Red and White Lesions of the Oral Cavity: An Update

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Abstract

In our oral cavity various pathological conditions have been reported which includes different type of lesions which require a proper diagnostic criteria, clinically correlation including radiographic & histological reports for its diagnosis. In this article we focus on the various types of red and white lesions of the oral cavity which have been classified based on its etiology, variation in structure, appearance, precancerous potentiality & etc. The lesion appears white due to changes in the epithelium which can be caused by an increase in the keratinization of normal keratinized mucosa, keratinization of non keratinized mucosa or thickening of the epithelium. The reduced vascularity or fibrosis of mucosa can also lead to the whiteness of the oral mucosa. The red appearance of the lesion appears because of the inflammation,atrophy, vascular dilation, and purpura or reduced in the keratinization of the oral epithelium. Generally the red and white lesions are benign and a large proportion of the normal population has been affected by it. The most common precancerous condition which comes under these lesions classification is Leukoplakia**.** A proper management of this condition is required to avoid its future complication. All conditions should be properly examined by taking a proper and careful history. However a biopsy is much needed for these conditions to be diagnosed accurately.

Keywords: *Red Lesion, White Lesion, Leukoplakia, Keratinization, Precancerous.*

Introduction

The red and white lesions are most commonly affected lesion in the oral cavity. To understand the various colors of this lesion one has to know, the color of oral mucous depends on the Degree of keratinization, dilation, and concentration of blood vessels, the amount of melanin pigment present in the epithelium and thickness of the epithelium. The whiteness of the oral mucosa can be due to acanthosis, hyperkeratosis, and necrosis in oral epithelium, vascularity reducing in the underlying lamina propria, and accumulation of fluid intracellular or extracellular in the epithelium. Same as the red appearance is caused by enlarged blood vessels, atrophic epithelium, and an increase in vascularisation and a decrease in the number of epithelial cells.[1]

Classification According to the Burkett's 11th Edition:

- **Red and White tissue reactions**
- **Infectious diseases,** which includes
  - Oral candidiasis
  - Hairy leukoplakia
- **Pre Malignant lesions**
  - Oral leukoplakia and Erythroplakia
  - Oral submucous fibrosis
- **Immuno Pathologic Disease**
  - Oral lichen planus
  - Drug induced lichenoid reaction

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  - Lupus Erythematosus
  - Lichenoid Reaction
- **Allergic Reactions**
  - Lichenoid contact reactions
  - Reaction to dentifrice and Chlorhexidine
- **Toxic Reactions**
  - Reactions to smokeless tobacco
  - Smokers palate
- **Reactions to mechanical trauma**
  - Morsicatio
- **Other red & white lesions**
  - Benign migratory glossitis
  - Leukoedema
  - White sponge nevus
  - Hairy tongue

Infectious Disease:

1. **Oral Candidiasis**:-It is also known as oral thrush. It is caused by yeast *Candida albicans*. The different species of Candida which are responsible for the infection are c. albicans, c. tropicalis, and c. glabrata thus contributing in the 80% of cases. The production of lipases facilitates the penetration of yeasts into the epithelial cells.[2]

   Pathogenesis:

   Yeast cells adheres to host cell

   ↓

   Host cells triggers yeast to hypha transition

   ↓

   Uptake of fungus by host cells through endocytosis

   ↓

   Penetration of fungal active into host cells

   ↓

   Formation of biofilm

Various traits also influence the fungal pathogenicity, which includes Hsps, induction of hyphal formation by uptake of amino acids, and extracellular alkalinization.

Classification includes Acute, Pseudomembranous, Erythematous, and Candida associated lesions such as denture stomatitis, angular cheilitis, and median rhomboid glossitis.

Pseudomembranous Candidiasis: The oral lesions are white, soft and plaques are elevated occurring on buccal mucosa, tongue, gingiva, palate, and floor of the mouth. Acute form belongs to classic Candida infection whereas chronic form is associated with HIV and steroid inhalers. It affects the people who are under medication for prolonged antibiotics and immunosuppressant drugs.[3]

Erythematous Candidiasis: It is also known as antibiotic stomatitis and occurs due to a long course use of broad-spectrum antibiotics, smoking and steroids inhalation. It can occur in any site and it's the only variety of oral candidiasis that is consistently painful.

Chronic plaque-type and nodular candidiasis: It is also known as chronic hyperplastic candidiasis. It is featured by a white plaque. The lesion is firm, white persistent plaques occurring in the lips, tongue, and cheeks. This form is associated with malignant transformation.[4]

Candida-Associated lesions:

I. Denture stomatitis

II. Angular Cheilitis

III. Median rhomboid glossitis

IV. Oral candidiasis associated with HIV infection, Management of following involves:

The treatment of denture stomatitis includes eliminating the predisposing factors, dentures should be kept in antimicrobial solutions and surgical excision.

