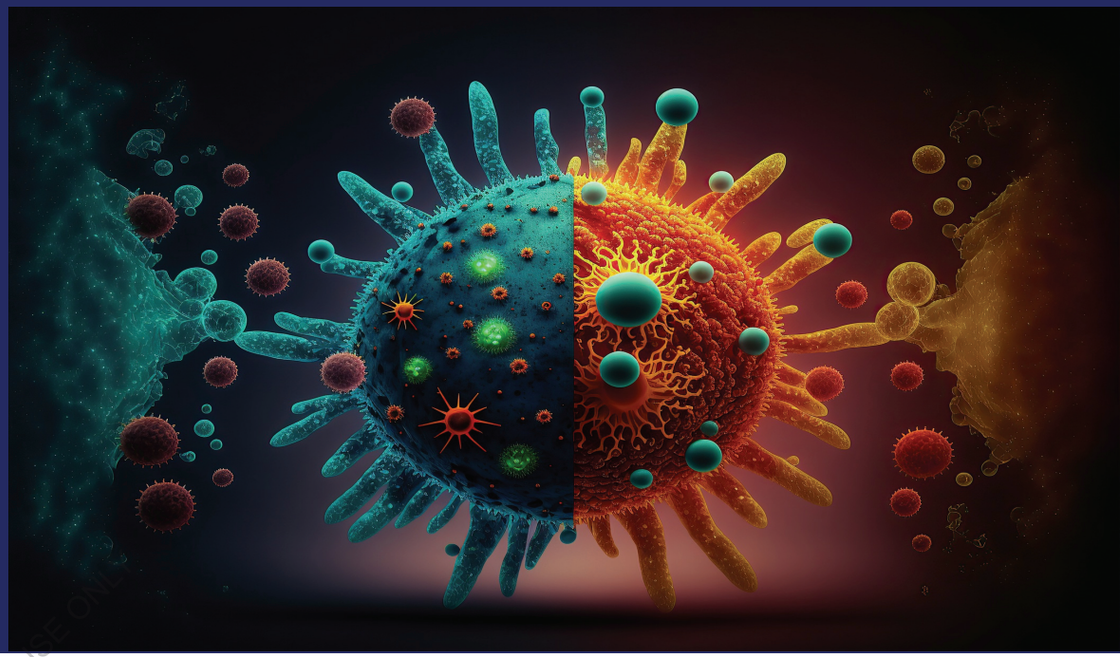
Potentially Malignant Oral Disorders (PMODS) represent a group of conditions of the oral mucosa that carry an increased risk of transformation into malignancy, most commonly oral squamous cell carcinoma. These lesions, including leukoplakia, erythroplakia, oral lichen planus, oral submucous fibrosis, and actinic cheilitis, often exhibit clinical and histopathological features that serve as early indicators of carcinogenic potential. Early detection and intervention are critical, as the progression to malignancy can be mitigated with appropriate clinical surveillance and management. This abstract provides an overview of the aetiology, risk factors, diagnostic approaches, and current therapeutic strategies associated with PMODs. Emphasis is placed on the role of biopsy and histopathological grading of epithelial dysplasia, as well as lifestyle modifications, such as tobacco and alcohol cessation, which are pivotal in reducing disease progression. A multidisciplinary approach, involving dental professionals, pathologists, and oncologists, is essential for optimal patient outcomes.



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Introduction[1]

Cancer is the second most common cause of death after heart diseases in developed countries, and the third leading cause of mortality following heart and diarrheal diseases in developing countries. Cancer of the oral cavity accounts for approximately 3% of all malignancies and found in 270,000 patients annually worldwide. It is the 12th most common cancer in women and M,the 6th in men. Almost 4–8.1% of females and 8–8.5% of males may develop oral cancer in their lives. Oral squamous cell carcinoma (OSCC) comprises 92–95% of all oral cancers.

