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Review Article

An overview of pigmented lesions of the oral cavity

Dalal Mufadhi Alanazi[1]*, Badria Moashi Alanazi[2], Hilalah Masoud Alanazi[1], Ghada Khairallah Al-Shahrani[3], Abeer Abdulhai Alanazi[1], Tamam Mohammed Alenazy[1], Amirah Hamoud Alruwaili[1], Reem Awwadh Almutairi[1], Suad Murdhi Alanazi[4]

[1]Dental Department, Eastern Riyadh Dental Center, Riyadh, Saudi Arabia
[2]Dental Administration Department, Eastern Riyadh Dental Center, Riyadh, Saudi Arabia
[3]Dental Department, Directorate of Health Affairs, Dammam, Saudi Arabia
[4]Dental Department, Al Yamamah Hospital, Riyadh, Saudi Arabia

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***Correspondence:**
Dr. Dalal Mufadhi Alanazi,
E-mail: dalonazi1234@gmail.com

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ABSTRACT

It might be difficult to diagnose pigmented lesions of the mouth and perioral regions. Although several lesions may be correctly identified on the basis of clinical findings alone and while epidemiology may be helpful in guiding the clinician, the histological examination is typically necessary for the final diagnosis. Oral hyperpigmentation may present exogenously/ endogenously; pathologically/physiologically. The differential diagnosis depends on factors like medication usage, familial history in addition to the position, spread, and length as well as hue and pattern variations. Physiological pigmentation, melanotic macule, melanocytic nevus, smoker's melanosis, oral melanoacanthoma, pigmentation caused by foreign matter or medicines, Peutz-Jeghers syndrome, Addison's disease, and oral melanoma are examples of dark or black pigmented discolorations that can be unifocal, multifocal, or dispersed macular lesions.

Keywords: Oral pathology, Oral medicine, Pigmentation, Melanin, Diagnosis

INTRODUCTION

The dentist may face a diagnostic conundrum when pigmented tissues are observed within the mouth. In the oral cavity, pigmented lesions are frequently discovered. These injuries can be physiological alterations, symptoms of systemic diseases/ malignant neoplasms, among other clinical entities. Therefore, it is crucial to comprehend the reasons of mucosal pigmentation and conduct proper patient evaluation. Physiological pigmentation, which is prevalent in African, Asian and Mediterranean people, is caused more by increased melanocytic function than by an increase in the total amount of melanocytes.[1]

LITERATURE SEARCH

This study is based on a comprehensive literature search conducted on November 14, 2022, in the Medline and Cochrane databases, utilizing the medical topic headings (MeSH) and a combination of all available related terms, according to the database. To prevent missing any possible research, a manual search for publications was conducted through Google Scholar, using the reference lists of the previously listed papers as a starting point. We looked for valuable information in papers that discussed the information about pigmented lesions of the oral cavity. There were no restrictions on date, language, participant age, or type of publication.

DISCUSSION

Benign pigmented lesions of the oral cavity

Physiologic pigmentation (racial pigmentation)

Physiological pigmentation, which is prevalent in African, Asian and Mediterranean people, is caused more by increased melanocytic function than by an increase in

the total amount of melanocytes.[1] Physiological pigmentation appears within the initial two decades of life, albeit it might not be noticeable to the individual right away. It is brownish, ranging from light to dark. The attached gingiva is the most prevalent intraoral location for this kind of pigmentation, where it manifests bilaterally as a clearly delineated, dark brownish zone that generally bypasses the marginal gingiva (Figure 1). The buccal mucosa (BM), hard palate (HP), labial mucosa, and tongue can all exhibit this phenomenon in the form of brownish areas with ill-defined boundaries. Since the pigmentation has no symptoms, no therapy is necessary.

