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Oral Premalignant Lesions

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Abstract:- This paper provides an general overview of oral premalignant lesions and conditions , reasons and causes behind this premalignant lesions and conditions and how to identify these conditions and differentiate them from other non cancerous lesions and this paper also provides information on early signs and Symptoms along with signs and symptoms during the later stages and complications associated and also provides information on etiopathogenesis and as of how to diagnose these lesions clinically and by different laboratory tests and also gives an overview on management a of these lesions.

I. INTRODUCTION

Precancerous lesion, It is an applied state of tissue often, but not always has a high potential to undergo malignant transformation. Some benign lesions or conditions for varying length of time, also generally precede oral cancer. Interestingly, these lesions or conditions share same etiological factors with oral cancer, particularly the use of tobacco and exhibit same habit and relationship .Many of them show high potential to become cancer and are, therefore, termed as precancerous lesion.

It is especially important to remember that a premalignancy is not guaranteed to eventually transform into cancer ,as is often but erroneously believed. Individual with oral precancer has 69 times greater risk of developing oral cancer as compared to tobacco users who do not have precancer.

➢ *Definition*

- Precancerous lesion: It is defined as a morphologically altered tissue in which cancer is more likely to occur, than its apparently normal counterparts.
- Precancerous condition: It is defined as a generalized state or condition associated with significantly increased risk for cancer development.

➢ *Some of oral precancerous lesions are:*

- Leukoplakia
- Erythroplakia
- Mucosal changes associated with smoking habits
- Carcinoma in situ
- Bowen disease
- Actinic keratosis, cheilitis and elastosis.

➢ *Some of precancerous conditions are :*

- Oral submucous fibrosis
- Syphilis
- Sideropenic dysplasia
- Oral lichen planus
- Dyskeratosis congenita
- Lupus erythematosus

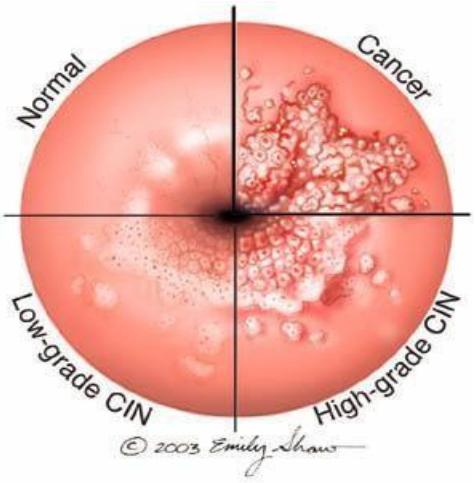
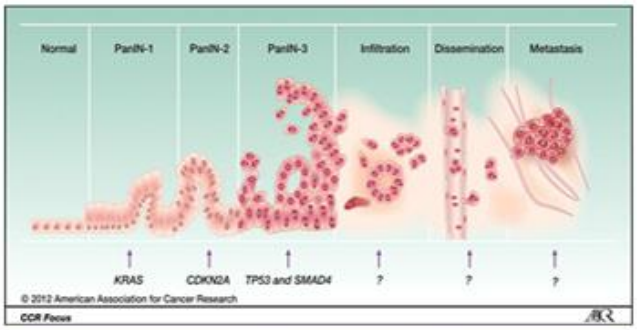


Fig 1 Showing Histological Chances In Different Grades Of Cancer

II. PRECANCEROUS LESIONS

➢ *Stages of Precancerous Lesions*



Lesion	Aetiology	Features
Erythroplasia	Tobacco/alcohol	Flat red plaque
Leukoplakia	Tobacco/alcohol	White or speckled plaque
Proliferative verrucous leukoplakia	Tobacco/alcohol/ human papillomavirus (HPV)	White or speckled or nodular plaque
Sublingual keratosis	Tobacco/alcohol	White plaque
Actinic cheilitis	Sunlight	White plaque/erosions
Lichen planus	Idiopathic	White plaque/erosions/red lesions
Submucous fibrosis	Areca nut	Immobile mucosa
Discoid lupus erythematosus	Idiopathic	White plaque/erosions/red lesions
Chronic candidosis	*Candida albicans*	White or speckled plaque
Syphilitic leukoplakia	Syphilis	White plaque
Atypia in immunocompromised patients	HPV	White or speckled plaque
Dyskeratosis congenita	Genetic	White plaques
Paterson–Kelly syndrome (sideropenic dysphagia; Plummer–Vinson syndrome)	Iron deficiency	Post-cricoid web

Potentially Malignant Oral Lesions

Fig 2 Showing Types And Aetiology Of Oral Cancer.

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III. LEUKOPLAKIA

➢ *Definition*

It is defined as any white patch on mucosa, which cannot be rubbed or scraped off and which cannot be attributed to any other diagnosable disease.

➢ *Who Definition*

It is a whitish patch or plaque that cannot be characterized, clinically or pathologically, as any other disease and which is not associated with any other physical or chemical causative agent except use of tobacco.

The term Leukoplakia originates from two greek words leuko means white and plakia means a patch and the white colour of mucosa results from the thickened surface of the keratin layer.

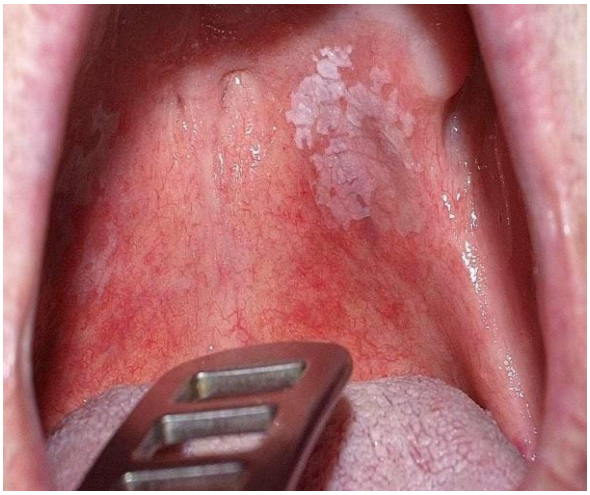

Fig 3 showing Leukoplakia of palate.

