



## Review

# Potentially malignant lesion – oral leukoplakia

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**Leukoplakia was considered as one of the premalignant lesion but now it was included under potentially malignant disorder. It is mainly associated with chewing and smoking tobacco habits. It has a risk of malignant transformation if the risk factors are not eliminated. In this review we discussed the classification, clinical features, malignant potential and various treatment modalities of oral Leukoplakia.**

**Keywords:** Leukoplakia, Homogenous, Speckled.

## INTRODUCTION

Oral premalignancy is considered as Intermediate stage. There are two types; they are premalignant lesions and premalignant conditions. Premalignant Lesions are defined as 'A localized area of morphologically altered tissue in which cancer is more likely to occur'. Example is Leukoplakia. Premalignant Conditions are defined as 'A generalized state for predisposition of malignancy'. Example is Oral submucous fibrosis. But recently WHO considering both premalignant lesions and conditions under a single group of disorders that is "Potentially Malignant Disorders" (Warnakulasuriya et al., 2007).: (leuko→white; plakia→patch) Leukoplakia is considered as one of the most common premalignant lesion or Potentially Malignant Disorder (van der Waal et al, 1997). According to WHO, it is defined as white lesions that cannot be characterized as being a result of any other specific disease of the oral mucosa (Seo et al., 2010). Risk factors include, tobacco- chewing and smoking, cigar / cigarette / beedi / pipe, alcohol, chronic trauma, candidiasis, galvanism, syphilis, vit deficiency, infections, bacterial, fungal, viral, ultra violet light, hormonal disturbances. (Haris CM)

There was a study conducted in china which reveals the prevalence in smokers was 23.43% and in non-smokers 1.93%. Among three variants of smoking, the traditional Hanyan pipe smoking carried the highest risk for the development of Oral Leukoplakia followed by cigarette and Shuiyan water pipe smoking. The rate of alcohol drinkers with OL was 54.50% and 22.21% in individuals without Oral Leukoplakia (Zhang et al., 2010).

## Classification

There are different clinical types in oral leukoplakias. They are as follows (Bailoor and Nagesh, 2005),

- Speckled leukoplakia and non speckled leukoplakia
- Homogenous, Ulcerative, Speckled
- Reversible / irreversible

It is also clinically classified in to six types,

- Thin or mild leukoplakia
- Thick or homogenous Leukoplakia (Figure 1)
- Nodular / granular leukoplakia
- Verrucous Leukoplakia (Figure 3)



Figure 1. Homogenous leukoplakia



Figure 2. Speckled leukoplakia



Figure 3. Proliferative verrucous Leukoplakia

- Proliferative verrucous leukoplakia
- Speckled leukoplakia (Figure 2)

### Clinical features

- Age: It occur in persons in their fifth to seventh decade of life. Approximately 80% of patients are older than 40 years.

- sex: Comparitively more in males with a male-to-female ratio of 2:1 (Cawson and Odell., 1998).

- site: Common site in the oral cavity are Lip, Vestibule, BM, Gingiva, and Tongue. More commonly in beedi smokers it presents in Anterior buccal mucosa and patients with chewing habits it is seen on the Posterior buccal mucosa. Individuals with oral leukoplakia are not symptomatic (Cawson and Odell, 1998)

- colour: clinically it appears gray, white or yellowish white
- thickness: it may be thin or thick
- appearance: it appears Fissure, Granular, Patch, Plaque, Verruciform or Erythematous.
- stages: Clinically there are three stages are described. In early stage lesion is nonpalpable, faintly translucent, with white discoloration. Next stage localized or diffuse, slightly elevated plaques with an irregular outline. These lesions are opaque white with fine, granular texture. Later in some instances, the lesions progress to thickened, white lesions, showing induration, fissuring, and ulcer formation.
- size: Varies from few millimeters to few centimeters
- shape is Irregular
- nonscrapable

Diagnosis: This type of lesions is diagnosed depending on clinical history and examination however the biopsy is necessary to confirm the diagnosis before starting any treatment plan. Tolluidine blue and vizelite are used to select the biopsy site. In case of small lesions excisional biopsy is indicated and in large lesions incisional biopsy including the adjacent normal tissue is needed.