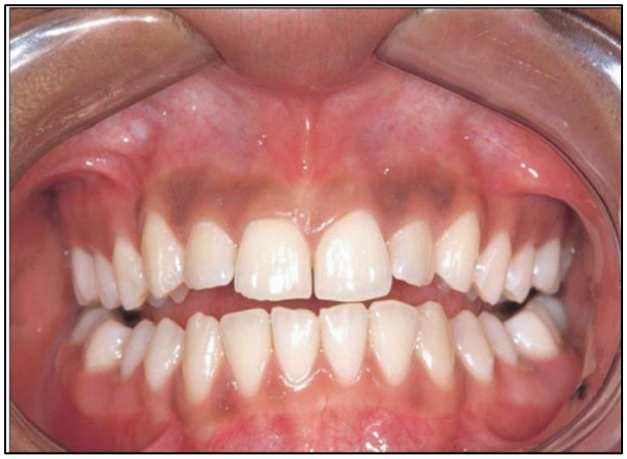

Figure 1: Physiologic pigmentation (racial pigmentation).[2]

Ephelides

Ephelides are freckles brought on by the sunlight and are most prevalent in fair-complexioned people, particularly those with reddish or auburn hair. They occur more frequently in young people and less frequently as people mature. They often have smooth margins, are consistent, numerous, pale tan colorwise, and below 3 mm in size. They are periodic and connected to sunlight exposure. They frequently show up on the labial vermilion margin, most frequently on the lower aspect. Ephelides do not develop inside the oral cavity because they need to be exposed to sunlight for development.[3] Histologically, the basal cells is more pigmented without hypermelanocytosis or an extension of the rete pegs (RP). Epidermis health is normal.[4]

Lentigo

Adults are more likely to experience lentigos, which last lifelong sometimes. They are frequent on the face and particularly around the mouth. Although they do not undergo an alteration of color due to sunlight, they are associated with long-term sunlight damage. They span from 2 mm to 20 mm in diameter and range colorwise from tannish to brownish. Histologically, basal melanocytes exhibit hyperplastic activity and have elongated RP. Elevated melanocytosis is related to the enhanced melanin deposits.[3] Compared to ephelides, lentigos show more erratic behavior colorwise and outline-wise. Lentigo alterations are suggestive of malignancy-related alterations and clearly indicate the need for a biopsy and histological investigation.

Oral melanotic macules

The labial mucosa, gingival mucosa, HP, and BM are the most frequent sites for the minute, well-defined oral melanotic macules, which are brownish to blackish colorwise. Patients vary age-wise from four years onwards, with a preponderance for women (1.9:1). Histological examination reveals basal melanocytes with regular morphologic features producing more pigment in situ.[5] In addition, melanophages in the top region of the lamina propria (LP) are seen to contain melanin.[5] To differentiate this from other melanocytic tissues intraorally, a biopsy is typically advised.

Smoking-associated melanosis

Even though hyperpigmentation in the HP and BM has also been predominantly linked to smoking pipes, the condition affects 25 to 31% of tobacco consumers and is marked by distinct or merging numerous brownish macular patches that typically involve the attached lower gingival mucosa on the labial side and the lower lip (Figure 2).[6] The enhanced melanin synthesis by melanin producing cells and its deposition inside the basal cell layer and LP are the causes of smoker-associated melanosis.[7] In the period after giving up the habit, a steady recovery to natural pigmentation across the span of many months to years can be seen.[8]

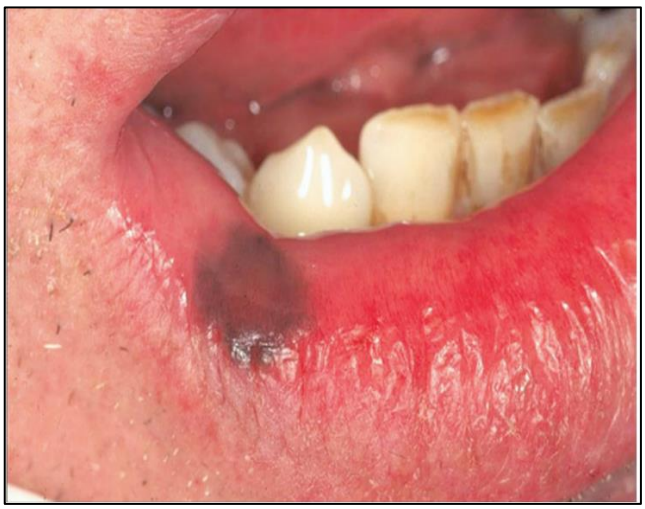

Figure 2: Lower lip showing smoker's melanosis.[2]