❖ *Clinical Aspects*

Pre leukoplakia is defined as a low-grade or very mild reaction of oral mucosa, appearing as a grey or greyish white ,but never completely white area with slightly lobular pattern and with indistinct borders blending into adjacent normal mucosa (Pindborg, et al,1968) Classification

➢ *According to clinical description:*

- *Homogenous*

✓ Flat : It has a smooth surface.
✓ Corrugated: like a beach at ebbing tide.
✓ Pumice like :with pattern of fine fines
✓ Wrinkled: like dry, craked mud surface.

- *Non Homogenous*

✓ Nodular or speckled,- characterized by white specks or nodules on erythematous base .
✓ Verrucous-slow growing papillary proliferations above the mucosal surface that may be heavily keratinized. Extensive lesions of this type is known as oral florid papillomatosis.
✓ Ulcerated- lesions exhibit red area at the Periphery of which white patches are present.

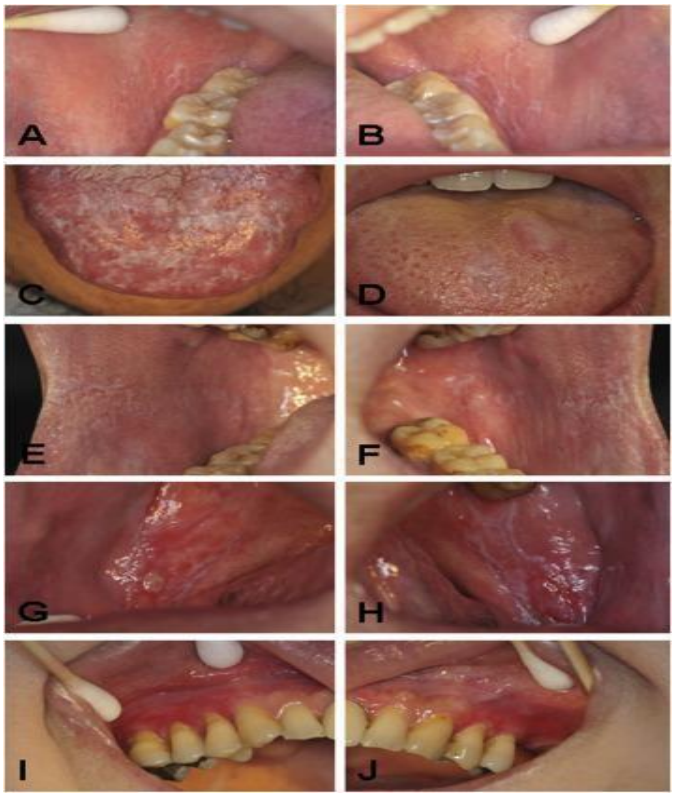

Fig 4 Showing Non Homogeneous Leukoplakia

✓ Erythroleukoplakia- leukoplakiai is present in Association with Erythroplakia.
✓ According to etiology
✓ Tobacco induced
✓ Non tobacco induced

➢ *According to High risk of future development of oral cancer*

● *High Risk Sites*

✓ Floor of mouth
✓ Lateral or ventral surface of tongue
✓ Soft Palace

● *Low Risk Site*

✓ Dorsum of tongue.
✓ Hard palate

● *Intermediate Group*

✓ All other sites or oral mucosa.
✓ According to Histology
- Dysplastic
- Non dysplastic

- According to extent

✓ Localised
✓ Diffused

➢ *Etiopathogenesis*

- *Local Factors Local Factors Include*

✓ Tobacco
✓ Alcohol
✓ Sanguinaria

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- ✓ Chronic irritation
- ✓ Candidiasis
- ✓ Electromagnetic reaction or galvanism

- *Regional Systemic Factors*

- ✓ Syphilis
- ✓ Vitamin deficiency
- ✓ Nutritional deficiency
- ✓ Xerostomia
- ✓ Hormones
- ✓ Drugs
- ✓ Virus
- ✓ Idiopathic

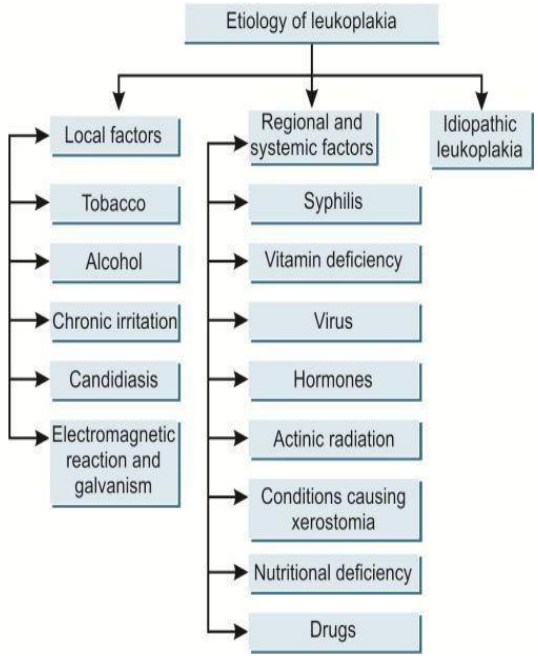

Fig 5 Chart Showing Etiology Of Leukoplakia.

