Oral Medicine

Sheet 14 by Ibrahim Khatib and Areen Afghani

Pigmented lesions of the oral mucosa

These are very common, **however the ones we encounter the most are racial pigmentation and smoker’s melanosis**.

Melanocytes are responsible for the secretion of melanin. They are dendritic cells which are present in the basal layer of epithelium and since they secrete melanin, they are responsible for the color of the skin. Their biochemistry is complex however the enzyme responsible for them is tyrosinase which converts tyrosine to melanin.

When we say pigmented lesion, we mean any lesion which is **black, brown, or yellowish**. White and red lesions are not considered pigmentation.

Pigmented lesions may be classified into melanocytic and non-melanocytic.

**A-** Melanocytic: the cause of the pigmentation is due to increased activity or number of melanocytes.

**B-** Non-melanocytic lesions have nothing to do with melanocytes such as the amalgam tattoo, also some drugs result in pigmentation. Some lesions such as mucoceles, hemangiomas and petechiae may appear pigmented.

Melanocytic lesions include racial pigmentation and smoker’s melanosis, as well as melanotic macules, nevus and melanomas.

We also have other causes such as post inflammatory and associated with systemic diseases.

**1- Racial pigmentation** (ethnic pigmentation) appears as brown patches on the oral mucosa or the gingiva. It is symmetrical and persistent (present at a young age), doesn’t affect gingival stippling and usually affects dark skinned patients.

The gingiva appears dark brown and we differentiate it from smoker’s melanosis by its symmetry and due to the fact that it is bilateral, the patient is usually a nonsmoker with dark skin.

**2- Smoking melanosis** affect smokers regardless of the type of smoking. It is dose and time related (increases with dose and time). The amount of pigmentation reflects the amount of smoking. It may affect children due to second hand smoking. The mechanism is unknown however smoking itself stimulates melanocytes and causes excessive production of melanin which appears as dark patches. (Local effect)

Smoker’s melanosis does not have a malignant tendency however it reflects the presence of other risk factors for oral cancers.

It is reversible with smoking cessation.

Patches are irregularly distributed along the buccal mucosa, gingiva, and are generalized, not symmetrical and the patient has a history of smoking.

**3- Melanotic macules** are well known, they are a localized area of increased production of melanin (if generalized = Racial pigmentation). It is asymptomatic and has no risk of malignant transformation and usually affects the upper or lower lips.

Note: Racial pigmentation usually affect black people but could also affect white people.

All the previous disorders are due to increased melanocyte activity and not an increase in number.

\*There is a syndrome known as **peutz jegher syndrome**, where the patient has cirumural pigmentation on the lips with intestinal polyps which are premalignant. This is a rare syndrome but we may encounter it. (Case study: a patient presented with macules on the lips, after taking her history we found out that her father died from colon cancer, after taking an endoscopy it was found that she has intestinal polyps)

**4- Some systemic diseases** cause oral pigmentation, the most important one is Addison’s disease. Here the patient has adrenal insufficiency due to reduction in the production of cortisone from the adrenal cortex. ACTH increase from the pituitary gland and this increases the melanocyte stimulation hormone and this increases melanin production which appears as melanin patches in the oral mucosa and the skin. (Generalized pigmentation in any area of the oral mucosa, but usually in areas which experience trauma such as the lateral border of the tongue and the buccal mucosa.

A patient who presents with new lesions matching that which was described should be asked about symptoms of Addison’s disease such as weakness, hypotension, abdominal pain, weight loss, nausea, and vomiting. We can measure the patient’s blood pressure in the clinics, if it is low then he should test his serum levels of cortisone or ACTH.

\*When does this occur, in patients with primary or secondary Addison’s? (Look it up)

**4-Nevus**

We should know about some rare disorders such as the nevus.

What is the difference between nevus and macules?

 Nevus is a benign **proliferation** of melanocytes (benign tumors), whereas in macules the activity of melanin producing cells increases. Clinically they are hard to differentiate however on the skin it is easier, the nevus are elevated and appear as pigmented lesions while macules are flat.

The nevus can be classified into 3 types according to its pathology (the location of melanocyte proliferation:

1-If proliferation is limited to the connective tissue 🡪 intramucosal nevus

2- If in the basement membrane 🡪 junctional nevus

3-If in both area 🡪 Compound nevus

Why is the melanocyte present in the connective tissue? (Its original place is in the basement membrane of the epithelium)

The melanocyte is a derivative of the neural crest cells (mesenchymal cell that migrates into the epithelium), so if for any reason it is trapped in the connective tissue, it may form a nevus.

So if proliferation is beneath the basement membrane 🡪 Intramucosal

On the basement membrane 🡪 Junctional

Both 🡪 Compound

There is a fourth type known as blue nevus, where the proliferation in the connective tissue is far from the basement membrane therefore it appears blue.

It is totally benign and sometimes cannot be diagnosed except after taking a biopsy since it looks like a melanotic macule.

**5- Melanoma**: Malignant tumor from melanocytes. It affects the skin but may affect the oral cavity. In the skin, its etiology is due to excessive exposure to the sun however in the oral cavity its etiology is unknown. It is very rare and usually affects the palate and the gingiva, it is very aggressive and is one of the worst types of tumors.

When do we suspect that a lesion is melanoma?

When it is asymmetrical, with irregular margins, large in size, and has different mixtures of colors. (Black/red)

In the early stages it appears similar to nevus or macules.

What distinguishes the melanoma are the **RAS** and **RAF** genes. They are tumor suppressor genes which when mutated, increase the risk of melanoma.

Note: not all lesions which are irregular in color and border are melanomas, they could be racial pigmentation.

In the end, we can distinguish them by taking a biopsy.

**6- Amalgam tattoo**: Iatrogenic form of pigmentation due to implantation of amalgam in soft tissues, it is very common and is localized.

What distinguishes it is its color which is **grey-blue** and it is adjacent to teeth restored with amalgam or extraction sites which had teeth restored with amalgam or near an apicoectomy.

**It grows larger with time!**

We can take an x-ray to diagnose it since amalgam is radio-opaque. Note that its texture is normal, it is **only a change in color**.

Implantation of amalgam 🡪 macrophages ingest amalgam 🡪macrophages release lysosomes 🡪 metals released from amalgam 🡪 metals reach connective tissue fibers and change its color.

**7- Drugs**, pigmentations may be due to drugs such as:

Amino-quinolones

Cyclophosphamide

AZT

Minocycline

OCP

The mechanism is variable, some drugs increase the production of melanin while other, when metabolized, deposit their metabolites in the oral mucosa.

Sometimes diagnosis is tough and we must take a thorough history.

The color of the pigmentation can help in diagnosis. (Melanin is brown black)

**8- Heavy metals** such as:

Lead, Mercury, Arsenic, Bismuth, Copper, and Cisplatin.

Cisplatin (Platinum) is a chemotherapeutic drug.

Occupational history is useful (Case study: A patient presented with a black lesion, after taking his history, we concluded that he was working in a battery factory where he was exposed to high amounts of lead which resulted in lead poisoning, other symptoms included anemia).

**What distinguishes heavy metal pigmentation is that it is a continuous line on the gingival margin.**

**9- Post inflammatory pigmentation:** A patient with an inflammatory mucosal disease such as lichen planus could have pigmentations. The mechanism is due to the production of interleukins and cytokines which are part of the inflammatory process, all which stimulate the melanocytes. Moreover, in lichen planus, the basement membrane undergoes degeneration which allows neutrophils and macrophages to reach the epithelium and therefore releases melanin.

There are some simpler cases where either a patient had drank a colored juice or had a tattoo inked in his oral cavity.