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Review Article

Spectrum of white lesions in the oral cavity- A review

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ABSTRACT

The white lesions occurring in the oral cavity consist of 5% of the oral pathoses but some of these like leukoplakia, lichen planus, proliferative verrucous leukoplakia, etc have a high potential of malignant transformation up to 0.5-100%. As they are visualized as shades of white, they are of diagnostic challenge. Some of the lesions are also associated with other skin lesions viz. lichen planus, pemphigus, etc. The etiology, pathogenesis, and mode of treatment varies with the different type of lesions. This spectrum consists of lesions from harmless reactive lesions to dysplastic and malignant entities. The white appearance of these lesions is may be because of hyperkeratosis, acanthosis, intracellular/intercellular edema, necrosis of the epithelial cell or increased fibrosis. They are seen as patches, papules, or plaques unilaterally or bilaterally in the oral cavity involving buccal mucosa, tongue, palate, labial mucosa, gingiva etc. While there are a few clinical and histological elements that assist in the identification of this wide range of white lesions to arrive at an accurate diagnosis, further lending a hand in providing appropriate treatment for the same.

1. Introduction

The white lesions of the oral cavity have a broad spectrum with different aetiology, presentation, and prognoses. They can be benign physiologic entities, systemic conditions, infections or malignancies.[1] Diagnosis of oral white lesion is very challenging since it has wide range of aetiology and presentation like papular, reticular, annular or erosive ulcerative or a blend of them.[2] This emphasizes the need for every dentist to have immense knowledge to diagnose a particular white lesion.[1]

2. Why White Lesions are White?

The whitish appearance of the oral mucus membrane can be

1. The epithelium may be stimulated to an increased production of keratin (hyperkeratosis).
2. An abnormal stratum spinosum widening (acanthosis
3. Extra and intracellular accumulation of fluid in the oral epithelium
4. Necrosis of the cells in the epithelium
5. Microbes, particularly fungi, can produce whitish, non-adherent pseudo membrane comprising of debris or epithelial cells, fungal mycelium, and neutrophils.[3]
6. Increased fibrosis of the connective tissue, reducing blood vessels.[4]

2.1. Leukoedema

The prevalence is up to 90% among blacks and ranges from 10–50% in whites, there is no sex predilection, mainly seen in smokers.

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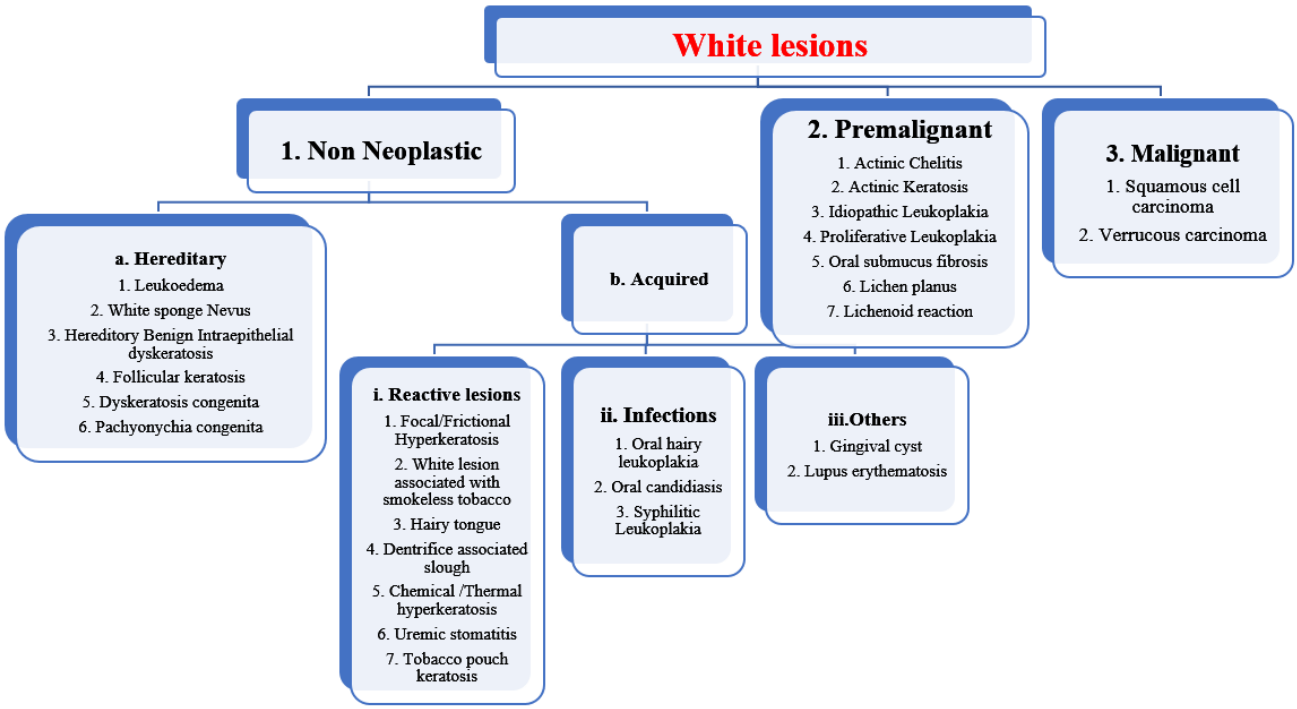

