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Pigmented lesions of head and neck: A Review

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Abstract

The phrase "pigmentation of oral mucosa" is used to describe a wide variety of diseases or disorders that cause a change in the colour of oral tissues. Petechiae, purpura, ecchymoses, hematomas, vascular tumours, and foreign substances are frequent sources of mucosal colouring but are not genuine pigmented lesions. As a real pigment, melanin, which is produced by melanocytes, gives the mucosa its characteristic colour of brown, blue, or black. The doctor may face a diagnostic conundrum if pigmented tissue is seen in the mouth cavity. The appearance of mucosal pigment varies and might take the form of a tiny nodule to a big mass or a focused to widespread macular colour. There is a physiological basis for pigmentation, it may indicate a cancerous process. Oral pigmentation requires a thorough examination of patient to rule out any malignancy associated with it. The present article reviews the oral pigmentations in detail, which will serve as a ready reference for the dentists.

Keywords: Pigmented Lesions, Melanin, Pigmentation, malignant pigmentation, malignant melanoma.

Introduction

Mucosal pigmented lesions in the oral cavity can manifest as indicators of various physiological changes, systemic illnesses, or malignant neoplasms, underscoring the importance of a thorough

patient evaluation.[1] A comprehensive understanding of the causes of mucosal pigmentation is crucial. The differential diagnosis for clinically pigmented lesions encompasses reactive, neoplastic, traumatic, and pigmentation-related disorders, including those linked to systemic conditions. Conditions originating from melanocytic, vascular, hematopoietic, or hemosiderotic sources should be considered.[2]

Though not authentic pigmented lesions, petechiae, purpura, ecchymoses, hematomas, vascular tumors, and foreign substances can contribute to mucosal pigmentation. Melanin, produced by melanocytes in the basal epithelial layer, is transferred to adjacent keratinocytes via membrane-bound organelles.[3] Additionally, nevus cells, derived from the neural crest and present in both skin and mucosa, have the capacity to generate melanin. Human skin pigmentation's intricate nature has evolved in response to regional environmental factors, with the distribution of skin color closely associated with the intensity of incoming UV radiation.[4]

It is noteworthy that, as a precautionary measure, the National Cancer Institute classifies "any pigmented lesion on the oral mucosa as melanoma" until proven otherwise.Pigmented lesions are often observed in the mouth.Among other clinical entities, these lesions might represent physiologic changes, signs of systemic illnesses, or malignant neoplasms.[4]Understanding the causes of mucosal pigmentation and conducting a thorough patient evaluation are therefore critical.[5]The differential diagnosis for a clinically pigmented lesion may include a number of reactive, neoplastic, traumatic, and pigmentation-related disorders as well as pigmentation connected to systemic illness. Lesions or diseases having melanocytic, vascular, hematopoietic, or hemosiderotic origins may be taken into consideration. While not true pigmented lesions, petechiae, purpura, ecchymoses, hematomas, vascular tumours, and foreign substances are frequently responsible for mucosal pigmentation.[6] Melanin is produced by melanocytes in the basal layer of the epithelium and is transported by membrane-bound organelles to neighbouring keratinocytes.[7] Nevus cells, which are generated from the neural crest and are present in the skin and mucosa, can also produce melanin.[8] The complex characteristic of human skin pigmentation developed in response to regional environmental factors. The intensity of incoming UV radiation is significantly associated with the distribution of human skin colour.Until proven otherwise, the institute of national cancer classifies "any pigmented lesion on the oral mucosa as melanoma". It is essential to routinely conduct histological exams of any pigmented lesion of the oral mucosa to confirm or refute the clinically hypothesised diagnostic hypothesis and formally exclude melanoma due to the variety of clinical types (Table-1), differential diagnoses (Table-2) and their similarities. [9]

Table-1: Classification of Pigmented Lesions

Focal melanotic pigmentation	Diffuse melanotic pigmentation
Freckle	Drug induced melanosis

Oral melanotic macule	Physiologic pigmentation
Oral melanocanthoma	Smoker's melanosis
Melanotic nevus	Melasma
Malignant melanoma	Iinflammatory hyperpigmentation
Associated with systemic or genetic disorder	Exogenous pigmentation
Addison's Disease	Amalgam tattoo
Cushing's Disease	Graphite pigmentation
Graves' Disease	Metal pigmentation
Peutz-Jeghers Syndrome	Ornamental tattoo
Café au Lait spots	Hairy tongue