Angular cheilitis is treated by topical miconazole or a mild steroid ointment suppresses the inflammation.[5]

The treatment of median rhomboid glossitis involves the use of topical antifungal clotrimazole, fluconazole, and topical corticosteroid which includes fluocinonide 0.05% & clobetasol 0.05%.

2. **Hairy Leukoplakia:** This lesion is a corrugated white lesion that occurs on the ventral or lateral surfaces of the tongue. The disease affects mostly the severe immunodeficiency patients. It is the

second most HIV associated lesion. It mostly affects men as compared to females.

Pathogenesis: The marker involves lowering of **CD4+ T- lymphocytes counts.** Greenspan and the co fellows in 1984 reported the first time. It is strongly associated with the Epstein Barr virus. The clinical features involve vertical white folds in the borders of tongue **shaggy orfrayed** appearance. The lesion is bilateral often, asymptomatic and cannot be scraped off. A palisading pattern can also be seen clinically.[6]

Histopathology Features: In the irregular surface severe hyperkeratosis can be noticed with acanthosis. Hairs can be seen projecting from the surface. Balloon cells can be observed in the spinous layer 7 pyknotic nuclei. The important microscopic features involve homogenous nuclear inclusions and EBV can be detected by in situ hybridization or by IHC. The lesion does not require any treatment. However antiviral drugs such as acyclovir, zidovudine is been used and topical application of podophyllin resin 25% solution is used. The malignant transformation is very low.[7]

Pre Malignant Lesion:

1. **Oralleukoplakia:** It is the most common premalignant condition. It is a white patch that can't be characterized pathologically or clinically as any other disease.

Pathogenesis: The cause of Oral leukoplakia is still unknown.

The various etiologic factors of leukoplakia include:- Use of tobacco, hot, cold and acidic foods, beverages, occlusal trauma, syphilis, presence of candida Albicans, sharp tooth, ethanol, and presence of viruses.

Oral leukoplakia is more common in men and it mostly occurs over 50 years of age.

Clinical Findings: It is usually asymptomatic and occurs in the floor of mouth, buccal mucosa, maxillary gingiva, hard palate, lip, soft palate, and lip vermilion. The borders are ragged or smoothly contoured. The mouth is scattered by solitary or multiple plaques. The most common occurring sites or at high risks isthe floor of the mouth and lateral borders of the tongue for malignant transformation.[8]

Classification: Oral leukoplakia can be classified as:

1. **Homogenous leukoplakia:** In this type no red component can be found and is asymptomatic and the lesion is white and consists of well-demarcated plaque. Surface fissures appear as cracked mud.
2. **Speckled Leukoplakia:** This form of leukoplakia consists of both red and white flecks of line.
3. **Erythroplakia:** In this form also a combination of both red and white patches can be observed.
4. **Verrucous Leukoplakia:** It is a lesion where verrucous areas are present. It consists of nodular or exophytic components. The lower gingiva is a predilection site. An aggressive form of this lesion can occur which is called proliferative verrucous leukoplakia in which the reoccurrence rate is high.

Diagnosis: The cause should be eliminated such as sharp tooth or restoration.

If the healing does not occur then a biopsy is must required.

Histopathology: The Features include hyperkeratosis, hyperplasia, and atrophy.

The malignancy rate of oral leukoplakia is between 4%-8%.

Differential Diagnosis of this lesion includes lichen planus, smokeless tobacco lesion, hairy leukoplakia, verruca Vulgaris, lupus erythematous, cheek biting lesion, white sponge nevus, etc.[9]

Management: The management involves first and furthermost to discontinue the habits. Different types of surgeries include cold knife surgical excision, laser surgery are widely used. Chemoprevention is used in the form of topical bleomycin. Antioxidants such as retinoic acid and beta carotene are administrated. Stripping procedure with free grafts is also used.

2. **Oral Submucous Fibrosis:** It comes under the classification of premalignant lesions. It is a chronic disease that is mostly caused by the use of arecanut. It has a high risk of malignancy. The metabolism of collagen is affected by arecanut which leads to increased fibrosis.

Clinical Features: The hallmark diagnosing feature is the Burning sensation in the patient mouth. Excessive salivation, dryness of mouth, generalized inflammation with ulcerations can also be seen. In the cheek and palate small vesicles can be observed. Bands are also

present where pain persists. In the advanced cases of this lesion in the entire oris or mouth orifice circular bands are found, difficulty in swallowing, fibrous bands appearance, difficulty in tongue movement and inability to whistle are observed.