Intraoral nevi

On the oral mucosa, these lesions are far less frequent than on the body. Oral nevi are minute, well-defined macular lesions in the clinical sense; however, they

frequently take the form of mildly elevated papules. They are sometimes nonpigmented and might be brownish, bluish, grayish, or nearly black.[9] They are noninvasive growths of the melanocytes present cutaneously that usually include alterations in the neuroblastoma ras viral oncogene homolog (NRAS) or the oncogenic serine/ threonine-protein kinase B-Raf (BRAF).

Malignant pigmented lesions of the oral cavity

Melanoma

Under 1% of all oral cancers are oral melanoma, making it an uncommon disease. Melanocytes with malignancy tendencies proliferate both inside the connective tissue (CT) and on the interface between the epithelium and CT. The HP, which represents nearly. 40% of occurrences, is the commonest site, succeeded by gingival mucosa, which represents one-third incidences. Additionally, more mucosal areas may be impacted intraorally. Oral melanoma often develops from the fourth to seventh decade of life, and males than females are likely to develop it. In clinical practice, this lesion may appear as a painless, slowly expanding brownish or blackish spot with asymmetrical and uneven boundaries, or as fast-growing masses accompanied by discomfort, ulcers, hemorrhage, and bone loss.

Neuroectodermal tumor of infancy

This is a rarely occurring benign tumor consisting of primordial pigment making cells and may develop from neural crest cells. Infants typically have growths discovered before six months of age. Though lower jaw and cranial malignancies have also been reported, growths in maxilla are more common. Infantile neuroectodermal tumors typically appear as a nonulcerative, sometimes darkly pigmented masses caused by melanocytes. Infants might or might not have emerging teeth, and radiographically, poorly defined lucencies may be observed. These neoplasms exhibit an alveolar structure histopathologically which is composed of colonies of tumor cells interspersed with minor quantities of CT. The outcomes of surgical removal are favorable.

Endogenous etiologies of oral pigmentation

Postinflammatory hyperpigmentation

This is frequently seen on the bodies of people with chronically presenting conditions with inflammation, can also be seen in the mouth, for instance, in cases of oral lichen planus. The distribution of pigmentation resembles the initial lichen planus growths in appearance. Reticulate and patchy pigmentation could therefore be the results of successfully addressing the primary diseases. Submucosally occurring pigmentation granules may be seen histologically.

Oral melanoacanthomas

This is a rarely occurring non-neoplastic hybrid growth composed of keratinocytes and pigment-rich branching melanocytes.[10-12] It is believed that this lesion has a reactionary character and typically reverts back on its own or following partial excision, such as incisional biopsy.[10-12] Oral lesions vary from their cutaneous equivalent in that they mostly affect Black people, impact a much younger demographic, evolve quickly, and typically have a smooth surface. The most often afflicted subsite is the BM.

Addison's syndrome

This disorder develops when an autoimmune illness, an infection, or a cancerous growth gradually destroys both sides of the cortical region of the adrenal gland.[13] Scattered hyperpigmentation of the skin and intraoral mucosa is caused by melanocyte-stimulating hormone. Scattered brownish spots on the tongue, BM, gingival mucosa, and HP may be seen which resemble normal pigmentation (Figure 3).[14] Pigmentation linked to Addison's disease, on the other hand, begins and advances during adulthood and is typically accompanied by systemic symptoms such fatigue, nausea and vomiting, abdominal discomfort, diarrhea and constipation. weight loss and fall in blood pressure. Therapy of the root issue and corticosteroid replacing medication comprise management.