Table 2: Differential Diagnosis of Oral Pigmented Lesions

Clinical Features of Pigmented Lesions

Diffuse and Bilateral Pigmentation	**Focal Pigmentation**
Physiologic pigmentation	Haemangioma and vascular pigmentation
Peutz -jeghers syndrome	Varix and thrombus
Addison's disease	Hematoma and other haemorrhagic lesions
Heavy metal pigmentation	Amalgam tattoo and other foreign pigmentation
Drug induced pigmentation	Melanotic macules
Kaposi's sarcoma	Oral melanoma
Postinflammatory pigmentation	Pigmented Nevi

The primary challenge in managing a solitary pigmented oral mucosal lesion lies in ruling out various potential diagnoses, particularly malignant melanoma. Such pigmented macules in the oral mucosa may originate either endogenously or exogenously. Endogenous causes encompass melanoma, essential melanosis lentigo, Laugier-Hunziker syndrome, nevocellular nevus, blue nevus, and melanoacanthoma.[10] Exogenous factors include metallic, ethnic, or medical tattoos, hemangiomas, Kaposi's sarcoma, and neuroectodermal tumors in children. A thorough clinical

and histological assessment is essential for systematically evaluating the characteristics of melanoma.[11]

When gathering a medical history, pertinent information includes the lesion's progression, duration, personal and family history of melanoma or other skin conditions, associated pathologies, previous drug consumption, occupation, ethnicity, and potential exogenous causes. Conditions like Peutz-Jeghers syndrome, characterized by intestinal hamartomatous polyposis and mucocutaneous macules, elevate the risk of various malignancies.[12]

"Pigmented lesions of the oral mucosa" can encompass a spectrum of conditions marked by changes in tissue color due to pigment accumulation. While oral melanoma is rare, comprising less than 1% of all oral cancers, it requires careful consideration due to its potential severity. The hard palate is the most common location, followed by the gingiva. The ABCD checklist, commonly used for cutaneous melanoma diagnosis, can aid in clinically assessing oral melanoma. Biopsy, especially when the lesion is on the palate, is often necessary.[12]

Various types of solitary pigmented melanocytic lesions exist, including melanocytic nevi, atypical melanocytic hyperplasia/proliferation, and melanoma. Melanocytic macules are the most common, primarily affecting the gingiva and lips. Oral melanoacanthoma typically presents as a single lesion, with lentigo appearing as a benign dark macule, often on the lower lip. Multiple macules may indicate syndromes like Peutz-Jeghers or others.[13]

Physiological pigmentation, often seen in individuals with darker skin, manifests as macular pigmented patches. Factors such as smoking, hormonal fluctuations, and systemic drugs contribute to increased pigmentation. No specific treatment is required for physiological pigmentation, diagnosed primarily through clinical evaluation. Similar features may be observed in conditions like pigmentation associated with medicine, Peutz-Jeghers syndrome, Addison's disease, and post-inflammatory pigmentation, more prevalent in dark-skinned individuals, often seen near lichen planus lesions.[13]

Addison’s disease

Addison's disease affects individuals across all age groups and is not influenced by gender. In the oral cavity, it typically presents as irregular melanosis affecting various regions. Prior to intraoral pigmentation, skin bronzing is often observed. Clinical symptoms include gradually worsening weakness, anorexia, mood fluctuations, nausea, vomiting, diarrhea, and weight loss. Additional indications may involve hyponatremia and hyperkalemia, leading to a craving for salt. Early recognition of Addison's disease is crucial as untreated cases can be life-threatening.[14]

To diagnose Addison's disease, serum cortisol and plasma ACTH levels are assessed through exogenous ACTH stimulation tests. Steroid replacement therapy is the primary treatment,

effectively resolving hyperpigmentation. Addison's disease is a rare endocrine disorder, predominantly linked to autoimmune disorders in developed nations, while it is commonly associated with tuberculosis in developing nations. Symptoms may include dysphagia, fatigue, weight loss, hypotension, abdominal pain, amenorrhea, nausea, vomiting, thin and brittle nails, as well as scanty body hair.[15]