➢ *Clinical Features*

- Sex and age distribution- It occurs more commonly in older age group I e 35 to 45 years and above males are more frequently affected than female, due to direct consequence of tobacco habit.
- Common site- It can occur anywhere on the oral mucosa, buccal mucosa and comissure are more commonly involved, lip lessons are more common in male and tongue lesions are more common in females.
- Extent -The extent of involvement may vary from small well localized irregular patches to diffuse lesions involving a considerable portion of oral mucosa, multiple areas of involvement are not uncommon.
- Colour- Lesson maybe white or a yellowish white but with heavy use of tobacco it may assume brownish colour.
- Symptoms -Some patients may report a feeling of increase thickness of mucosa, those with ulcerated and nodular type may complain of burning sensation, enlarged cervical lymph nodes maybe single occurrence of metastasis.

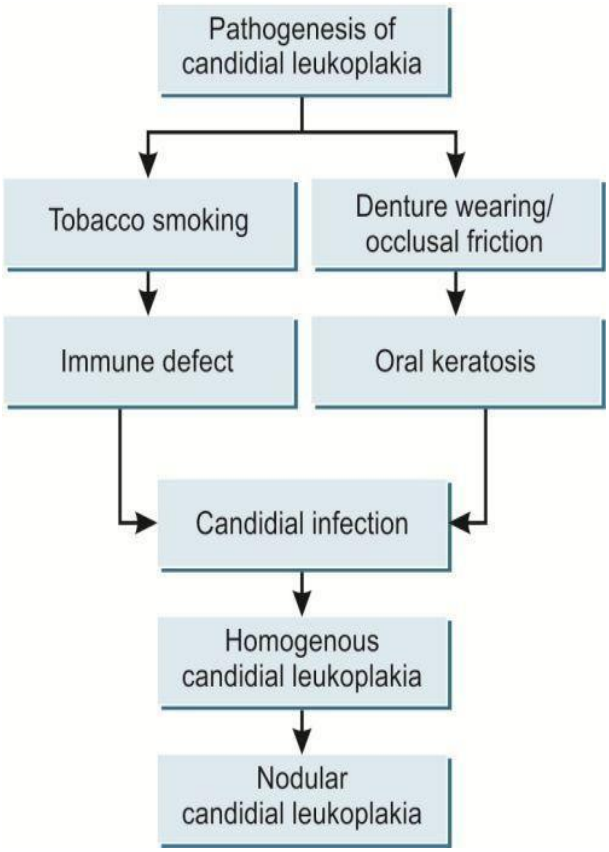

Fig 6 Showing Pathogenesis Of Candida Leukoplakia.

➢ *Sharp Staging*

- Stage 1 -Earliest lesion non palpable faintly translucent white discoloration.
- Stage 2- Localized or diffuse slightly elevated plaque of irregular outline.
- It is opaque white and me have fine granular texture.
- Stage 3-Thickened white lesion showing induration and feasuring.

➢ *Diagnosis*

- *Clinical Diagnosis*

Clinically any white patch with a history of tobacco chewing which cannot be rubbed of is a Diagnostic indicator for leukoplakia.

- *Laboratory Diagnosis*

In biopsy hyperorthokeratosis of epithelium, epithelial dysplasia, liquefaction degeneration, Basal cell hyperplasia can be seen ,scanning electron microscopy will show epithelial dysplastic changes.

Staging Before Treatment(Olep)	No Of Cases	Percentage Before Treatment	Staging After Treatment (C)	No Of Cases	Percentage after treatment
L1P0	20	40.0	L1C1	20	40.0
L2P0	8	16.0	L2C1	0	0
			L1C1	19	38.0
L3P0 or L1L2P1	16	32.0	L3C1	0	0
			L2C1	1	2.0
			L1C1	4	8.0
			L3C2	4	8.0
L3P1	6	12.0	L3C1	0	0
			L2C1	2	4.0
			L1C1	0	0

L1 Size of single or multiple leukoplakias together ≤ 2 cm
L2 Size of single or multiple leukoplakias together 2±4 cm
L3 Size of single or multiple leukoplakias together ≥4 cm
P (pathology)
P0 No epithelial dysplasia
P1 Distinct epithelial dysplasia (includes "mild to moderate" and "moderate to possibly severe" epithelial dysplasia; equals OIN grades 1 and 2)
C1=homogeneous; C2=non-homogeneous

Fig 7 Chart Staging of Leukoplakia.

❖ *Malignant Potential*

It is higher in women i e 6% than men i e 3.9% due to involvement of endogenous factors.

➢ *Differential Diagnosis*

- Lichen planus
- Chemical burn
- White sponge nevus
- Discoid lupus erythematosus
- Psoriasis
- Leukoedema
- Hairy leukoplakia
- Cheek biting lesion
- Electro Galvanic white lesion.

❖ *Management*

➢ *Elimination of Etiological Factors*

- Prohibition of smoking
- Removal of chronic irritant
- Elimination of other etiological factors

➢ *Conservative Treatment*

- Vitamin therapy
- Vitamin A + vitamin E
- 13 cis retinoic acid
- Antioxidant therapy
- Vitamin A palmitate
- Nystatin therapy
- Vitamin B complex
- Antibiotic preparation
- Estrogen