Diagram 1: Suggested classification

The lesion is noted on buccal mucosa bilaterally in most patients. Other areas like tongue (ventral surface), labial mucosa, alveolar mucosa, floor of the mouth, and soft palate can also be affected.[5] It is an opalescent change of the oral mucosa presenting as a gray to white, diffuse, non-scrapable condition appearing like veil. It is asymptomatic and it fades or disappears upon stretching the mucosa.[1]

Histologically epithelial layer thickening and broadening of rete pegs, intracellular edema of the intermediate cell layer, and retention of the superficial cells either as a layer of parakeratotic cells or as a layer of ballooning cells.[6] (Figure 1 A)

Leukoedema is diagnosed clinically, and a biopsy is not required. No treatment is necessary.[3]

2.2. White sponge nevus/cannon disease/familial white folded dysplasia

It is an autosomal dominant disorder that involves point mutation of either keratin 13 or keratin 4 genes[7,8] resulting in defective keratinization of the oral mucosa, rarely anogenital, laryngeal, oesophageal and nasal mucosa.[9]

It is present in early childhood, sometimes during adolescence[10,11] with no sex predilection.[4] It presents as bilateral asymptomatic, white corrugated or velvety diffuse plaques on the buccal mucosa and also tongue (ventral surface), labial mucosa, floor of the mouth, soft palate.[11,12]

Histologically superficial parakeratosis,[4] intracellular and intercellular edema, acanthosis, and the perinuclear space have eosinophilic condensation in spinous layer.[9] (Figure 1 B)

No treatment is indicated.[4]

2.3. Hereditary benign intraepithelial dyskeratosis / Witkop-Von Sallmann syndrome

It is an autosomal dominant hereditary disorder of the oral mucosa and conjunctiva.[13]

Seen in early childhood with oral lesions which are corrugated and asymptomatic white plaques on the buccal, labial mucosa or floor of the mouth, tongue (lateral border),[14] gingiva, palate[4] preceding the ocular.[15,16] Ocular lesions appear opaque, white plaque on the bulbar conjunctiva along with photophobia, itching,[14] blindness because of vascularization of the cornea.[15]

Histologically there is keratosis, acanthosis, and dyskeratosis. Cell within the cell appearance is seen in some areas as one cell is engulfed by the other. The lower part of the epithelium appears to be normal. The histological features are similar in both ocular and oral lesion.[4] (Figure 1 C)

No treatment is needed for oral lesions. Patients with ocular lesions are referred to an ophthalmologist.[4]

2.4. Follicular keratosis /Darier's disease/ Darier-White disease

It is an autosomal-dominant associated with the mutation of ATP2A2 gene.

Seen in childhood and adolescence cutaneous/mucosal lesions involving the mouth, pharynx, female genitalia (13% 0ral lesions) with equal gender predilection.[17]

Papules on the face, trunk, and seborrheic areas which may coalesce and get infected. Nails appear fragile with subungual keratosis and linear white and red streaks. Oral lesions most commonly occur in palate, gingiva, buccal mucosa presenting as whitish plaques or papules with central depression giving grainy/pebbly appearance and tend to coalesce occasionally.

Histologically epithelium with acantholysis and suprabasalar clefts is seen with parakeratotic and dyskeratotic cells in the cleft in the form of corps, ronds, and grains. Ronds and corps are keratinized squamous cells with uniformly basophilic nuclei and cytoplasm which is intensely eosinophilic. Grains are small parakeratotic cells having pyknotic, hyperchromatic nuclei. Basal cell proliferation is also seen. (Figure 1 D)

2.4.1. Treatment

Generalized skin lesions are treated with topical and systemic retinoids and oral lesions do not require any specific treatment.[18]

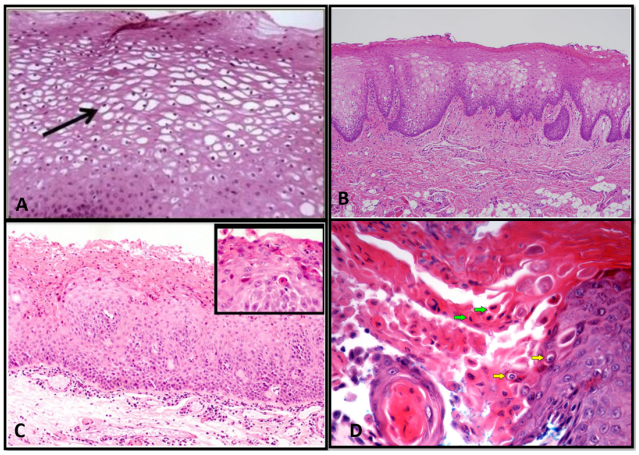

Figure 1: A): The histological picture of leukoedema shows intracellular edema of the intermediate cell layer.[19] **B)**: Histologically white sponge nevus shows superficial parakeratosis, intracellular and intercellular edema, acanthosis, perinuclear space with eosinophilic condensation in the spinous layer.[20] **C)**: HBID shows parakeratosis, acanthosis and dyskeratotic cells appreciated in the upper spinous layer. A mild lymphoplasmacytic infiltrate in the subepithelial lamina propria is typical. Inset: High-power photomicrograph shows dyskeratotic cells with hypereosinophilic cytoplasm.[21] **D)**: Corps and ronds are seen histologically in Dariers disease.[22]