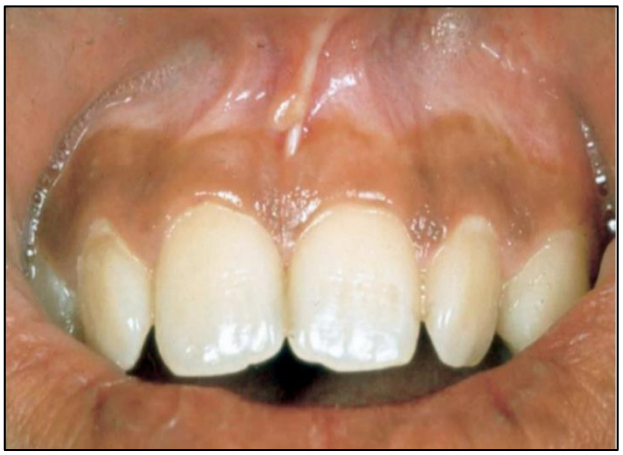

Figure 3: Oral manifestation of Addison disease (courtesy of Dr. J. van Hooff, The Netherlands).

Peutz-Jeghers syndrome

This is an uncommon genetic condition known triggered by a mutated LKB1 gene on chromosome 19.[15,16] It is distinguished by hamartomatous polyposis in the intestine, pigmented mucocutaneous macular lesions, and a higher likelihood of malignancy in the small intestine, colon, stomach etc.[17] Periorally, the generally minute and numerous melanotic patches of Peutz-Jeghers syndrome are quite noticeable. Additionally, there are pigmented

patches on body extremes, conjunctivally, the rectally, and the mucosally in the nose.[18] The melanotic patches don't need to be treated, and they don't raise your risk of developing melanoma. The patients must be watched carefully for the emergence of any malignant internal growths though.

Laugier-Hunziker syndrome

Brownish macules on the lip, mouth, and acral surfaces are the primary symptoms of this uncommon, benign acquired pigmentary condition. Lips, BM, HP and gingival mucosa are the most common sites for many pigmented macules, which can occur alone or in clusters. Additionally, patients may get lengthwise, deeply pigmented bands on their fingernails and, less often, on their toenails. On the neck and reproductive organs, brown coloration can sometimes be noticed. The macules have brownish and blackish tones. No systematic discoveries have been made. Histological examination reveals a buildup of melanin in the basal layer cells and a rise in the quantity of melanophages in the papillary dermis. Investigations using electron microscopy have revealed developed melanosomes in the keratinocytes' basal layer. There is no need for treatment since macules do not have malignant tendencies

Aspergillus infection

A fungal disease called aspergillosis can appear clinically as a confined or invading infectious disease. In the vast majority of patients, an infection may present as a sinus or bronchopulmonary allergy. An aspergilloma is a tumor that develops when a fungal disease concentrates in the maxillary sinus. Patients who undergo root canal therapy or tooth extractions may be more susceptible to sinus infection. Nasal discharge together with regional discomfort and soreness are common signs. These infections cause facial edema and perforate palate due to necrosis, which manifests as a yellowish or blackish ulceration. Microscopic histological analysis shows branched, septate hyphae that infiltrate vasculature, obstruct regular circulation, and cause necrosis. Substantial tissue damage may occur because immunocompromised people are incapable of producing a granulomatous inflammatory response. The preferred method of care is administration of amphotericin B systemically. On the other hand, afflicted areas can require forceful surgical cleaning.

