referred to as melasma or chloasma.

The cause is unknown, and the pigment may remain for quite some time after withdrawal of the incriminated drug. Microscopically, basilar melanoses without melanocytic proliferation is observed, and melanin incontinence is commonly seen.
Physiologic Pigmentation
Black people, Asians, and dark-skinned Caucasians frequently show diffuse melanosis of the facial gingiva. In addition, the lingual gingiva and tongue may exhibit multiple, diffuse, and reticulated brown macules.

racial pigmentation, representing basilar melanosis, evolves in childhood and usually does not arise de novo in the adult. Therefore, any multifocal or diffuse pigmentation of recent onset should be investigated further to rule out endocrinopathic disease.

Café au Lait Pigmentation
In neurofibromatosis, an autosomal dominant inherited disease, both nodular and diffuse pendulous neurofibromas occur on the skin and (rarely) in the oral cavity.

A concomitant finding is the presence of “café au lait” pigmentation. As the term implies, these lesions have the color of coffee with cream and vary from small ephelis-like macules to broad diffuse lesions. They tend to appear in late childhood and can be multiple; many overlie the neurofibromatous swellings on the skin. Rarely, oral pigmentation is encountered. Microscopically, café au lait spots represent basilar melanosis without melanocyte proliferation.

Smoker’s Melanosis
Diffuse macular melanosis of the buccal mucosa, lateral tongue, palate, and floor of the mouth is occasionally seen among cigarette smokers (Figure 6-8).

It is probable that in certain individuals, melanogenesis is stimulated by tobacco smoke products. Studies have disclosed that tobacco use stimulates an increase in oral pigmentation. The lesions are brown, flat, and irregular.

**Pigmented Lichen Planus**

Lichen planus is a disease that generally presents as a white lesion, with variants showing red and desquamative lesions.

Rarely, erosive lichen planus can be associated with diffuse melanosis. In such instances, the classic lesions of lichen planus remain recognizable, usually in the buccal mucosa and vestibule. White patches, with diffuse brown macular foci.

Histologically, the usual features of lichen planus are observed, along with basilar melanosis and melanin incontinence.

**Endocrinopathic Pigmentation**

Bronzing of the skin and patchy melanosis of the oral mucosa are signs of:

1. Addison’s disease.
2. Pituitary-based Cushing’s syndrome.

In both of these endocrine disorders, the cause of hyperpigmentation is oversecretion of ACTH, a hormone with melanocyte-stimulating properties.

In Addison’s disease, adrenocortical insufficiency evolves as a consequence of destruction of adrenal cortex due to granulomatous infection of the cortex, autoimmune cortical destruction or Ca.

Alternatively, if the hypercorticism is the consequence of a pituitary ACTH-secreting tumor that secondarily induces an adrenal hypersecretion, then melanocyte-stimulating effects may evolve.
Clinically

The skin may appear tanned, and the gingiva, palate, and buccal mucosa may be blotchy. These changes in pigmentation are due to an accumulation of melanin granules as a consequence of increased hormone-dependent melanogenesis. Serum steroid and ACTH determinations will aid the diagnosis, and the pigment will disappear once appropriate therapy for the endocrine problem is initiated.

**HIV Oral Melanosis**

HIV-seropositive patients with opportunistic infections may have adrenocortical involvement by a variety of parasites, which manifests signs and symptoms of Addison’s disease.

Such patients undergo progressive hyperpigmentation of the skin, nails, and mucous membranes. Most HIV-seropositive patients presenting with diffuse multifocal macular brown pigmentation of the buccal mucosa microscopically characterized by basilar melanin pigment, with incontinence into the underlying submucosa.

**Peutz-Jeghers Syndrome**

- Multiple focal melanotic brown macules are concentrated about the lips.
- The macules usually measuring < 0.5 cm in diameter.
- Lesions may occur on the anterior tongue, buccal mucosa, and mucosal surface of the lips.
  - The skin lesion usually develop in early childhood which is multiple dark freckle.
- Intestinal polyposis” not premalignant”. Leading to intestinal obstruction. most of them are self correcting but surgery is indicated to prevent ischemic necrosis of bowel.
- GIT adenocarcinoma may develop in the area other than that of polyp.