Characterized by hyperpigmentation due to ACTH melanogenesis, oral manifestations of Addison's disease include pigmentation over the gingiva, vermilion border of the lip, buccal mucosa, palate, and tongue. Notably, oral pigmentation may precede dermatological signs, making dental professionals often the first to encounter the disease. Early diagnosis by dental surgeons is crucial for appropriate medical management, given the potential severity of Addison's disease if left untreated. [15]

Peutz – jehgers syndrome

Pigmentation of the lips and perioral skin, resembling black freckles, is often an early indicator of Peutz-Jeghers syndrome (PJS), a genetic disorder typically emerging in childhood or adolescence. Additionally, this pigmentation may manifest intraorally, especially on the buccal mucosa, and on the extremities. In the differential diagnosis, Laugier-Hunziker syndrome (LHS) is considered due to a similar pattern of oral and perioral pigmentation, although LHS pigmentation tends to appear in adulthood.[16]

Apart from distinctive pigmentation, individuals with PJS may experience anemia, gastrointestinal bleeding, and abdominal pain attributed to the development of hamartomatous polyps in the gastrointestinal tract.[17] Treatment involves managing gastrointestinal symptoms and vigilant monitoring for potential cancer development, as PJS is associated with an increased cancer risk.[18]

The pigmentation in PJS, both oral and perioral, is permanent and typically doesn't necessitate treatment. However, if cosmetic intervention is desired, laser therapy can be employed. Seeking medical advice is crucial for accurate diagnosis and appropriate management of genetic syndromes such as PJS.[18]

Drug related discolorations

The pigmentation of the oral mucosa has been associated with various systemic drugs, either due to the formation of melanin or the deposition of the drug or its metabolites on the mucosal surface. Medications such as amiodarone, minocycline, zidovudine, clofazimine, ketoconazole, hormones, oral contraceptives, phenothiazines, and chemotherapy have been implicated in this phenomenon. Commonly affected areas include the buccal mucosa, gingiva, and hard palate.[19] The pigmentation can present as widespread, multifocal, or localized in clinical settings,

exhibiting hues of brown, blue, gray, or black. Specifically, antimalarial drugs, frequently used in the treatment of systemic lupus erythematosus and rheumatoid arthritis, are often linked to pigmentation of the hard palate.[20]

Minocycline, when taken for an extended period, can cause blue-black staining of the gnathic bones in approximately 20% of individuals, although this doesn't truly represent mucosal pigmentation despite the bluish appearance it may give to the surrounding tissue.[21] Diagnosis relies on the temporal correlation between the pigmentation and the initiation of a medication known to induce this side effect.[22] Discontinuation of the drug can lead to a significant fading of the lesions. In cases where oral melanoma risk is a concern due to the overlap in affected areas, a biopsy may be necessary to confirm the diagnosis. Histopathologically, the characteristics of drug-induced pigmentation may resemble those of a melanotic macule or manifest as small brown-yellow granules in the lamina propria, believed to be deposition of the drug or its products.[22]

Smoker's melanosis

The use of cigarettes or pipes can lead to smoker's melanosis, a common reactive and benign condition that results in increased pigmentation of the oral mucosa. This reaction is thought to be triggered either by the heat stimulating melanocytes to produce protective melanin or by the harmful compounds present in cigarette smoke.[23] Approximately 21.5–30% of smokers, predominantly adults, are observed to experience this condition, with a higher likelihood in women, suggesting a potential hormonal link.[24] While the anterior labial mandibular gingiva is the most frequently affected area, smoker's melanosis can also manifest on the buccal mucosa, lips, hard palate, and tongue. Typically, multiple brown macules are present, varying in color from light brown to brown-black depending on the duration and intensity of tobacco use. Although no specific treatment is required for this condition, it is advisable to discuss the associated health risks of smoking with the patient. The pigmented spots may gradually diminish upon smoking cessation.For individuals concerned about the appearance of pigmented areas, surgical excision or laser ablation can be considered.[24]

However, it's important to note that if the smoking habit persists, the pigmentation may recur. Emphasizing the importance of quitting smoking is crucial for both oral health and overall well-being.[24]

Black hairy tongue

The benign and acquired condition known as "Black hairy tongue" impacts the dorsal tongue, featuring elongated, darkly stained filiform papillae.[25] While comprehensive population studies on black hairy tongue are limited, information on hairy tongue, in general, has been documented. According to a Turkish study encompassing 5150 patients, 11.3% exhibited hairy tongues, with

prevalence increasing with age, smoking, excessive black tea consumption, male gender, and inadequate dental care. Individuals with this condition typically do not experience pain, and some may not even be aware of its presence, while others may seek medical attention due to the unusual appearance.[26]