IV. GUIDELINE FOR MANAGEMENT OF LEUKOPLAKIA

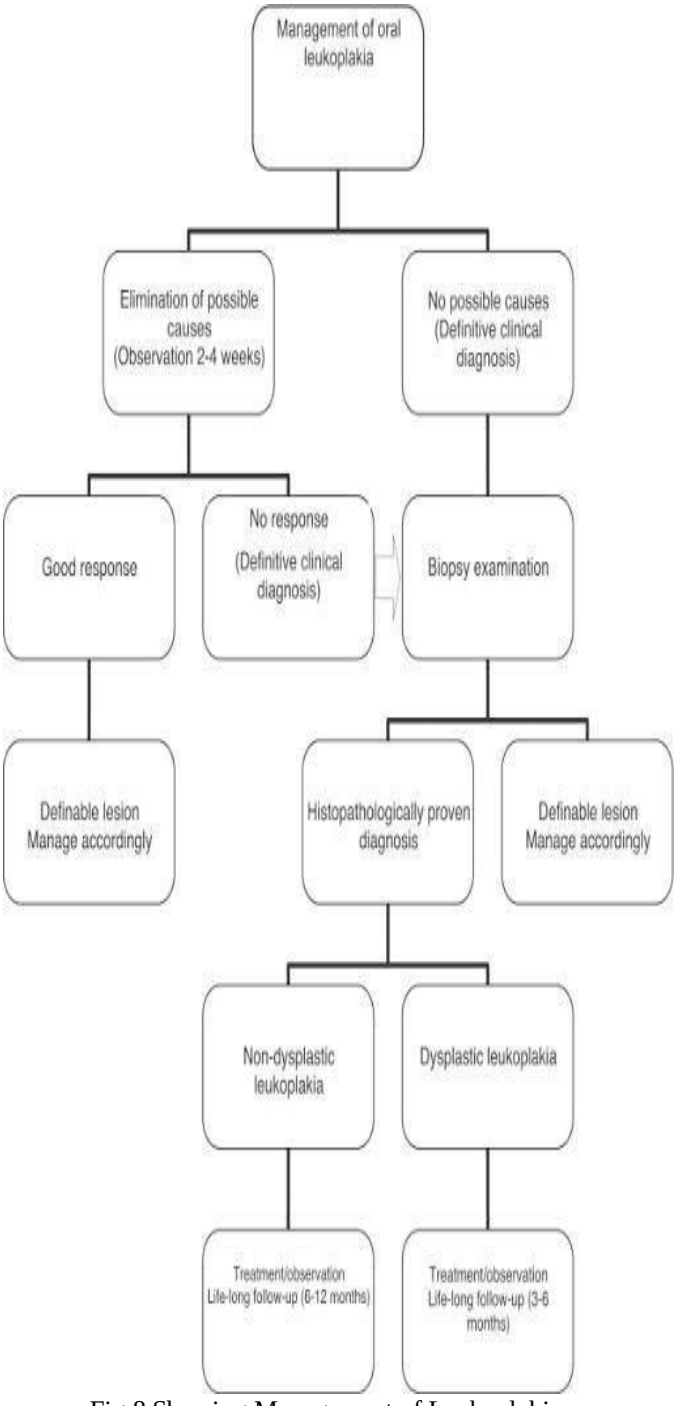

Fig 8 Showing Management of Leukoplakia.

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❖ *Erythroplakia*

It is also called as erythroplasia of Queyrat, erythroplasia is a persistent velvety red patch. Reddish colour results from absence of surface keratin layer and due to presence of connective tissue papillae containing enlarged capillaries projected close to the surface.

❖ *Definition*

It is applied to any area of red and velvet textured mucosa that cannot be identified on the basis of clinical and histopathological examination as being caused by inflammation or any other disease process.

A chronic red mucosal macule which cannot be given any other specific Diagnostic name and cannot be attributed to traumatic, vascular or inflammatory causes

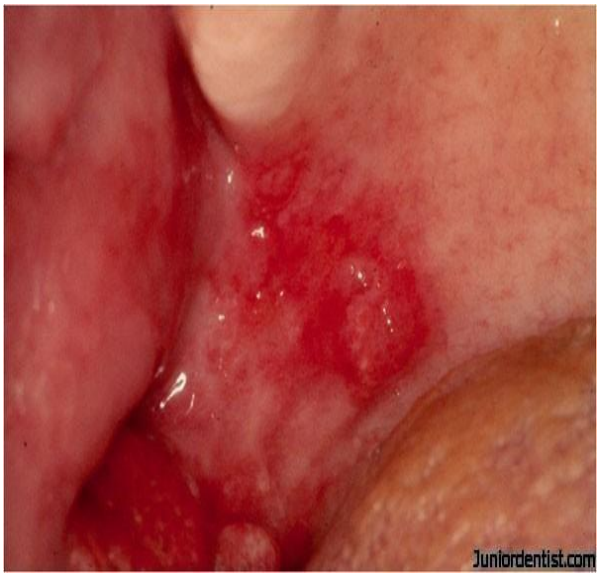

Fig 9 Showing Erythroplakia.

➢ *Classification*

- Homogeneous

✓ These commonly occur on buccal mucosa with a well demarcated margin.

- Erythroleukoplakia

✓ Erythroplakia interspersed with leukoplakia.

✓ Granular or speckled these are elevated lesions.

➢ *Etiology*

- Idiopathic
- Alcohol and smoking
- Candida infection.

➢ *Clinical Features*

- Age and sex- Male prediliction is seen and most common in 6th and 7th decades of life.
- Site- Occurs on all mucosal surface of head and neck area, half of all cases however are found on the vermillion or intra oral surfaces, with the rest being eventually divided between larynx and pharynx.
- Symptoms -As name obviously implies is asymptomatic
- Extent- unlike leukoplakia and erythroplakia is seldom multiple and seldom covers extensive areas of mouth ,also unlike leukoplakia, erythroplakia seldom expand laterally after initial diagnosis ,because most lesions are completely removed or destroyed immediately after formal diagnosis .

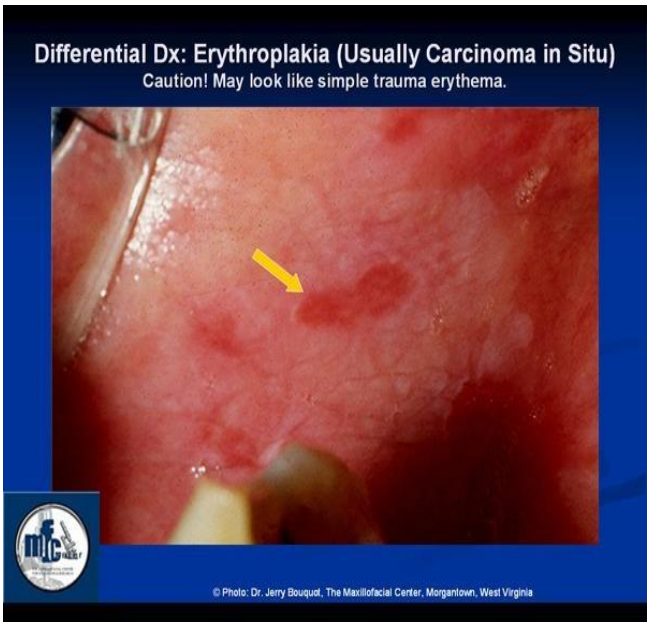

Fig 10 Showing Erythroplakia.