2.5. Dyskeratosis congenita /Coleengman syndrome / Zinsser-Colleengman syndrome

Rare inherited disorder characterized by mucosal hyperpigmentation of the skin, nail dystrophy and leukoplakia.[23,24] The inheritance pattern can be autosomal dominant, autosomal recessive, or x-linked (commonly exhibited) with mutation of the DKC1 gene.[25–27]

Seen in first decade with male predilection.[14] The important clinical manifestation is bone marrow failure leading to anemia by the second decade. There is abnormal skin pigmentation, nail dystrophy and oral bullae that later rupture and form leukoplakic white plaques. There is discomfort with hot and spicy food swallowing and have chances of malignant transformation.[25,26]

Histologically hyperkeratosis and epithelial dysplasia are the features initially, frank malignant changes are seen as the lesion develops.

Regular follow up is necessary for the oral lesions and hematopoetic stem cell transplantation is the treatment of choice for bone marrow failure.[27]

2.6. Pachyonychia congenita

It is a rare autosomal dominant disorder characterized by subungual and palmoplantar hyperkeratosis, nail dystrophy, and oral leukoplakic lesions.[28,29] There are two subtypes type 1 (Jadas- sohn-Lewandowsky form) and type 2 (Jackson-Lawler form).[30] Mutations of keratin 16 & 17 gene are implicated as the cause of type 1 & type 2 respectively.[31,32]

Clinically nail dystrophy and palmoplantar and follicular keratosis along with oral leukoplakic lesions on the tongue and buccal mucosa are present.[28,33] In type 1 neonatal teeth can be seen.[33]

Histologically hyperkeratosis and acanthosis of the epithelium are seen.

No treatment is indicated for oral lesions. Cutaneous lesions has no satisfactory treatment regimen.[34]

2.7. Focal/frictional hyperkeratosis

It is caused frequently by friction from the teeth, seen on the buccal mucosa at the level of occlusion and tongue.[35]

Seen mostly in female adults (with temporomandibular dysfunction) as an area of white plaques and papules with erosions and shredded keratin which is ill-defined with rough surface having high risk for OPMD.[36]

Histologically epithelial hyperplasia, hyper parakeratosis, intracellular edema, acanthosis, bacterias are seen in the biopsy from the tongue but less often from lip and buccal mucosa, long rete ridges are evident.[36] (Figure 2 B)

2.8. White lesion associated with smokeless tobacco /Snuff Dipper's lesion/Snuff pouch /Spit tobacco keratosis

Placing of the smokeless tobacco product commonly in the lower buccal vestibule leads to keratotic changes.[37]

Clinical appearance varies from an early grey opalescent lesion to progressive keratotic thickening and furrowing of the mucosa.[37,38]

Histologically the surface is either orthokeratotic or parakeratotic with chevron parakeratosis imparting a wavy keratotic layer.[36,38,39] The epithelium shows acanthosis, vacuolated spinous cells, and hyperchromatic nuclei in the basal layer without dysplasia. Collagen appears homogenous, eosinophilic, and acellular with or without inflammation. (Figure 2 C)

2.8.1. Treatment

Discontinuation of the habit, if not resolved surgical removal is advised.[40,41]

2.9. Hairy tongue

It is filiform papillae overgrowth of the tongue by long-term use of oxygenating mouthwashes, broad-spectrum antibiotics, intense smoking or radiotherapy altering the microbiome.

Clinically it is asymptomatic except for the tingling sensation and gagging. Colour of the tongue varies from white to tan to deep brown depending on the diet and oral hygiene.

Microscopically there is elongation of the filiform papillae, harbouring microorganisms and fungi. Mild inflammation can be seen in the underlying connective tissue. (Figure 2 A)

Treatment involves identification of etiological factors and discontinuation. Brushing with slurry of sodium bicarbonate in water and a gentle scraping of the dorsum of the tongue.[42]

2.10. Dentifrice-associated slough

It is associated with using various toothpastes or mouthwashes caused by the components of the dentifrices like flavoring agent, detergent, or any essential oil.[42]

There is no gender and age predilection. Commonly involved sites are buccal mucosa, vestibule, and gingiva. Painless superficial whitish slough which peels off associated with pain while peeling.[43]

Histologically epithelium shows acanthosis, intracellular oedema, and parakeratosis. Intraepithelial cleft without acantholysis can also be seen. Inflammation is minimal or absent.[44,45] (Figure 2 D)