The elongation of papillae is attributed to reduced desquamation and/or increased keratin synthesis. Research by Manabe et al. suggests that epithelial cells expressing hair-type keratins, particularly at the termini of filiform papillae, are responsible for the formation of these elongated spires of keratin.[27] Black hairy tongue generally does not necessitate treatment, although individuals often seek it for reasons related to halitosis or cosmetic concerns.[28] Managing the condition begins with identifying potential causal factors. Recommendations include breaking detrimental habits, improving oral hygiene practices, increasing dietary roughage, and, if feasible, discontinuing relevant medications. In many cases, the condition can be completely resolved with a simple toothbrush stroke or tongue scrape.[29]

Investigation & Management

The majority of pigmented lesions typically do not warrant investigation. However, in cases where malignancy is suspected, histopathological examination remains the gold standard diagnostic procedure. Histological analysis often reveals epithelial hyperplasia, acanthosis, melanic pigmentation of basal layers (hypermelanocytosis), and the presence of melanophages in the underlying layers of the epithelium.This examination is crucial, especially when clinically distinguishing between a nevocellular nevus and a melanoma is challenging.[30]

A histopathological study identified an increase in nevus cells, uniformly spherical and arranged in layers or thecas within the basal lamina propria and membrane. This histological investigation is vital for ruling out early melanomas or preventing their progression.[30]

Exogenous pigmentation can be either unintentional or intentional. Accidental pigmentation may result from tar, metal fillings, crowns, or other factors. Occasionally, a mucosal breach with an intramucosal dental material deposit may be observed. Involuntary pigmentation can arise from tattoos causing pigmented scars on the cheeks or buccal gingiva, ethnic pigmentations in African tribes, or other causes.[30]

Dark red or purple pigmentation with a vascular origin tends to appear nearly black. Examples of such lesions include bruises, angiomas, and Kaposi's disease. Vascular lesions often exhibit variations in volume, location, sensitivity to pressure and heat, and nocturnal changes. Kaposi's disease lesions are typically macular or nodular, displaying dark purple coloring, a hazy appearance, and possibly extending over the body. Surgical excision is the primary treatment, with topical chemotherapy and radiation as secondary options.[31]Understanding the histological features, such as epithelial hyperplasia, acanthosis, and melanic pigmentation, is essential for

accurate diagnosis and appropriate management. In certain instances, distinguishing between nevocellular nevi and melanomas may require histopathological scrutiny.[31]

Exogenous pigmentation, whether unintentional or intentional, adds another layer of complexity to the spectrum of pigmented lesions. Accidental pigmentation can arise from various sources, including dental materials, while involuntary pigmentation may be associated with tattoos or ethnic factors.[31]

Vascular lesions, characterized by dark red or purple pigmentation, present another category of pigmented lesions, with conditions like angiomas and Kaposi's disease demonstrating distinct features. Surgical excision often serves as the primary treatment for these lesions, complemented by topical chemotherapy or radiation in certain cases.[31]

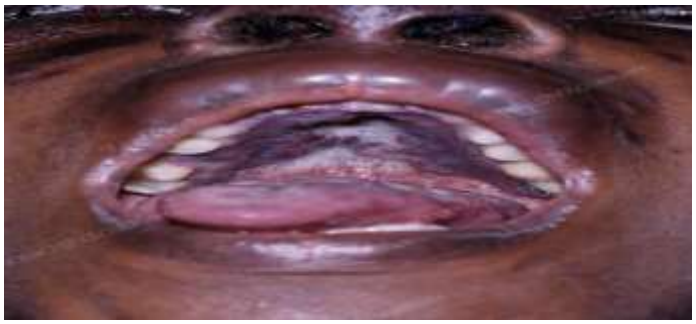

Figure 1:- Kaposi's Sracoma of Oral cavity) Source :- Burkitt – Oral Medicine and Radiology

The management of pigmented lesions of the head and neck involves a comprehensive approach, considering both benign and potentially malignant conditions. [31] Following are some of the key aspects of the management:[31]