▼ BROWN HEME-ASSOCIATED LESIONS

Ecchymosis
Traumatic ecchymosis is common on the lips and face yet is uncommon in the oral mucosa. Immediately following the traumatic event, erythrocyte extravasation into the submucosa will appear as a bright red macule or as a swelling if a hematoma forms. The lesion will assume a brown coloration within a few days, after the hemoglobin is degraded to hemosiderin.

The lesion should be observed for 2 weeks, by which time it should have resolved if it represents a focus of ecchymosis.

When multiple brown macules or swellings are observed and ecchymosis is included in the differential diagnosis,

- **Hemorrhagic diathesis** should be considered. (hereditary coagulopathic disorders and in chronic liver failure.
- Patients taking anticoagulant drugs may present with oral ecchymosis, particularly on the cheek or tongue.

**Petechia**

Capillary hemorrhages will appear red initially and turn brown in a few days once the extravasated red cells have lysed and have been degraded to hemosiderin.

- Petechiae secondary to platelet deficiencies, Autoimmune or idiopathic thrombocytopenic purpura (ITP), HIV-related ITP, disorders of platelet aggregation, aspirin toxicity, and myelosuppressive chemotherapy all will lead to purpura.
- Oral petechiae are not associated with thrombocytopenia or thrombocytopenia; rather, they are usually confined to the soft palate, where 10 to 30 petechial lesions may be seen and can be attributed to suction. Excessive suction of the soft palate against the posterior tongue is self-inflicted.
- Palatal petechiae can also appear following fellatio.
- When traumatic or suction petechiae are suspected, the patient should be instructed to cease whatever activity may be contributing to the presence of the lesions. By 2 weeks, the lesions should have disappeared.
Hemochromatosis

The deposition of hemosiderin pigment in multiple organs and tissues occurs in:

1- Primary heritable disease.
2- Secondary to a variety of diseases and conditions, including:
   A- Chronic anemia.
   B- Porphyria.
   C- Cirrhosis.
   D- Excess intake of iron.

Clinically:

The oral mucosal lesions of hemochromatosis are brown to gray diffuse macules that tend to occur in the palate and gingiva.

▼ GRAY/BLACK PIGMENTATIONS

Amalgam Tattoo

- The lesions are solitary macular and bluish gray or even black and are usually seen in the buccal mucosa, gingiva, or palate.
- Found in the vicinity of teeth with large amalgam restorations. Such iatrogenic lesions occur when the dentist introduce amalgam particles in to tissue during the removal of amalgam or during multiple tooth extractions.
- They are identifiable on radiographs of the area.
- No treatment is required but biopsy is recommended when a gray pigmented lesion suddenly appears.
- The differential diagnosis must include nevi and melanoma in such instances.

**Graphite Tattoo**
- Graphite tattoos tend to occur on the palate and represent traumatic implantation from a lead pencil.
- The lesions are usually macular, focal, and gray or black.
- Microscopically, graphite resembles amalgam in tissue although special stains can differentiate them.

**Hairy Tongue**
Hairy tongue is a relatively common condition of unknown etiology.

- The lesion involves the dorsum, particularly the middle and posterior one-third. The papillae are elongated, sometimes markedly so, and have the appearance of hairs.
- The hyperplastic papillae then become pigmented by the colonization of chromogenic bacteria, which can impart a variety of colors ranging from green to brown to black.
- Various foods, particularly coffee and tea, probably contribute to the diffuse coloration.
- Microscopically, the filiform papillae are extremely elongated and hyperplastic with keratosis.
- **Treatment** consists of having the patient brush the tongue and avoid tea and coffee for a few weeks.
**Pigmentation Related to Heavy-Metal Ingestion**

Ingestion of heavy metals or metal salts can be an occupational hazard since many metals are used in industry and in paints. Lead, mercury, and bismuth have all been shown to be deposited in oral tissue if ingested in sufficient quantities or over a long course of time. These ingested pigments tend to extravasate from vessels in foci of increased capillary permeability such as inflamed tissues.

In the oral cavity, the pigmentation is usually found along the free marginal gingiva, where it dramatically outlines the gingival cuff, resembling eyeliner. This metallic line has a gray to black appearance. The heavy metals may be associated with systemic symptoms of toxicity, including behavioral changes, neurologic disorders, and intestinal pain. This condition is now rarely seen.

▼ **BLUE/PURPLE VASCULAR LESIONS**

**Hemangioma**

Vascular lesions “tumorlike hamartomas “presenting as proliferations of vascular channels.