Treatment includes discontinuation of the dentifrice responsible.[43–45]

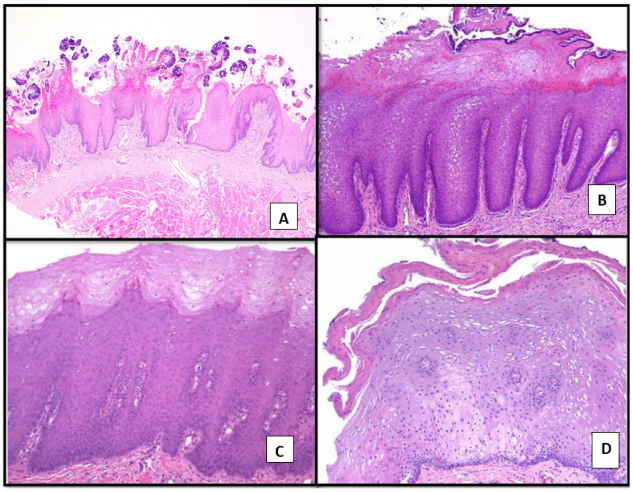

Figure 2: A): Histopathology of oral hairy tongue shows elongation of the filiform papillae, harboring microorganisms.[22] **B)**: Microscopically frictional keratosis shows epithelial hyperplasia, hyperparakeratosis, intracellular edema, acanthosis, bacterias.[46] **C)**: Epithelium shows para keratinization and chevron type of hyperkeratosis with vacuolated cells in the spinous layer and without any inflammation in the connective tissue.[46] **D)**: Histologically intraepithelial linear clefting of the superficial parakeratin, is seen in dentrifrice-associated slough

2.11. Chemical /Thermal hyperkeratosis

Some chemicals cause burning of the oral mucosa leading to hyperkeratosis. These lesions are commonly seen on the vestibule and gingiva. Some of the chemicals are sodium hypochlorite, aspirin, hydrogen peroxide, formocresol, paraformaldehyde, cavity varnish, and mouthwashes.[4]

Thermal keratosis is due to heat from excessively hot food or smoking. Lesions are seen on the palate, and tongue.

Nicotine stomatitis both chemical and thermal keratosis caused by tobacco.[4]

2.11.1. Clinical features

Thermal keratosis focal keratosis with ulcerations, mild pain may be present.

Chemical keratotic lesions are white with irregular shape associated with the pain.

Nicotine keratosis causes opacification of the hard palate with red spots representing inflamed and metaplastically altered salivary duct openings.[4]

Histologically chemical and thermal keratoses display a superficial pseudomembrane composed of necrotic tissue and an inflammatory exudate.

2.11.2. Treatment

Removal of the causative agent.

2.12. Uremic stomatitis

In advanced renal failure, white plaques with sudden onset appears on oral mucosa including dorsal and ventral surface of the tongue, floor of the mouth, buccal and labial mucosa, gingiva.[47] The suggested etiology is that urea is converted to ammonia by salivary urease which in turn causes mucosal irritation.

2.12.1. Clinical features

Four clinical forms of the lesions are seen viz. hyperkeratotic, hemorrhagic, ulcerative, pseudomembranous and they are associated with burning sensation and unpleasant breath of urea and ammonia.

2.12.2. Histological feature

Epithelium exhibits hyperkeratosis, acanthosis along with ballooning keratinocytes and the underlying connective tissue shows minimal inflammation unless ulceration where it shows dense inflammatory infiltrate.[48] (Figure 3 C)

2.12.3. Treatment

Lesions resolve on the treatment of renal treatment. Scaling and hydrogen peroxide mouthwashes are helpful.

2.13. Oral hairy leukoplakia

It presents as non-scrapable white plaques on the lateral border of the tongue either unilaterally or bilaterally in HIV infections, immunocompetent patients**.** Other sites in the oral cavity are buccal mucosa, floor of the mouth, and soft palate.[4]

Asymptomatic white plaques with diffused demarcation and corrugated surface are noted on the lateral border of the tongue, sometimes associated with burning sensation.[49]

Histologically irregular hyperkeratosis and acanthosis is seen along with koilocytes.[4] (Figure 3 A,B)

Superficial epithelial cells exhibiting nuclear beading.[50,51]

No treatment required. Antivirals can resolve the lesion but reappear once discontinued.[4]

2.14. Oral candidiasis

It is the most common type of fungal infection by candida albicans, commensal in the oral cavity. Hyperplastic and pseudomembranous forms appears white.[1]

Clinically it presents as creamy white plaques, patches, or papular lesions that are scrapable leaving behind an erythematous area.[14] The pseudomembranous type gives curdled milk appearance. The lesion may be associated with foul taste and burning sensation. The buccal mucosa is frequently affected by pseudomembranous candidiasis followed by the tongue and the palate.[14]

Gender distribution among oral leucoplakia varies, with M:F ratios ranging from 4:1 to 85:1 in different parts of India.