The clinical concept of malignant transformation in oral mucosa has been proposed for more than 100 years. **Sir James Paget** first described malignant transformation of an oral lesion into tongue carcinoma in 1870. [2]

Schwimmer also reported the same finding in 1877. Several years later, the term "potentially malignant disorders" was defined by World Health Organization (WHO) as the risk of malignancy being present in a lesion or condition either during the time of initial diagnosis or at a future date.[3]

Although little information is available regarding the real prevalence of PMDs in the general population, a commonly accepted prevalence of 1–5% has been reported. Average age of patients with PMDs is 50–69 years, which is 5 years before occurrence of oral cancer. Unfortunately, in recent years 5% of PMDs has been observed in persons under 30. Premalignant disorders are usually found on the buccal mucosa, followed by gingivae, tongue and floor of the mouth.[4]

Etiology:

No single factor has been identified as the causative factor for potentially malignant disorders. But a number of high risk factors has been put forwarded which has greater than normal risk of malignancy at a future date.[4]

A. Extrinsic Factors

1. Tobacco in any form (smoking or chewing) is the single most major extrinsic cause (people who smoke more than 80 cigarettes per day have 17-23 times greater risk).
2. Alcohol regardless of beverage type and drinking pattern – synergistic action along with tobacco (risk of smokers who are also heavy drinkers is 6-15 times than that of abstainers).
3. Virus infection – HPV, EBV, HBV, HIV, HSV.
4. Bacterial infection – treponema pallidum.
5. Fungal infection – candidiasis.
6. Electro-galvanic reaction between unlike restorative metals.
7. Ultraviolet radiation from sunlight – associated with lip lesions.
8. Chronic inflammation or irritation from sharp teeth or chronic cheek-bite (tissue modifiers rather than true carcinogens).

B. Intrinsic Factors

1. Genetic (5% are hereditary).
2. Immunosuppression – organ transplant, HIV.
3. Malnutrition – iron (anemia), vitamin A, B, C deficiency.

Epidemiology

Anyone can develop cancer, however the risk of being diagnosed with cancer increases with age. Longer people live the more likely it is for a sporadic mutation to occur in their genome, leading to genetic alterations that may lead to a malignant phenotype. Among the genders, PMDs have traditionally shown a predilection for males. But recent studies show a 1:1 male to female ratio. This could be due to the increased habitual use of tobacco and alcohol among women.

Average age of population affected with PMDs is 50-69yrs, occurring about five years earlier than oral cancer. However recent studies show that 15% of PMDs affect the younger age group of 30 years. This may be due to the fact that various extrinsic and intrinsic etiological factors are now more prelevant in today's younger population.

Most common sites for PMDs in India are buccal mucosa followed by tongue, palate and floor of the mouth. Location of PMDs differs from distribution of OSCC, for which the tongue, alveolar ridge and floor of mouth are the most common sites.[5]

WHO also classified PMDs into two sub groups as follows:

Precancerous lesion: A precancerous lesion is a morphologically altered tissue in which oral cancer is more likely to occur than in its apparently normal counterpart, for example, Leukoplakia, Erythroplakia etc.

Precancerous condition: A precancerous condition is a generalized state associated with a significantly increased risk of cancer, for example, submucous fibrosis, Lichen planus etc. However, in a World Health Organization (WHO) Workshop, held in 2005, it was decided to use the term "potentially malignant disorders (PMD)" as it conveys that not all disorders described under this term may transform into cancer.

The following were identified as Potentially Malignant Disorders by the World Health Organisation′s working group on Oral Cancer.

- Leukoplakia
- Erythroplakia
- Palatal Lesion Of Reverse Cigar Smoking
- Oral Lichen Planus
- Oral Submucous Fibrosis (SMF)
- Discoid Lupus erythematos

Leukoplakia

WHO in 1994 defined leukoplakia as “a predominantly white lesion of oral mucosa that cannot be characterized as any other definable lesion clinically or pathologically, often associated with tobacco products, some of which will transform into cancer”. [6]

The WHO (1997) described leukoplakia as “a predominantly white lesion of the oral mucosa that cannot be characterized as any other definable lesion.”[7]

Later in 2005 WHO defined it as “a white plaque of questionable risk having excluded other known diseases or disorders that carry no increased risk of cancer”. Multiple studies over the years have shown a malignant transformation rate of 3.6-17.5%, while few Indian studies have shown a transformation rate as low as 0.3-0.5%.