❖ *Diagnosis*

➢ *Clinical Diagnosis*

- Red well demarcated patch with no sign of infection and inflammation give rise to diagnosis of erythroplakia.
- Toluidine blue test -Differentiation of erythroplakia with malignant changes and early squamous cell carcinoma, from benign inflammatory lesions of oral mucosa is enhanced by use of 1% toluidine blue test. Laboratory Diagnosis.
- Biopsy exhibits epithelial changes ranging from mild dysplasia to carcinoma In Situ and even invasive carcinoma.

➢ *Differential Diagnosis*

- Candidiasis
- Denture stock
- Tuberculosis
- Histoplasmosis
- Area of mechanical irritation
- Macular haemangioma
- Telangiectasia
- Traumatic lesion

❖ *Management*

✓ Removal of suspected irritate

✓ Incisional Biopsy

✓ Surgical stripping

✓ Destructive techniques such as laser electro coagulation, cryotherapy have also proven to be effective.

✓ Clinical follow up

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V. CARCINOMA IN SITU

Also called intra epithelial carcinoma .Severe dysplastic changes in a white lesion indicate considerable risk of development of Cancer. The most severe grade of dysplasia merges with the condition known as carcinoma Insitu. It is more common on skin but can also occur on mucous brane.

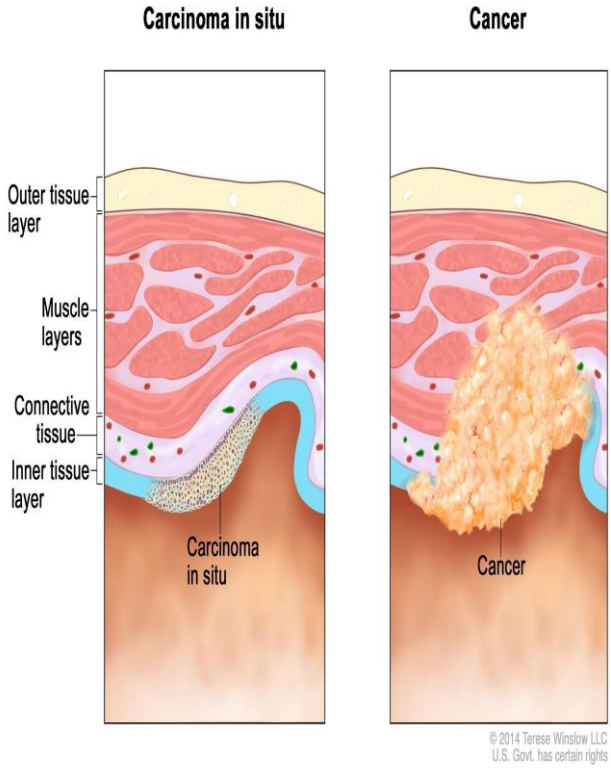

Fig 11 Showing Histological Chances In Carcinoma Insitu And Cancer.

➢ *Clinical Features*

- Age and sex -Male predilection ia seen and occurs more commonly in elderly person.
- Site- Common site are floor of mouth, tongue and lips.
- Appearance- Appearance of lesion maybe like leukoplakia and erythroplakia.

➢ *Diagnosis*

- Clinical diagnosis clinically cannot be differentiated from leukoplakia.
- Laboratory diagnosis

In biopsy keratin may or may not be present on the surface of lesion but if present if more apt to be parakeratin rather than Orthokeratin, loss of orientation of cell and loss of polarity .Sharp line of division between normal and altered epithelium extending from surface down to connective tissue rather than blending of epithelium and increase in nuclear cytoplasmic ratio nuclear hyperchromatism are sometimes seen.

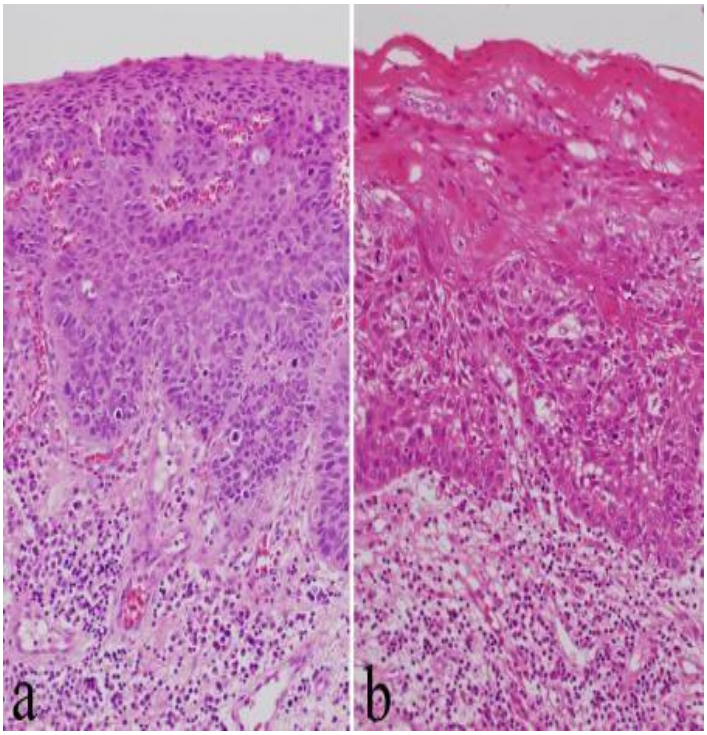

Fig 12 Histological Image Showing Carcinoma Insitu.