Chronic hyperplastic candidiasis (or candidal leukoplakia) appears as a tough plaque on buccal commissures, cheeks, palate, and tongue that cannot be rubbed. It can be distinguished only by histology from other forms of leukoplakia.[40]

Histologically Gram and PAS staining show candidal hyphae embedded in clumps of detached epithelial cells. This type of lesion has an increased propensity for dysplastic change and warrants close monitoring.[40] Another characteristic histological feature of CHC is the collection of polymorphonuclear leukocytes forming "microabscesses" associated with candidal hyphae.[52] The stratum spinosum shows acanthosis with hyperplasia of the rete ridges. (Figure 3 D)

2.14.1. Treatment

Eliminate predisposing factors. Medical management in the form of antifungal therapy or topical application of retinoids, bleomycin, beta carotene or mixed tea, and surgical methods.[53]

2.15. Syphilitic leukoplakia

Syphilis is an acute and chronic sexually transmitted disease which is caused by an anaerobic bacterial species, Treponema pallidum.[54] Based on its activity and infectivity phase, acquired syphilis can be classified into four stages: primary, secondary, latent, and tertiary.[55,56]

Oral lesions are principally associated with secondary syphilis, although all stages can give rise to oral manifestations.[57,58] most common is called “mucous patches” with two subtypes: slightly elevated-type plaques and, occasionally, oval ulcerations covered with a gray or white pseudomembrane; or multiple mucous patches that may coalesce to form serpiginous lesions (snail track ulcers).It is unclear whether white plaques with verrucous aspect, “leukoplakia like” truly reflect syphilis, or more likely a tobacco smoking habit—indeed this was observed by Hutchinson in the 19th century.[43]

Syphilitic leukoplakia would represent a homogenous white patch affecting huge regions of the dorsum of the tongue.[57]

2.16. Gingival cyst

It is believed that the remains of dental lamina within the alveolar ridge mucosa after tooth formation proliferate to form these small keratinized cysts.

2.16.1. Clinical features

Gingival cyst of the newborn or Bohn’s nodules, can present as few or many, white to yellowish, round to oval nodules in the maxillary and/or mandibular gingiva and alveolar ridge of newborns. They are generally asymptomatic, without any

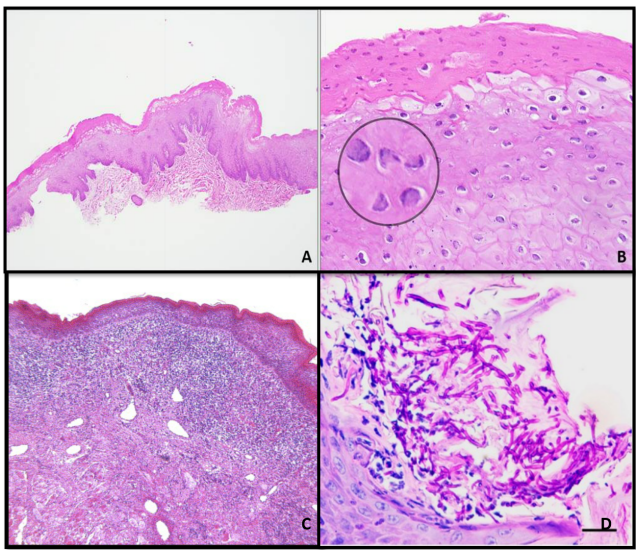

Figure 3: A): Oral hairy leukoplakia shows Hyperkeratosis, acanthosis, with prominent intracellular edema are noted at low power, magnification.[59] **B):** Peripheral "beading" of the chromatin is noted in superficial keratinocytes.[59] **C**): Epithelium exhibits hyperkeratosis, acanthosis, ulceration, and the underlying connective tissue shows dense inflammatory infiltrate in uremic stomatitis.[60] **D**): PAS-stained image showing significant accumulation and penetration of C. albicans hyphae through the hyperkeratotic surface of the tongue dorsal epithelium. Neutrophilic Munro microabscesses in response to the infection are seen.[61]

discomfort for the infant.[62]

2.16.2. *Histologic features*

It is lined by thin epithelium and a lumen usually filled with desquamated keratin, occasionally containing inflammatory cells.[62] (Figure 4 A)

2.16.3. *Treatment*

These are self-limiting, follow-up is needed.

2.17. *Lupus erythematosus*

It is an autoimmune disease involving immune complexes. Environmental factors which can aggravate the disease are sun exposure, drugs, chemical substances, and hormones.

2.17.1. *Clinical features*

The oral lesions in Systemic LE and Discoid LE are similar in their characteristics, both clinically and histopathologically. The typical clinical lesion comprises white striae with a radiating orientation, and these may sharply terminate toward the erythematous center of the lesions. The most affected sites are the gingiva, buccal mucosa, tongue, and palate. Oral mucosa lesions compatible with LE may be the first sign of the disease.

2.17.2. *Histologic features*

On histopathological examination by H & E, lupus erythematosus shows hyperkeratosis, basal cell layer degeneration, increased basement membrane thickness, chronic inflammatory infiltrate in the connective tissue with diffuse, deep and perivascular distribution.[17] (Figure 4 B) Systemic or topical steroids are given.