Histopathology: It involves hypertrophic fibroblasts, epithelial atrophy, loss of rete pegs, edema, and dilated & congested blood vessels.[10]

Management It involves furthermost the elimination of habit. In treatment plan vitamin B complex and high proteins and calories should be taken. Glucocorticoids which act as immunosuppressive agents is been used. Local injections of hyaluronidase, dexamethasone, and placental extract are used. In surgical management involving the excision of the fibrotic bands by fresh human placental grafts, followed by the injection of dexamethasone in the advanced cases.

Immunopathologic Diseases:

1. **Oral Lichen Planus:** It is one of the most common diseases. The cause of this disease is still unknown. It can consist of both red and white components with different textures.

The autoreactive T lymphocytes play a vital role in the development of OLP. Severe pruritis is a primary symptom of this disease. The surface is covered by very fine grayish-white lines called **Wickham's Straie.** One of the classical hallmarks of these skin lesions is **pruritic erythematous to violaceous papules**. Koebner phenomenon is associated with this disease. Genital mucosa is the most common extraoral mucosa site. The OLP has different forms which include Reticular Form, popular form, plaque form, Bullous form, Erythemateous form, and ulcerative form.

Histological Features: It includes Liquefaction degeneration, hyper ortho keratosis, and sawtooth appearance of retepegs. Beneath the basement membrane one can notice an eosinophilic band and thickening of the granular cell layer.

Management: It involves the use of Corticosteroids, Calcineurin inhibitors, Tacrolimus, Pimecrolimus Retinoids, Dapson, Mycophenolates Enoxaparin, Efalizumab. The different nonpharmacological modalities include PUVA therapy, Photodynamic therapy, and LASER therapy.

2. **Drug:** Induced Lichenoid Reactions-It is a type of lesion which exhibits similar histopathological features as lichen planus and clinically it is very difficult to distinguish between drug-induced lichenoid reactions and lichen planus. It can be differentiated from the OLP based on drug administration, contact with a metal or systemic disease & when the factor was eliminated, on resolution. The causes include Gold therapy, NSAIDs, Other hypertensives, etc. Clinically ulcerative reaction pattern can be seen and unilateral.[11]

Management: The treatment involves discontinuation of drug and topical steroids are used.

3. **Lupus Erythematosus:** It is an autoimmune disorder, which is chronic. The etiopathogenesis of SLE is not all so clear but some research fin that it is due to the interaction between genetic and hormonal factors, and hormonal exposures. Epstein Barr virus ad cytomegalovirus is commonly associated with this disease. In some researches it has been found that ROS, which is reactive oxygen species, triggers the production of autoantigen and T cells which are involved in the pathogenesis of SLE. Different diagnostic criteria are made for SLE which includes Neurological involvement, arthritis, anti-double-stranded DNA, APLA, ANA are now considered in the inclusion criteria. The management involves the use of corticosteroids, Hydroxychloroquine, Cyclophosphamide, and other immunosuppressive agents are used.

Allergic Reactions: This classification presents:

- **Lichenoid Contact Reactions:** It is a type of hypersensitivity reaction which occurred due to the reaction of amalgam fillings. The most important disguising feature to differentiate between OLP and LCE is **the extensions of lesions.** It is usually asymptomatic. The management includes the replacement of dental materials and the healing period is 1-2 months.
- **Reactions to Dentifrice and Chlorhexidine:** It is a very rare disorder. It is a type of allergic reaction that includes flavor additives such as carvone and cinnamon or preservatives. Clinically both ulcerations and white lesions can occur. The common sites involve buccal, labial, and tongue mucosa. The healing of the lesion is seen after the withdrawal of allergic contained agents.[8-11]

Toxic Reactions: Under this classification;

- **Reactions to smokeless Tobacco:** It is divided into 3 groups; Moist snuff, chewing tobacco, and Dry snuff. It is a white and leathery lesion and gingival retractions can be seen in smokeless tobacco habit. Wrinkles at the site of application can be observed in the mild form. Discontinuation of the habit is the proper treatment regarding this lesion.
- **Smokers Palate:** It is also known as stomatitis Nicotina or Leuukokeratosis. This is a white patch diffused in nature occurring in the Hard Palate. It is usually caused by smoking like cigars or pipe smoking. It is painless and the response of chronic heat forms this patch, during smoking. It has not an increased rate of transferring into oral cancer. Clinically one can observe gray or white nodules and the presence of red dots in the center. In some severe cases dried lake **bed appearance** can be seen in the mucosa. In this lesion a biopsy is not required usually but in some cases where red patches can be seen i.e. Erythroplakia then a biopsy is required. Stopping the habit of smoking can lead to an eradication of patch, but if the lesion persists even after the stopping then a biopsy is required must and leukoplakia condition can be diagnosed in those cases.