➢ *Management*

- Surgical removal: Lesions may be surgically excised, cauterized and even exposed to solid carbon dioxide.

VI. PREMALIGNANT CONDITION LICHEN PLANUS

The term lichen planus is derived since the lesion looks like lichen on rocks and planus stands for flat, various mucosal surfaces may be involved either independently or concurrently with cutaneous involvement or serially.

❖ *Definition*

Lichen planus is a common inflammatory disease of skin presenting with characteristic violaceous, polygonal, pruritic papules. The disease may also affect the mucosa, hair and nails.

It is a relatively common dermatological disorder occurring on skin and oral mucous membrane refers to the Lace -like pattern produced by symbiotic algae and fungal colonies on the surface of rocks in nature. Prevalence of lichen planus in general population is about 0.9% to 1.2% and prevalence of oral lichen is reported in between 0.1% and 2.2%

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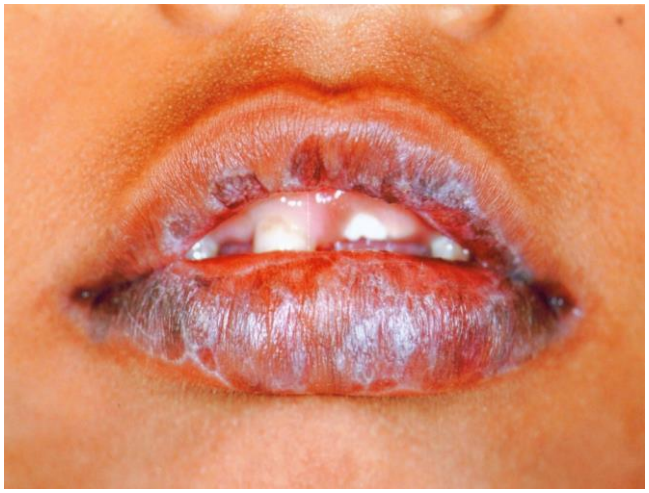

Fig 13 Showing Lichen Planus Of Lip.

➢ *Etiology*

- Cell mediated immune response
- Auto immunity
- Immune deficiency
- Genetic factors
- Infection
- Psychogenic factor
- Habit.

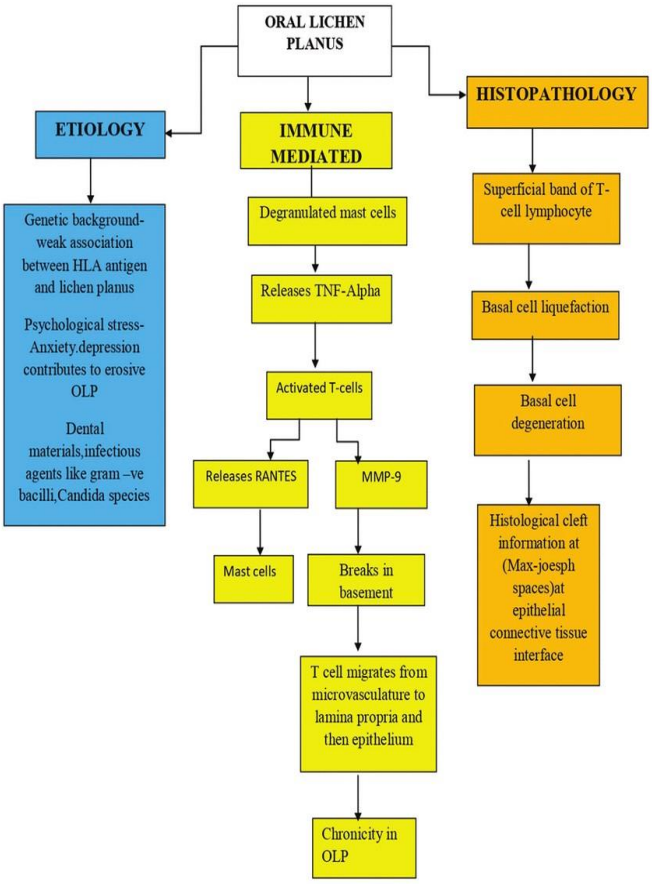

Fig 14 Showing Etiology And Management Of Lichen Planus.

➢ *Types*

- ✓ Reticular
- ✓ Papular
- ✓ Atrophic
- ✓ Classical
- ✓ Plaque
- ✓ Erythematous
- ✓ Ulcerative
- ✓ Hypertrophic
- ✓ Erosive
- ✓ bullous
- ✓ Hypertrophied
- ✓ Annular
- ✓ Actinic
- ✓ follicular
- ✓ linear

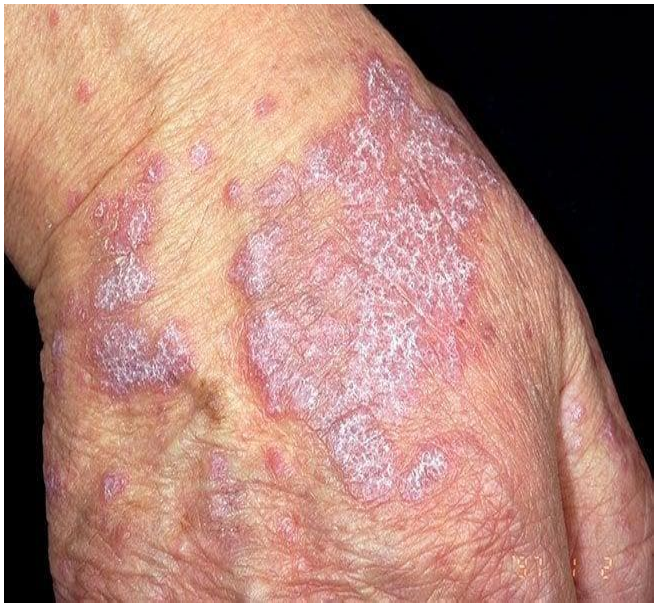

Fig 15 Showing Lichen Planus Involving Skin.