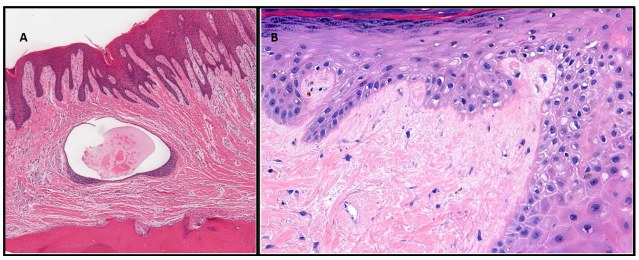

Figure 4: A): Gingival cyst shows cystic lining and lumen filled with desquamated keratin.[22] **B**): Cutaneous lupus erythematosus shows intraepithelial edema and thickening of the basement membrane.[22]

2.18. *Actinic cheilitis*

Actinic cheilitis occurs as a result of excessive exposure to ultraviolet sunlight. It is typically found on the vermillion border of lower lip, mostly in who works outdoors.[4] Some studies have shown fibroblast growth factor receptor 3 gene (FGFR3). Some lesions (6%–10%) have malignant transformation.[4]

2.18.1. *Clinical features*

Male predilection is of 10:1[14]

Moreover, the border between vermilion and the adjacent skin cannot be established and the lesion may be solitary well-demarcated or multiple poorly demarcated .95,97,98 g men. The patient presents with dryness, swelling, and cracks with smooth, blotchy, pale atrophic regions.[62] The lesions progress to rough, scaly keratotic plaques, Symptoms include burning and itching.

2.18.2. *Histologic features*

The epithelial changes range from simple hyperorthokeratosis without dysplasia to CIS. Varying degrees of cytologic atypia such as increased nuclear/cytoplasmic ratios, loss of cellular polarity and orientation, chronic inflammation, and vasodilatation are also characteristic of actinic cheilitis. (Figure 5 C)

2.18.3. *Treatment*

Surgical intervention is the current treatment of choice.99 Chemotherapy with 5-fluorouracil, CO2 laser, and cryotherapy have also been recommended.

2.19. Actinic keratosis

It is the cutaneous counterpart of actinic cheilitis, lesions are seen in light-complexioned individuals who have had long-term exposure to sunlight.

2.19.1. Clinical features

Presents as oval plaques with rough surface which are smaller than 1 cm in diameter most commonly found on the forehead, cheeks, temples, ears, and lateral portions of the neck. The color of the lesion varies from white yellow, and brown to red.

2.19.2. Histological features

There is nuclear atypia, increased nuclear-cytoplasmic ratio, and atypical proliferation of basal cells. The dermis generally contains a lymphocytic inflammatory cell infiltrate. Elastotic or basophilic changes in collagen and irregular clumps of altered elastic fibers and regenerated collagen are noted in these areas. (Figure 5 A)

2.19.3. Treatment

Treatment includes cryotherapy, surgical excision, topical application of 5-fluorouracil.[42]

2.20. Idiopathic Leukoplakia

Idiopathic leukoplakia should be differentiated from tobacco-associated leukoplakia.

Most commonly seen in females on the tongue,but can develop on the gingiva.

2.20.1. Clinical features

Homogenous greyish white plaque with surface showing cracked mud appearance

2.20.2. Histological features

Histologic features include hyperkeratosis, dysplasia features like irregular stratification, increased and abnormal mitotic figures, premature keratinization, nuclear pleomorphism and hyperchromatism, and an increased nuclear-cytoplasmic ratio.[42] (Figure 7 B)

2.20.3. Treatment

Periodic examination and re-biopsy of suspicious lesions. Surgical excision is the treatment of choice.[42]

2.21. Proliferative Verrucous Leukoplakia

Was coined in 1985 by Hansen and colleagues. Some studies showed it is associated with HPV 16 and 18 and 8 and Epstein-Barr Virus are associated with it and tobacco seems to play no role.[14]

PVL is more prevalent in women in their sixth decade of life, with the gingiva and tongue being the most common sites

2.21.1. Clinical features

PVL may be solitary or multiple, with wide clinical manifestations ranging from a flat verrucous appearance in its early stages to a more exophytic appearance with an erythematous component in the late stages

Non-homogeneous multifocal areas with speckled and rough surface might appear in the form of exophytic, wart-like, verrucous, polypoid projections or erythematous feature.[14]

2.21.2. Histologic features

PVL is a continuously developing lesion with the early lesions exhibiting only hyperkeratosis and late lesions representing epithelial dysplasia, verrucous carcinoma, or squamous cell carcinoma–like changes. (Figure 5 B)

2.21.3. Treatment

Treatment modalities ranging from surgery, irradiation, and chemotherapy

2.22. Oral submucous fibrosis

It is a progressive, chronic, and premalignant condition characterized by fibroelastic changes and inflammation in the mucosa.[4] The aetiology is associated with consumption of spicy food, chilies, and/or areca nuts, as well as vitamin B deficiency and protein malnutrition.[63] According to some there is a genetic predisposition involving human lymphocytic antigen (HLA) A10, DR3, DR7, and B7.[64]

2.22.1. Clinical features

The most commonly involved sites are the buccal mucosa, labial mucosa, soft palate, floor of the mouth, and tongue.