Neville BW, Day TA (2002) quoted definition of Leukoplakia according to WHO (1978) that Leukoplakia is “a white patch or plaque that cannot be characterized clinically or pathologically as any other disease.”[8]

Rajendran R (2004) defined Leukoplakia as “a predominantly white lesion of the oral mucosa that cannot be characterized as any other definable lesion; some oral Leukoplakia will transform into cancer.”[9]

Warnakulasuriya et al. (2007) defined this lesion as “a white plaque with an increasing questionable oral cancer risk after excluding other known diseases and disorders that do not increase the risk.”[10]

CLASSIFICATION:[11]

By Pindborg (1974)

Homogenous- Flate

Corrugated

Pumice-like

Wrinkled

Non- homogenous- Verrucous

Proliferative and verrucous

Nodular

Erthroleukoplakia

Banoczy (clinical classification-1977) [12]

Leukoplakia simplex-56%

Leukoplakia verrucose-27%

Leukoplakia erosive-17%

Faske (Histopathological classification-1958) [13]

Group1- showing epithelial hyperplasia-15%

Group2- superficial keratosis-31%

Group3- combination of hyperplasia and keratosis-18%

Group4- epithelial dysplasia-36%

Burkhardt and Seifert (Histopathological classification-1977)

Leukoplakia flat-70%

Leukoplakia papillary-endophytic -22%

Leukoplakia papillomatous-exophytic -8%

Hornstein (Etiological classification- 1977)

Leukoplakia in broad sense (Hereditary and endogenous)

Leukoplakia in narrow sense (Exogenous- irritative and precancerous leukoplakia).

MODIFIED CLASSIFICATION AND STAGING SYSTEM FOR ORAL LEUKOPLAKIA [14]

L (size of the leukoplakia)

- Lx: Size not specified.
- L1: Single or multiple lesions together <2 cm.
- L2: Single or multiple lesions together 2-4 cm.
- L3: Single or multiple lesions together >4 cm.

P (pathology)

- Px: Epithelial dysplasia not specified.
- P0: No epithelial dysplasia.
- P1: Mild to moderate epithelial dysplasia.
- P2: Severe epithelial dysplasia.

OL-staging system

- Stage I: L1 P0.
- Stage II: L2 P0.
- Stage III: L3 P0 or L1/ L2 P1.
- Stage IV: L3 P1 or any L P2.

ETIOLOGY:

Poate TWJ, Warnakulasuriya S (2006) in a study, examined the risk factor among patients attending a dysplasia clinic in South London to evaluate the outcomes for the intervention of tobacco habits in this population. They found that the major risk factors for oral epithelial dysplasia are smoking and excess alcohol consumption and these risk are shared by cases with oral squamous cell carcinoma. If untreated, 10-15% of leukoplakia will develop in to cancer over a period of time.[15]

Usta U, Berberoglu U, Helvaci E, Altaner S, Sut N, Ozdemir C (2008) into their study found that tobacco smoking and tobacco chewing are the known risk factor for oral leukoplakia. However, dysplasia is not necessarily limited to Leukoplakia. It was found that 4.5% of clinicaliy benign-appearing lesion have dysplastic or carcinomatous features.[16]

Pimenta FJ, Cordeiro GT, Pimenta LGGS, Viana MB, Lopes J, Gomez MV et al. (2008) observed that the development of oral leukoplakia is strongly associated with the exogenous exposure to carcinogens, mainly smoking, chewing tobacco and betal nut. Of these, tobacco use is the most important etiology factor and is present in 80% of all cases. Oral Leukoplakia may show histologically the presence of dysplasia which may undergo malignant transformation to Oral Squamous Cell Carcinoma.[17]

Brzak et al. conducted study including 12,508 patients between 1998 and 2007 and found the highest frequency of leukoplakia in smokers.[18]

CLINICAL FEATURES:.

Leukoplakia usually affects persons older than 40 years of age. Prevalence increases rapidly with age, especially for males and as many as 8% of men older than 70 years of age reportedly are affected.

Leukoplakia may be found in almost any location in the oral cavity, it is more prevalent of the buccal mucosa, gingiva and vermilion border of the lip (actinic cheilitis). The lips and palate, maxillary mucosa, retromolar area, floor of the mouth and tongue are less likely sites. Two latter sites account for 93% of leukoplakia with dysplasia or carcinomatous change.

Sex distribution is variable. Men are more affected in some countries, while this is not the case in the western world. Less than 1% of men below the age of 30 have leukoplakia. The male to female ratio is reported to be about 3:1 to 6:1. Leukoplakia can be either solitary or multiple.