Histopathology: The main histopathological changes are (Liu et al, 2010),

- Keratinization of the epithelium (Hyperortho keratinization or Hyperpara keratinization)
- Increased thickness of epithelium → Acanthosis
- Basement membrane becomes thin
- Inflammatory component in Connective Tissue
- Change in cellular layer

- Increased nuclear cytoplasmic ratio
- Hyperchromatic nuclei
- Nuclear hyperplasia
- Abnormal mitotic figures
- Increased mitosis
- Pleomorphic nuclei
- Basillar hyperplasia
- Drop shaped rete pegs (Figure 7)
- Loss of polarity

L C P STAGING: (L → size C → Clinical P → Pathological) (Bailoor and Nagesh, 2005).

Resently the Leukoplakia was graded according to size, clinical and pathological stages it is known as LCP Staging.

- L x → size not specified
- L 1 → less than 2cm, single/ multiple
- L 2 → 2 to 4 cm, single/ multiple
- L 3 → more than 4cm, single/ multiple
- > C 1 → Homogenous
- > C 2 → Non homogenous
- ✓ P x → Not specified
- ✓ P 0 → No epithelial dysplasia
- ✓ P 1 → distinct epithelial dysplasia

	Pathological	Clinical
STAGE 1	L1 P0	L1 C1
STAGE 2	L2 P0	L2 C1
STAGE 3	L3 P0	L3 C1
STAGE 4	L3 P1	L3 C2

## Malignant potential

Oral leukoplakia is considered to be one of the common potentially malignant lesions of the oral mucosa, with a malignant transformation rate in various studies and locations that range from 0.6 to 20%.

- It is more in females (6%) than male (3.9%)
- More in patients with chewing tobacco habit.
- Oral Leukoplakia among non smokers have an increased rate of malignant transformation.
- Epithelial Dysplasia: Moderate and severe dysplastic lesions had a higher risk of malignant transformation than Oral Leukoplakia with or without epithelial dysplasia (Figure 4,5,6).
- Site: lesions in the floor of mouth, ventrolateral tongue and soft palate have a high risk of malignant transformation. Buccal Mucosa and commissures up to 1.8%, Lip and tongue 16% to 38.8%.
- Five clinical criteria demonstrate a particularly high risk of malignant change. They are (Haris CM)
- The verrucous type is considered high risk.
- Erosion or ulceration within the lesion is highly suggestive of malignancy.
- The presence of a nodule indicates malignant potential.
- A lesion that is hard in its periphery is predictive of malignant change.
- Oral Leukoplakia of the anterior floor of the mouth and undersurface of the tongue is strongly associated with malignant potential. (Einhorn and Wersall, 1967; Haya-Fernández et al., 2004; Napier and Speight, 2008; Zhang et al., 2001; van der Waal, 2009; Reibel, 2003)

## Differential diagnosis

Differential diagnosis considered are (Haris CM)

- Lichen planus
- Chemical burn
- Leukoedema
- White sponge nevus
- Discoid lupus erythematosus
- Syphilitic mucous patch
- Veruca vulgaris
- Cheek bite

## Guidelines for treatment

We have to follow the following guidelines during treatment of Leukoplakia. They are, (Jeong et al., 2011)

- Elimination of risk factors like alcohol and Smoking and advise Nicotine substitutes. Enameloplasty in case of any broken sharp tooth and replace faulty metal restoration.
- Biopsy is a must before any treatment plans
- Should consider Conservative and surgical treatment, if the lesion do not heal in 2 to 3 weeks after elimination of risk factor.
- High risk lesion requires excision of the lesion with follow-up

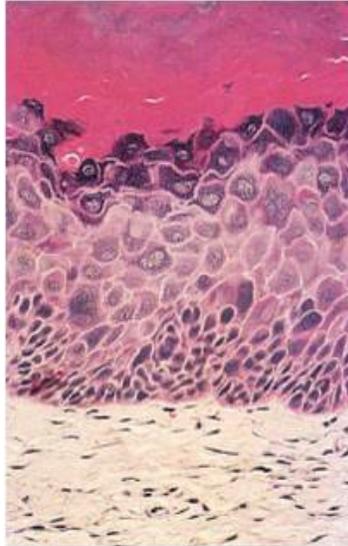


Figure 4. Mild dysplasia



Figure 5. Moderate dysplasia

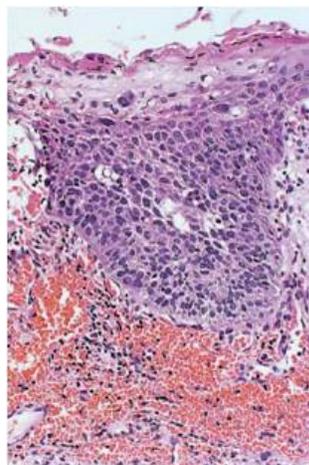
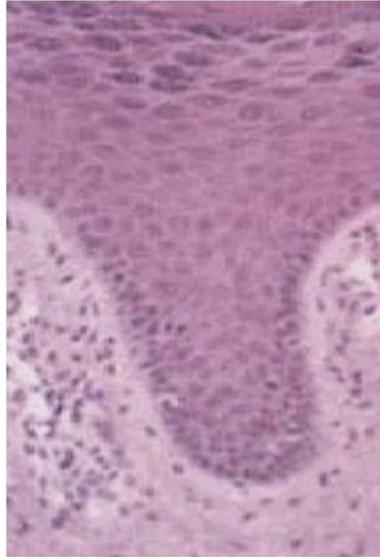