Mucor infection

This is an opportunistic infectious disease caused by a fungus. It is brought on by *Mucor* and *Rhizopus*, two members of the class Zygomycetes. Immunocompromise, unchecked insulin-dependent diabetes, or related ketoacidosis can precipitate zygomycosis. It can affect any part of the body, although the rhinocerebral kind is the most prevalent. In addition to proptosis, patients also experience nasal blockage, bloody nasal discharge, facial paresthesia, visual disturbances etc. Without therapy, it may worsen and lead to blindness, convulsions, and death. Histopathologically, the peripheral area has widespread necrotic findings and several sizable nonseptate hyphae. Minor arteries are invaded by the fungus causing tissue injuries, altered circulation and necrosis. Extensive surgical removal and systemically delivered high concentrations of amphotericin B are the main components of the therapy, which must be started right away. The root disease processes need to be treated if the individual has poorly managed diabetes or immunological impairment. Typically, the prognosis is dismal.

Cancers: bronchogenic disease

Intraoral hyperpigmentation could indicate a dangerous underlying condition. Discoloration on the soft plate laterally may be an indicator for chronic lung disease as well as bronchogenic cancer.[19]

Carney syndrome (Carney complex)

This is an autosomal dominant disorder marked by the development of potentially fatal cardiac myxomas, patchy pigments present mucocutaneously, and excessive hormonal function. The blotchy hyperpigmentation on the face and pigmented labial macular lesions may be seen in half the patients that may exist for many years. Several different thyroid and adrenal tumors can be observed among the endocrinologic findings.

Exogenous etiologies of oral pigmentation

Pharmacologic agents

Drug therapy may cause multifocal, pigmented lesions on the oral mucosa as a side effect. Zidovudine, clofazimine, estrogen, cyclophosphamide, ketoconazole, minocycline, estrogen, busulfan, doxorubicin, 5-fluorouracil, and antimalarial drugs such quinacrine hydrochloride, chloroquine, and hydroxychloroquine are among the medications frequently linked to oral mucosal pigmentation.[20,21] Medications can also trigger a reactionary inflammation in susceptible people, resulting in post-inflammatory hyperpigmented lesions in fixed drug reactions.[22] Fixed medication outbreaks appear as clearly defined hyperpigmented regions that typically impact the labial and oral mucous membrane. Medications like arsenic, which combine with sulfhydryl groups in epidermis, directly cause hyperpigmentation by boosting the activity of tyrosinase.[2] Medications like phenothiazines and minocycline, can sometimes interact directly with melanin to establish a medication-melanin complex. Minocycline hyperpigmentation most frequently affects the bones and results in osseous hyperpigmentation that permeates into the mucosal membranes and gives them a grayish tinge.

Amalgam tattoos (focal argyrosis)

One of the more frequent causes of oral hyperpigmentation is an amalgam tattoo, which manifests medically as a circumscribed, flattened, bluish-grey lesion with varied diameters. The most typical areas of affliction are the gingival and alveolar mucosa; however, these abnormalities can also affect the BM and the floor of the oral cavity (Figure 4). The findings of the diascopy ought to be negative because there are no indications of inflammation around the edge of the discoloration. When this occurs, the identification of amalgam tattoo can be determined based on the clinical and radiographic findings. This is particularly true when the amalgam fragments are sizable enough to be discernible by intraoral radiography.

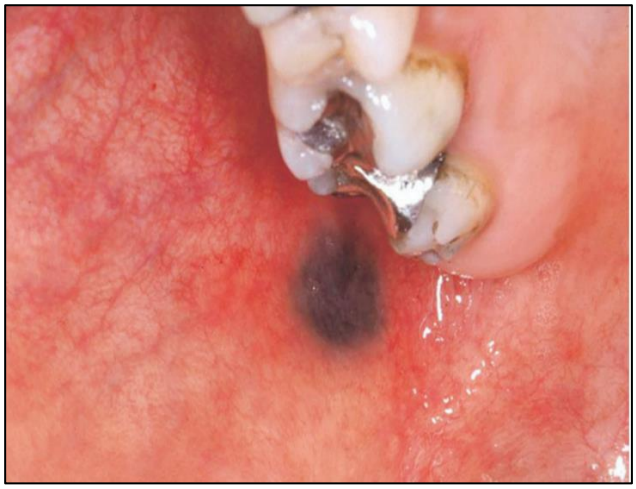

Figure 4: Amalgam tattoo.[2]