- The hemangiomas of childhood are found on the skin, in the scalp. Approximately 85% of childhood hemangiomas shows spontaneously regress after puberty.
- Depending on the depth of the vascular proliferation, the lesion may appear reddish blue or, if a little deeper in the connective tissue, a deep blue.
- Intramuscular hemangiomas may fail to show any surface discoloration.
- Hemangiomas on the facial skin, may be flat, macular, and diffuse, are referred to as port-wine stains and may involve the oral mucosa.
- It may be raised and nodular. Most oral hemangiomas are located on the tongue, where they are multinodular and bluish red. Tongue angiomas frequently extend deeply between the intrinsic muscles of the tongue.
- The lip mucosa is another common site for hemangiomas in children.
- Tend to blanch under pressure; indeed, placing a microscope glass slide over the pigmented area and adding pressure will often demonstrate this feature dramatically.
- Thrombi in angiomas may eventually calcify, and such lesions will feel hard on palpation. The calcified nodules, or phleboliths, may be radiographically evident.

Since many hemangiomas spontaneously involute during teenage years, treatment may be withheld in children.

- Patients who require treatment can undergo conventional surgery, laser surgery, or cryosurgery.
- Sclerosing agents such as 1% sodium tetradecyl sulfate may be administered by intralesional injection. Cutaneous port-wine stains can be treated by argon laser.

**Varix**

Pathologic dilatations of veins or venules are varices or varicosities.
- The ventral tongue is the most commonly involve orally and appear as tortuous blue, red, and purple elevations that course over the ventrolateral surface of the tongue.
- Varicosities become progressively prominent with age.
- When occur on the lower lip, appearing as a focal painless raised pigmentation. They may be blue, red, or purple, and the surface mucosa is often lobulated or nodular.
- Some can be blanched, others are not, due to the formation of intravascular thrombi.

Treatment
- The lesion can be excised or removed by other surgical methods, including electrosurgery and cryosurgery.
- Intraleisonal 1% sodium tetradecyl sulfate injection is effective as well.

Angiosarcoma
Malignant vascular neoplasms,
The oral cavity is an extremely rare site for such tumors, those that occur will (if superficial) appear red, blue, or purple. They are rapidly proliferative and therefore present as nodular tumors. Angiosarcomas can arise from blood or lymph vessel endothelial cells. They have a poor prognosis and are treated by radical excision.

Kaposi’s Sarcoma
A tumor of putative vascular origin, Kaposi’s sarcoma (KS) there are two distinct clinical settings:

(1) Elderly men “classic form (in the oral mucosa and on the skin of the lower extremities).

This classic form as originally described by Moritz Kaposi
- Indolent tumor with slowly progressive growth.
- Does not show a great tendency for metastasis.
- The oral tumors are red, blue, and purple, and the hard palate is the favored site.
- The skin tumors tend to localize in the dorsal aspect of the feet and great toe.
- In the early stages, the differential diagnosis includes pyogenic granuloma and giant cell granuloma.
- Nodular lesions may become unsightly and interfere with mastication; in this situation, therapy may be desirable

(2) Children in Africa (in lymph nodes).
- Is characterized by lymph node enlargement and can progressively involve many node groups, being an aggressive.
- The most common neoplastic process to accompany HIV infection.
- HIV seropositive subjects constitutes a diagnostic sign for acquired immunodeficiency syndrome (AIDS).
- Surgical excision is not usually attended by severe hemorrhage, but electrocautery is recommended, either as a primary form of surgery or as adjunct to conventional excision.
- Intralralional injection of 1% sodium tetradecyl sulfate will result in necrosis of the tumor.
- Intralralional 1% vinblastine sulfate is also beneficial.

**Hereditary Hemorrhagic Telangiectasia**

Is a genetically transmitted disease that represent multiple microaneurysms, owing to a weakening defect in the adventitial coat of venules.

- The lesions are so distinct as to be pathognomonic and characterized by multiple round or oval purple **papules** measuring less than 0.5 cm in diameter.
- More than 100 such purple papules on the vermillion and mucosal surfaces of the lips as well as on the tongue and buccal mucosa.
- Nasal mucosa reveals similar lesions and the Past history of epistaxis may be a complaint.
- The facial skin and neck are also involved.
- Microscopically, HHT shows numerous dilated vascular channels with some degree of erythrocyte extravasation around the dilated vessels.
- Treatment: There is no treatment for the disease. Papules can be cauterized by electrocautery in a staged series of procedures using local anesthesia.