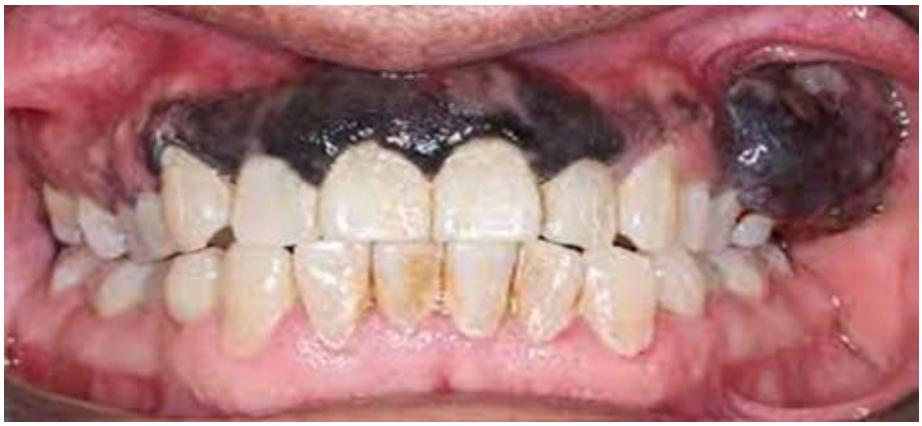

Figure 2 :- Malignant Melanoma of Oral Cavity. Source :- Burkitt – Oral Medicine and Radiology

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1. Clinical Assessment:

- A thorough clinical examination is crucial to evaluate the characteristics of pigmented lesions.
- Key features to consider include size, color, borders, symmetry, and any changes over time.

2. Dermatoscopy:- Dermatoscopy (also known as dermoscopy or epiluminescence microscopy) is a non-invasive technique that can aid in the examination of skin lesions, providing more detailed information about pigmented structures.

3. Biopsy and Histopathological Evaluation:

- For lesions with suspicious features or changes, a biopsy may be performed.
- Histopathological examination by a pathologist is essential for an accurate diagnosis and to differentiate between benign and malignant lesions.

4. Management of Benign Lesions:- Most benign pigmented lesions do not require specific treatment.

However, lesions causing cosmetic concerns or discomfort may be managed with interventions like laser therapy or surgical excision.

5. Management of Malignant Lesions:

- Early detection is crucial for better outcomes. Suspicious lesions may be biopsied for definitive diagnosis.
- Treatment options for malignant lesions include surgery, radiation therapy, and in some cases, systemic therapies like immunotherapy or targeted therapy.

6. Monitoring and Follow-Up: Regular monitoring is essential for any pigmented lesion, especially those with features suggesting the potential for malignancy.

7. Patient Education:

- Educate patients about the importance of self-examination and the need to report any changes in existing lesions or the appearance of new lesions.
- Promote sun protection measures to prevent the development of new pigmented lesions.

It's important to note that management strategies may vary based on the specific diagnosis, and individualized care plans are developed based on the characteristics of each lesion and the

patient's overall health. Always consult with healthcare professionals for accurate diagnosis and tailored management plans.[31]

Conclusion

In conclusion, pigmented lesions of the head and neck encompass a diverse range of conditions, each with unique characteristics and implications. While the majority of these lesions may not necessitate investigation, careful clinical examination is crucial for identifying potential malignancies. Histopathological analysis remains the gold standard for definitive diagnosis, especially in cases where clinical differentiation between benign and malignant lesions is challenging.Understanding the histological features, such as epithelial hyperplasia, acanthosis, and melanic pigmentation, is essential for accurate diagnosis and appropriate management. In certain instances, distinguishing between nevocellular nevi and melanomas may require histopathological scrutiny.

Exogenous pigmentation, whether unintentional or intentional, adds another layer of complexity to the spectrum of pigmented lesions. Accidental pigmentation can arise from various sources, including dental materials, while involuntary pigmentation may be associated with tattoos or ethnic factors.

Vascular lesions, characterized by dark red or purple pigmentation, present another category of pigmented lesions, with conditions like angiomas and Kaposi's disease demonstrating distinct features. Surgical excision often serves as the primary treatment for these lesions, complemented by topical chemotherapy or radiation in certain cases.

In managing pigmented lesions of the head and neck, a comprehensive approach involves not only accurate diagnosis through histopathology but also addressing underlying causes, breaking detrimental habits, and educating patients about potential risks. Regular monitoring and early intervention are crucial to ensure optimal outcomes and prevent potential complications associated with malignant transformations.

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