Symptoms include burning sensation on eating hot and spicy food and restricted mouth opening.[63,64]Oral lesions present with vesicles, excessive salivation, ulcers, dryness of the mouth, and pigmentation.[63] As it progresses there are vertical and horizontal fibrous bands palpable and ‘shrunken hockey’ stick uvula,

2.22.2. Histologic features

Early findings include the presence of chronic inflammatory cells, with several eosinophils in the lamina propria. Epithelial atrophy, hyalinized subepithelial collagen, and loss of vascularity is seen in established cases. Fibrosis of minor salivary glands is also evident.[65] (Figure 5 D)

2.22.3. Treatment

Submucosal injections of steroids and collagenases, as well as topical steroid application, oral iron preparations, and topical vitamin A applications have been tried for palliative relief. Severe cases need surgical intervention.[64]

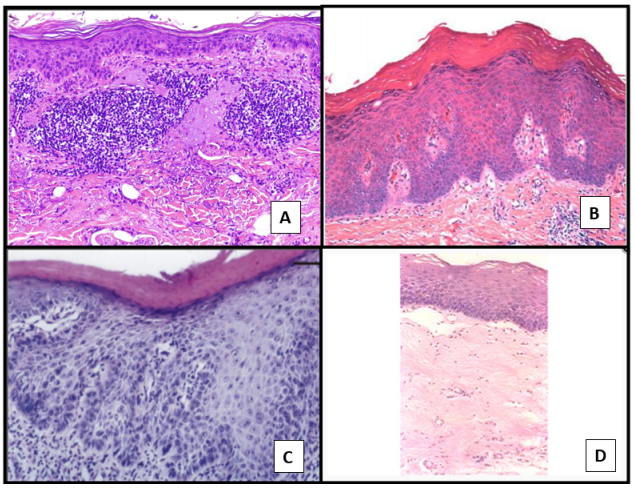

Figure 5: A): Epithelial dysplasia with dense amount of inflammatory infiltrate is seen in actinic keratosis.[22] **B)**: PVL shows hyperkeratosis, prominent granular layer with dysplastic changes.[46] **C)**: Actinic cheilitis shows dysplastic changes. **D)**: OSMF shows epithelial atrophy, hyalinized subepithelial collagen, and loss of vascularity.[22]

2.23. *Lichen planus*

The term lichen planus (LP) is derived from the Greek word lichen meaning tree moss and the Latin planus meaning flat

2.23.1. *Clinical features*

Clinically, there are six clinical subtypes of OLP that can be seen individually or in combination like: reticular, plaque, atrophic, erosive, popular and bullous.

The reticular lesions, the most recognized form of OLP, are often asymptomatic and appear as multiple papules with a network of small, raised, whitish–grey, lacy lesions referred to as Wickham striae.[66]

2.23.2. *Histological features*

liquefactive degeneration of the basal cells, colloid bodies (Civatte, hyaline, cytoid), homogeneous infiltrate of lymphocytes and histiocytes in a dense, band-like pattern along the epithelium-connective tissue interface in the superficial dermis, cytologically normal maturation of the epithelium, saw-tooth rete ridges and hyperkeratosis.[67] (Figure 6 A & B)

2.23.3. *Treatment*

Reticular lesions that are asymptomatic generally require no therapy but only observation for change.

2.24. *Lichenoid reaction*

Oral lichenoid reaction reactions present with clinical and histological overlapping features, hence diagnosis is difficult. The etiology can be drugs, restorative material,

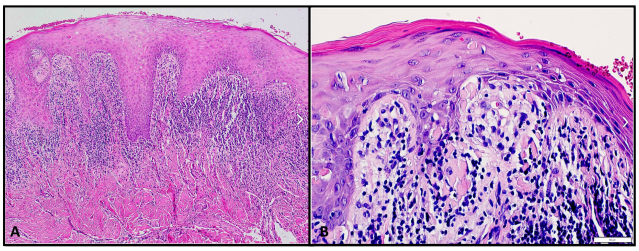

Figure 6: A): Lichen planus shows saw tooth rete ridges and **B)**: Colloid bodies.[68]

autoimmunity and can occur in Graft Vs Host reaction.

Lichenoid contact reactions are rare, but when present, are most commonly associated with dental amalgam due to type IV hypersensitivity. Corrosion products of amalgam have to penetrate the epithelial lining and bind with host keratinocyte surface proteins, resulting in a cell-mediated response directed at basal keratinocytes.[69] Most hypersensitivity is related to mercury.