Cultural or medical tattooing

A quarter of the people worldwide have at least one tattoo, commonly in the oral cavity, and this tattooing is either customary or voluntary. Some societies choose to permanently tattoo their gingival mucosa. In women in Ethiopia, anterior upper labial gingival is where tattoos are most prevalent.[23] For the purpose of displaying landmarks or radiation ports, healthcare practitioners purposely add tattoos.

Heavy metal-induced pigmentation

If accumulated in the mucous membranes, heavy metals like arsenic, bismuth, platinum, lead, and mercury may lead to pigmentation without releasing melanin. The majority of heavy metals could also lead to sialorrhea and induce neurological problems. Leukoplakia can be caused by arsenic. On the gums, lead causes the recognizable widespread greyish tint or streaks. Slate-grey discoloration of the gingiva is brought on by mercury. A bluish black to brownish darkening of the gums is caused by gold and bismuth.[24]

Miscellaneous foreign materials

Many different foreign items, including pencils, dye, ink, plant products, and gingival tattoos, can cause pigment like alterations when they are introduced in the oral cavity.

Hairy tongue

The filiform papillae of the tongue's faulty shedding and reactionary hypertrophy result in the pain free, innocuous condition known as "black hairy tongue".[25] The elongated keratinized papillae which give off the hairy look can display a range of hues, from yellowish brown to blackish, based on extrinsic elements like tobacco, caffeine, tea, and foodstuff as well as internal factors like chromogenic microorganisms in the microbiome.[26] Uncertainty surrounds the precise pathogenesis. In light of the typical clinical picture, a biopsy is typically not required for confirmation. Quitting smoking and tongue brushing or scraping both improve the healing. In severe circumstances, the papillae may need to be trimmed.[27]

Dental discoloration

The sources of tooth staining are both extrinsic and intrinsic. Bacteria stains, tobacco, food and beverages, gingival bleeding, and restorative agents are examples of the former. Amelogenesis imperfecta, dentinogenesis imperfecta, injury, amalgam fillings, fluorosis, erythropoietic porphyria, and hyperbilirubinemia are types of the latter.

CONCLUSION

The oral mucous membrane can develop pigmented lesions ranging from the relatively commonplace and non-lethal (like amalgam tattoos) to the uncommon and lethal (like malignant melanoma). The clinical manifestations of different pigmented lesions can be identical, creating a diagnostic challenge for the dental professional. A biopsy is part of the confirmatory diagnosis toolkit in these cases.

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REFERENCES

1. Gaeta GM, Satriano RA, Baroni A. Oral pigmented lesions. Clin Dermatol. 2002;20(3):286-8.
2. Meleti M, Vescovi P, Mooi WJ, Van der Waal I. Pigmented lesions of the oral mucosa and perioral tissues: a flow-chart for the diagnosis and some recommendations for the management. Oral Surg Oral Med Oral Pathol Oral Radiol Endodontol. 2008;105(5):606-16.