Figure 6. Severe dysplasia



**Figure 7.** Drop shaped rete pegs

- Reexamination of the patient every six months.
- Re-biopsy is required after 5 to 6 months to rule out any recurrence and dysplasia.

Nicotine substitutes: There are few nicotine substitutes available such as Nicotine PATCH (Nicotinell and Novartis -Transdermal patches), Nicotine chewing gums (Nicorette), Nicotine spray and Nicotine inhaler which can be used to stop the habits.

### **Conservative treatment**

The conservative treatment includes (Lippman et al., 1993; Garewal et al., 1999; Naidu, 2003; Azulay and Azulay, 1999).

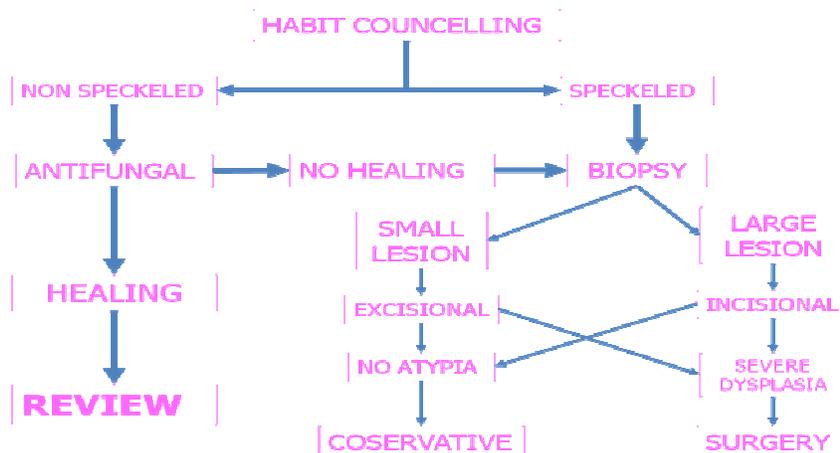
- Vitamin therapy (Vitamin C, Vitamin E, 13-cis – Retinoic acid and Vitamin B Complex) - Current recommended daily allowance for ascorbic acid ranges between 100–120 mg/per day for adults, daily intake of at least 140 mg/day is required for smokers because they usually present a reduction of the L-Ascorbic acid concentration in serum leukocytes. Dosage of vitamin E was 800 IU/day from 6 to 9months. In the systemic use with dosage of 300.000 IU of retinoic acid (Vitamin A), a clinical resolution of the 50% has been demonstrated. In topical use with dosage range from 0.05% to 1% a

clinical resolution from 10% to 27% has been obtained - Beeta-carotene and lycopene - Dosage of beta-carotene is 20 to 90mg/day with time periods from 3 to 12 months and lycopene was 4 to 8 mg/day.

- Antioxidants
- Nystatin therapy to prevent any secondary fungal infections.

### **Surgical treatment**

- CONVENTIONAL SURGERY – to remove the lesions surgically.
- CRYOSURGERY - Tissue exposed to extreme cold to produce irreversible cell damage. Cell death occurs at – 20 degree centigrade. Cryoprobe refrigerated by liquid nitrogen (Lin et al., 2011).
- ELECTROCAUTERY - Tissue distruction by high voltage current. Main advantage is less bleeding. And disadvantages are Foul odor, Hazarda of explosion, Under LA or GA, Slow healing, Pain and Scar (Jeong et al., 2011).
- CO2 LASER - Commonly used in case of leukoplakia. CO2 Lasers contain CO2, nitrogen and helium gases. Cutting large surface area. Nd:YAG lasers also used (Chu et al., 1988).



Treatment flow chart

## CONCLUSION

Oral Leukoplakia is one of the potentially malignant disorders. This can be diagnosed with the clinical history and examination. Biopsy of such lesions is important before starting any treatment because there are many white lesions which look like Leukoplakia so rule out such lesions are very important.

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