2.24.1. *Clinical features*

Asymmetrical unilateral reticular white patches, plaques or papules, with or without ulcerated areas. The lesions can be symptomless, or when ulcerated, painful; especially on eating hot, salty, spicy or citrus food.[69]

2.24.2. *Histological features*

Hyperkeratosis, vacuolar degeneration of basal keratinocytes mixed inflammatory infiltrate of plasma cells.(Figure 7 A)

2.24.3. *Treatment*

Removal of the cause.[69]

2.25. *Squamous cell carcinoma*

Oral squamous cell carcinoma (OSCC) comprises 92–95% of all oral cancers.[70] The incidence is higher among men, older than 65 years.

The etiology of OSCC is multifactorial including smoke &smokeless tobacco, alcohol, betel quid, phenol, viral, bacterial, and fungal infections, electro-galvanic reaction, radiation, genetics, immunosuppression, expression of oncogenes, deactivation of tumor suppressor genes, malnutrition, iron-deficiency anemia, and hereditary.[7,70]

2.25.1. *Clinical features*

Present as red, white, or in combination with elevated, rough, papillary, or flat surface.

Site: floor of the mouth, posterior lateral borders and ventral surface of the tongue. Involvement of submandibular and digastric lymph nodes due to cancer causes lymphadenopathy with firm to hard consistency,

which converts to fixed nodes in later stages.[10]

2.25.2. Histological features

It has variation in the histologic appearance. The well-differentiated SCC consists of sheets and nests of cells with obvious origin from squamous epithelium with dysplasia. There is the individual cell keratinization and the formation of keratin pearls. Few atypical mitotic figures are also seen. (Figure 7 C)

Moderately differentiated carcinomas lose certain features so that their resemblance to squamous epithelium is less pronounced. The shape arrangement of the cells is altered along with increased mitotic figures.

The poorly differentiated carcinomas bear little resemblance to their cell of origin with lack of cohesiveness and no keratin formation.[70]

2.25.3. Treatment

Initial stages are treated with surgery and advanced with radiation therapy or combined chemoradiation therapy with or without surgery. Five-year survival rate of OSCC is about 53–56%.[71]

2.26. Verrucous carcinoma (Ackerman's tumor, Snuff Dipper's cancer, Buschke-Loewenstein tumor)

Verrucous carcinoma is a subtype of OSCC having different clinical and histopathological features and found as 2%–9% of all oral carcinomas.[72] It has slow growth rate, local invasion, and a low tendency to metastasize.[73]

Its etiology is not understood completely but can be associated with smoking, alcohol consumption, betel nut chewing, smokeless tobacco, and the HPV virus.[73]

2.26.1. Clinical features

More commonly found in elderly male above 55 years on vestibule, buccal mucosa, gingivae, tongue, and hard palate.

This presents as an asymptomatic, diffuse, well-demarcated, thick white plaque with papillary projections on the surface[73] sometimes appears pink due to inflammation.[3]

2.26.2. Histological features

OVC has papillary growth, epithelial cells are highly proliferative with weak cellular atypia. The epithelial pegs are blunt and droplets shaped & form pushing borders. The basement membrane remains intact. Many lymphocytes and plasma cells are infiltrated into the connective tissue.[74] (Figure 7 D)

A malignant transformation comprises less than 1% to 16% of OSCC. It is reported that the rate of malignant transformation in gingival lesions is about 21 times higher than in other sites.

2.26.3. Treatment

Surgical excision.

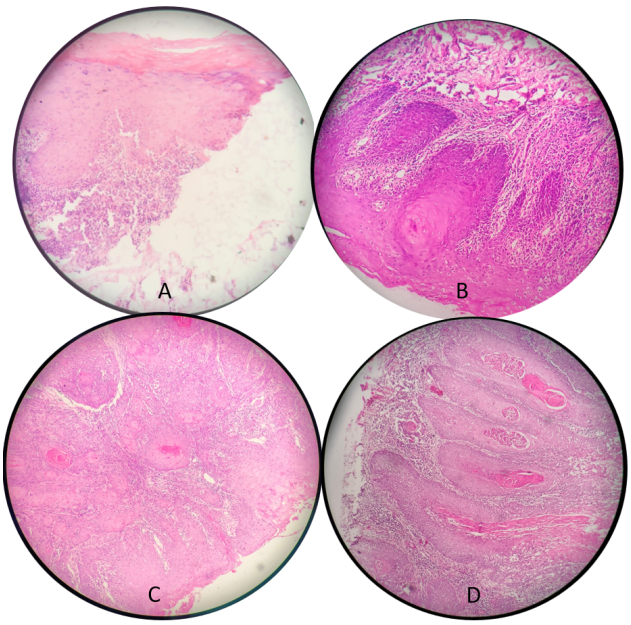

Figure 7: A): Lichenoid reaction showing dense inflammatory infiltrate. **B)**: Leukoplakia with broad rete ridge and dysplastic changes. **C)**: Squamous cell carcinoma with tumour invasion in the connective tissue. **D):** Verrucous carcinoma with endophytic growth and parakeratin plugging.

3. Conclusion

Many white lesions of the oral cavity share clinical features which makes it difficult for diagnosis. This review provides an overview of most white lesions, microscopic evaluation of the white lesions and is helpful in improving the knowledge regarding these lesions and the management of the same.

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None.

5. Conflict of Interest

None.

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