➢ *Clinical Features*

- Age and sex- It occurs in adulthood with age range for males is 35 to 44 years and females is 45 to 54 years, it has more female prediction
- Oral and other mucous membrane symptoms -chief complaint is usually of intense pruritus, itching associated with lichen planus usually provokes rubbing of lesion, rather than scratching.
- Signs- Lesions have characteristic violet hue. They are flat topped Shiny polygonal papules and plaques.

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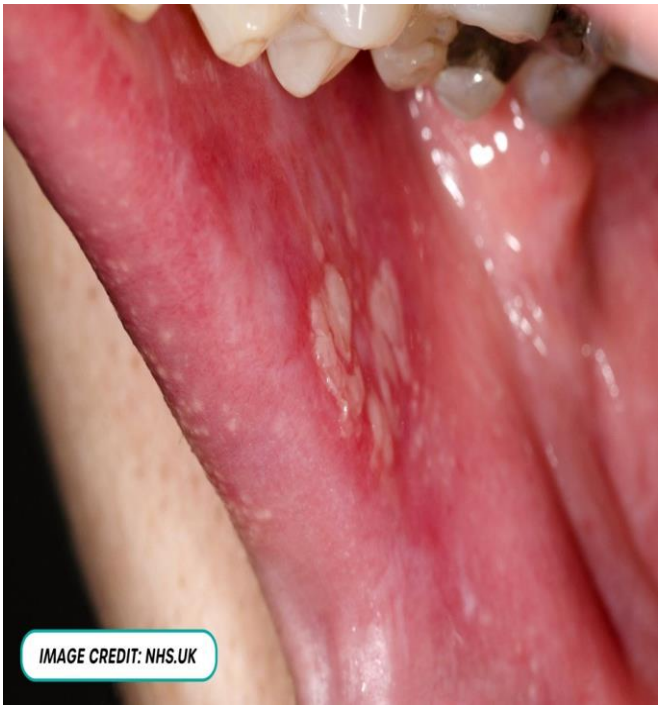

Fig 16 Showing Lichen Planus of Buccal Mucosa.

VII. ORAL LICHEN PLANUS

- Site- Common sites are buccal mucosa (84%)and to lesser extent tongue, lips, gingiva, floor of mouth and palate
- Symptoms- Patient may report with burning sensation of oral mucosa
- Appearance -oral lesion is characterized by radiating white or grey velvety thread like papules in a linear, angular or retiform arrangement forming typical lacy reticular patterns, rings and streaks over buccal mucosa and to a lesser extent on lip, tongue and palate.
- Malignant potential- The incidence of malignant transformation ranges from 0.4% to 12.3% .In India the incidence of malignant transformation is 0.4% .Carcinoma development is more common in women than in men. Atrophic, erosive and ulcerative lesion showing Erythroplakia components and tobacco are indicated to be more cancer prone.

❖ *Clinical Scoring System For Oral Lichen Planus*

- 0= No lesions.
- 1= White striae only.
- 2= White striae and erosions less than 1 cm square.
- 3=white striae and ulceration more than 1 cm square.
- 4=white striae and ulceration less than 1 cm square.

➢ *Diagnosis*

- *Clinical Diagnosis*

The interlacing white striae appearing bilaterally presence of Wickham striae and koebner phenomenon is also diagnostic.

- *Laboratory Diagnosis*

There is hyper orthokeratosis, hyperparakeratosis, acanthosis with intercellular oedema of spinous cells. Biopsy also shows civatte bodies in spinous and basal cell layers and lamina propria saw tooth appearance of rete pegs is seen.

Immuno fluorescent study- Positive IgA and IgM and IgG Antisera.

- *Differential Diagnosis*

✓ leukoplakia
✓ candidiasis
✓ Pemphigus
✓ Lupus Erythematosus
✓ Drug induced lesions
✓ Ectopic Geographic tongue
✓ Cheek biting
✓ Lichenoid drug reaction

- *Management*

✓ Removal of a cause
✓ Steroids
✓ Steroid spray
✓ Steroid coating in soft custom tray
✓ Topical delivery regimen
✓ Topical application of fluocinolone acetonide
✓ combination of prednisolone and levamisole
✓ Topical application of antifungal agent
✓ Vitamin A therapy
✓ Cyclosporin
✓ surgical therapy and psychotherapy
✓ Dapsone therapy
✓ PUVA therapy

VIII. ORAL SUBMUCOUS FIBROSIS

It Is A Chronic High Risk Precancerous Condition, Prevalent In Days Of Sushruta.

❖ *Definition*

An Insidious, chronic disease affecting any part of the oral cavity and sometimes pharynx. Although occasionally preceded by and or associated with a vesicle formation. It is always associated with juxta epithelial inflammatory reaction followed by fibro elastic changes of lamina propria with epithelial atrophy leading to stiffness of oral mucosa and causing trismus and inability to eat.