Reactions to Mechanical Trauma:

Morsicatio: It is also known as chronic cheek biting. In this trauma the buccal mucosa is injured due to chronic irritation due to repetitive biting or chewing. It is bilateral and the lesion is white with thickened mucosa. Erythema (redness) and ulcerations can also be seen. No treatment is required for this trauma, however if the problem prolongs then one can seek medical attention.[10,11]

Other Red and White Lesions:

1. **Benign Migratory Glossitis:** It is also known as geographic stomatitis. It is more common in females as compared to males. It mostly common in the age group between 20-30 years. Etiopathogenesis includes genetic like B15, DRW6, & CW6, Nutritional deficiency, hormonal and psychological disturbances. Allergy can also be a cause of this lesion. No treatment is required however mouthwash like tantum or benzydamine hydrochloride 0.15% spray can be used.
2. **Leukoedema:** It is a white lesion and occurs frequently in the buccal mucosa. The etiology is still now not clear. Bilaterally in nature and usually asymptomatic. No treatment is required.
3. **White Sponge Nevus:** Canon in 1935 first described this lesion. It is an autosomal dominant disorder. Epithelial keratin gene playing a vital role in its pathogenesis. It is a very rare disorder. Clinically a white lesion with irregular surface can be noticed in the buccal mucosa. The mucosa gets swollen in this disorder like a sponge, hence the name Sponge Nevus. It is benign with no treatment is required.
4. **Hairy Tongue:** The etiology is unknown but the predisposing factors include antibiotics, excess alcohol consumption, poor oral hygiene, immunosuppressive drugs, the microflora in mouth, and oral candidiasis. Clinically hair-like appearance can be seen due to impaired desquamation of filiform papillae. The treatment involves elimination or reduction in predisposing factors.[8-11]

Conclusion

The red and white lesions include different type of lesions and the professional require a skillful knowledge to diagnose and distinguish between these lesions. However clinical correlation plays a very important role in diagnosing apart from histological reports. The malignancy rate is not so high of this lesion except in the cases of leukoplakia or oral submucous fibrosis. Researches are done to know the etiological factors of some of these lesions.

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References

1. Warnakulasuriya S. White, red, and mixed lesions of oral mucosa: A clinicopathologic approach to diagnosis. Periodontol 2000. 2019;80(1):89-104.
2. Mortazavi H, Safi Y, Baharvand M, Jafari S, Anbari F, Rahmani S. Oral White Lesions: An Updated Clinical Diagnostic Decision Tree. Dent J (Basel). 2019;7(1):15.
3. Scully C, Porter S. ABC of oral health. Swellings and red, white, and pigmented lesions. BMJ. 2000;321(7255):225-228.

4. Simi S, Nandakumar G, Anish Ts. White lesions in the oral cavity: a clinicopathological study from a tertiary care dermatology center in Kerala, India. Indian J Dermatol. 2013;58(4):269-274.
5. Lipsker D, Chosidow O. Lésions blanches de la muqueuse buccale [White lesions of the oral mucosa]. Rev Prat. 2002;52(4):389-393.
6. Bai YD, Sankarapandian S, Aditi R. A Wide Spread Red Lesion on the Surface of the Tongue-A Case Report and Review of Differential Diagnosis. J Clin Diagn Res. 2017;11(6):ZD07-ZD09.
7. McNamara KK, Kalmar JR. Erythematous and Vascular Oral Mucosal Lesions: A Clinicopathologic Review of Red Entities. Head Neck Pathol. 2019;13(1):4-15.
8. Yardimci G, Kutlubay Z, Engin B, Tuzun Y. Precancerous lesions of the oral mucosa. World J Clin Cases. 2014;2(12):866-872.
9. Mortazavi H, Safi Y, Baharvand M, Rahmani S. Diagnostic Features of Common Oral Ulcerative Lesions: An Updated Decision Tree. Int J Dent. 2016; 2016:7278925.
10. Ferreli C, Giannetti L, Robustelli Test E, Atzori L, Rongioletti F. Linear white lesion in the oral mucosa. JAAD Case Rep. 2019;5(8):694-696.
11. Carrard VC, van der Waal I. A clinical diagnosis of oral leukoplakia; A guide for dentists. Med Oral Patol Oral Cir Bucal. 2018; 23(1):e59-e64.