3. Buchner A, Hansen LS. Melanotic macule of the oral mucosa: a clinicopathologic study of 105 cases. Oral Surg Oral Med Oral Pathol. 1979;48(3):244-9.
4. Lenane P, Powell F. Oral pigmentation. J Eur Academy Dermatol Venereol. 2000;14(6):448-65.
5. Ishikawa I, Aoki A, Takasaki AA. Potential applications of Erbium: YAG laser in periodontics. J Periodontal Res. 2004;39(4):275-85.
6. Hedin CA. Smokers' melanosis: occurrence and localization in the attached gingiva. Arch Dermatol. 1977;113(11):1533-8.
7. Brown FH, Houston GD. Smoker's melanosis. A case report. J Periodontol. 1991;62(8):524-7.
8. Hedin C, Pindborg J, Axell T. Disappearance of smoker's melanosis after reducing smoking. J Oral Pathol Med. 1993;22(5):228-30.
9. Buchner A, Hansen LS. Pigmented nevi of the oral mucosa: A clinicopathologic study of 36 new cases and review of 155 cases from the literature: Part I: A clinicopathologic study of 36 new cases. Oral Surg Oral Med Oral Pathol. 1987;63(5):566-72.
10. Contreras E, Carlos R. Melanoacantosis oral (melanoacantoma): reporte de un caso y revision de literatura. Medicina Oral, Patología Oral y Cirugía Bucal (Ed impresa). 2005;10(1):09-12.
11. Fatahzadeh M, Sirois DA. Multiple intraoral melanoacanthomas: a case report with unusual findings. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiol Endodontol. 2002;94(1):54-6.
12. Wright JM. Intraoral melanoacanthoma: A reactive melanocytic hyperplasia: Case report. J Periodontol. 1988;59(1):53-5.
13. Kim H. Generalized oral and cutaneous hyperpigmentation in Addison's disease. Odonto-stomatologie tropicale-Trop Dental J. 1988;11(3):87-90.
14. Neville BW, Damm DD, Allen CM, Bouquot JE. Oral and Maxillofacial Pathology. 2 [sup] nd ed. Philadelphia, PA: Saunders. 2002: 337-369.
15. Hemminki A, Markie D, Tomlinson I. A serine/threonine kinase gene defective in Peutz-Jeghers syndrome. Nature. 1998;391(6663):184-7.
16. Hemminki A, Tomlinson I, Markie D. Localization of a susceptibility locus for Peutz-Jeghers syndrome to 19p using comparative genomic hybridization and targeted linkage analysis. Nature Genetics. 1997;15(1):87-90.
17. Hemminki A. The molecular basis and clinical aspects of Peutz-Jeghers syndrome. Cellular Molecular Life Sci CMLS. 1999;55(5):735-0.
18. McGrath DR, Spigelman AD. Preventive measures in Peutz-Jeghers syndrome. Familial Can. 2001;1(2):123-7.
19. Merchant HW. Oral pigmentation associated with bronchogenic carcinoma. Oral Surg Oral Med Oral Pathol. 1973;36(5):675-7.
20. Fornatora ML, Reich RF, Haber S, Solomon F, Freedman PD. Oral melanoacanthoma: a report of 10 cases, review of the literature, and immunohistochemical analysis for HMB-45 reactivity. Am J Dermatopathol. 2003;25(1):12-5.
21. Barrett A, Raja A. The immunohistochemical identification of human oral mucosal melanocytes. Arch Oral Biol. 1997;42(1):77-81.
22. Sharma VK, Dhar S, Gill AN. Drug related involvement of specific sites in fixed eruptions: a statistical evaluation. J Dermatol. 1996;23(8):530-34.
23. Neville BW, Damm DD, Allen CM, Chi AC. Oral and maxillofacial pathology. Elsevier Health Sci. 2015.
24. Wood NK, Goaz PW, Sawyer DR. Intraoral brownish, bluish, or black conditions. Differential Diagnosis of Oral and Maxillofacial Lesions Saint Louis: Mosby-Year Book. 1997:82-208.
25. Ioffreda MD, Gordon CA, Adams DR, Naides SJ, Miller JJ. Black tongue. Arch Dermatol. 2001;137(7):968-9.
26. Tamam L, Annagur BB. Black hairy tongue associated with olanzapine treatment. Mt Sinai J Med. 2006;73(6):891-4.
27. Mirbod SM, Ahing SI. Tobacco-associated lesions of the oral cavity: Part I. Nonmalignant lesions. J Canadian Dental Association). 2000;66(5):252-6.

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