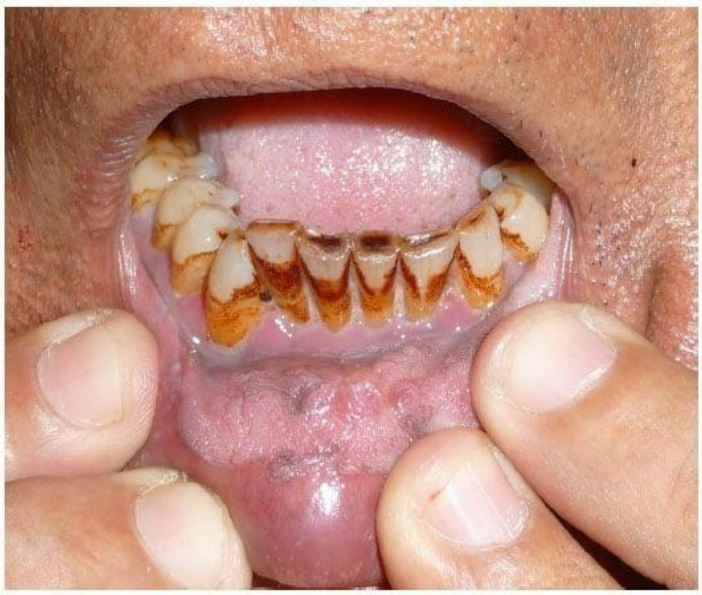

Fig 17 Showing Decreased Mouth Opening In Osmf.

❖ *Epidemiology*

OSMF is very common in India and in Indian subcontinent and other Asian people ,the prevalence rate of oral Fibrosis in India, Burma ,South Africa ranges from 0 to 1.2%, in India overall incidence is 0.2 0.5% .Its incidence is high in southern parts of India, where the incidence of oral cancer is also high.

IX. ETIOPATHOGENESIS

- Chillies - Capsaicin in chillies act as local irritants.
- Tobacco
- Lime
- Betel nut
- Nutritional deficiency
- Defective iron metabolism
- Bacterial infection
- Collagen and disorders
- Immunological disorders
- Altered salivary composition
- genetic susceptibility

Fig 18 Showing Vertical Bands On Buccal Mucosa In OSMF Case.

➢ *Clinical Features*

- Age and sex distribution- It affects both the sexes. The age group varies although majority of patients are between 20 and 40 years of age.
- Site Distribution- The most frequent location of osmf retro molar area, it also commonly involves soft palate ,palatal fauces, tongue and labial mucosa, sometimes it involves floor of mouth and Gingiva.
- Prodromal symptoms- The onset of condition is insidious and is often of 2 to 5 years of duration the most common initial symptom is burning sensation of oral mucosa, aggravated by spicy food followed by either hyper salivation or dryness of mouth. Vesiculation, ulceration pigmentation, recurrent stomatitis and defective sensation have also been indicated as early symptoms.
- Late symptoms – Trismas, difficulty in swallowing, difficulty protrusion of tongue, referred pain, blanching of mucosa, fibrous band formation
- Soft palate and uvula- Involvement of soft palate is marked by fibrotic changes, uvula when involved is shrunken and in extreme cases it becomes bud like or hockey stick appearance.

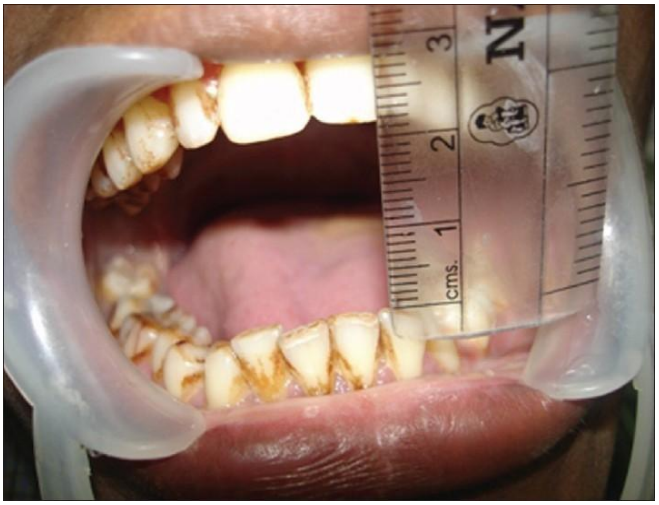

Fig 19 Showing Decreased Mouth Opening In OSMF Case.

➢ *Clinical Stages Of Oral Submucous Fibrosis*

- Stage of stomatitis and vesiculation.
- Stage of Fibrosis.
- Stage of sequelae and complication.

❖ *Diagnosis*

➢ *Clinical Diagnosis*

- Clinically reduced mouth opening with palpable fibrous bands is enough to make a diagnosis.

➢ *Laboratory Diagnosis*

- Oral epithelium is markedly atrophic which exhibits intracellular edema, signet cells and epithelial atypia. The inflammatory cells are mostly mononuclear; eosinophils and occasional plasma cells may be seen.

➢ *Malignant Potential*

- The carcinoma patients exhibiting osmf have a frequency which exceed 1.2% of submucous Fibrosis in a General population.

Grading/ Staging	Maximium Interincisal mouth opening
Stage I	Maximum interincisal mouth opening up to or >35 mm
Stage II	Maximum interincisal mouth opening between 25 and 35 mm
Stage III	Maximum interincisal mouth opening between 15 and 25 mm
Stage IV	Maximum interincisal mouth opening 5 and 15mm
Stage V	Maximum interincisal mouth opening <5 or nil

Fig 20 Showing Correlation of Mouth Opening With Grade of OSMF.

❖ *Management*

➢ Restriction of habit and behavioural therapy
➢ Medicinal therapy
➢ Supportive treatment
➢ Vitamin rich diet
➢ Iodine B- Complex preparation
➢ Steroids
➢ Local Hydrocortisone injection
➢ Systemic therapy with Hydrocortisone 25 mg tablets in doses of 100 mg per day .
➢ Placental extract
➢ Hyaluronidase
➢ Lycopene (Tab lycopene , OD for 3 months)
➢ Vitamin E therapy
➢ Other therapies include vasodilator injection and injection of Gamma interference, laser therapy, cryosurgery ,oral
➢ Physiotherapy and diathermy.

X. CONCLUSION

Prompt diagnosis of Oral premalignant lesion itself reduces the chance of conversion or progression of lesion into malignant lesion by more than fifty percent further more immediate identification of the cause and correction of the cause can further aid in control of progression of the lesion into malignant lesion.

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