Early or thin leukoplakia appears as a slightly elevated grayish-white plaque that may be either well-defined or may gradually blend into the surrounding normal mucosa. As the lesion progresses, it becomes thicker and whiter, sometimes eukoplakias develop surface irregularities and are referred to as granular or nodular leukoplakias. Other lesions develop a papillary surface and are known as verrucous or verruciformleukoplakia.[19]

Clinical diagnosis:

Leukoplakia usually present as a single or multiple lesion, localized change of the oral mucosa. The site distribution shows world-wide differences that are partly related to gender and tobacco habits. In fact, any oral site may be affected. Two clinical variants of leukoplakia such as homogeneous and the non-homogeneous type.

Daftary et al. (1972) conducted a study among leukoplakia patients and observed that 32% had nodular leukoplakia, 16% had ulcerated leukoplakia, and 52% had homogeneous leukoplakia.[20]

Brouns et al. (2013) found that 52.7% had homogeneous leukoplakia and 47.27% cases had non-homogeneous leukoplakia. The reasons for the higher incidence of homogenous leukoplakia in the present study are difficult to explain as they are multifactorial. It could be due to variation in the availability of tobacco products, consumption of tobacco with or without slaked lime, duration and frequency of tobacco products combined with alcohol usage in the Indian population.[21]

Diagnosis:

A provisional diagnosis of leukoplakia is made when a predominantly white lesion at clinical examination cannot be clearly diagnosed as any other disease or disorder of the oral mucosa. So, a biopsy is mandatory. The various diagnostic aids used are as follows:

Clinical Methods:[22]

A. *Vital Staining*

i. Toluidine Blue
ii. Lugol's Iodine Vizilite

Photodiagnosis

i. 5-Aminolevulinic acid mediated fluorescence endoscopic imaging
ii. 5-Aminolevulinic acid mediated digitized fluorescence endoscopic imaging
iii. Autofl,muorescence spectroscopy

Histopathological Methods/Cytological Methods

i. Exfoliative cytology
ii. Oral CDx system
iii. Biopsy

Differential diagnosis:[23]

White lesions of oral mucosa often present problems of differential diagnosis, which are of primary importance when assessing precancerous changes in the mouth. The precancerous character of oral leukoplakia is well established, and the "high-risk" type: erosive-dysplastic leukoplakia of greater malignant potential has been thoroughly investigated. Because of their possible association with oral carcinoma, some clinical types of oral lichen planus, namely, the atrophic-erosive forms indicate caution in their treatment and supervision. Epithelial dysplasia is often associated with candidiasis and discoid lupus erythematosus, but neither this, nor such other white lesions as white sponge naevus or morsicatio buccarum, are considered to be preneoplastic. All these white lesions may be clearly identified, differentiated, and circumscribed as clinicopathological disease-entities, by clinical, histopathological and ultrastructural methods, thus facilitating early diagnosis, treatment and prevention of possible malignancy.

- Leukoedema
- Lichen planus
- Chemical burn
- Morsicatio buccarum (habitual cheek biting)
- Candidosis
- Psoriasis
- Lupus erythematosus
- White sponge nevus

Etiopathogenesis: [20]

Local Factors:

TOBACCO - It is the main etiologic agent for leukoplakia. It is available in two forms: smoked and smokeless. The smoked form contains carbon monoxide, thiocyanate, hydrogencyanide, nicotine and the metabolites of these constituents whereas smokeless tobacco contains nitrosamine, polycylic aromatic hydrocarbons and nitrosoproline. The smoked tobacco is available in the forms of bidi, chilum and cigarette whereas the smokeless tobacco is available in the forms of dry snuff, moist snuff, niswar, naas, mishri, khaini quid (tobacco + slaked lime). The chemical constituents of tobacco and its combustion end products as tars and resins are irritating substances capable of causing leukoplakia. Over 300 carcinogens have been identified in tobacco smoke or in its water-soluble components which can be expected to leach into saliva. The major and most studied among them include aromatic hydrocarbons, benzopyrene and the tobacco specific nitrosamines, N-nitrosonornicotine (NNN), nitrosopyrrolidine (NYPR), nitrosodimethylamine (NDMA) and 4-(methylnitrosamine)-1-(3-pyridyl)- 1-butanone (NNK).Benzopyrene is a powerful carcinogen and is found in amounts of 20-40mg per cigarette. The mainstream smokes of a cigarette contains 310 mg of NNN and 150 ng of NNK. These agents act on keratinocytes, stem cells and are absorbed and act in many other tissues in the body.

Alcohol: It seems to have a strong synergistic effect with tobacco relative to oral cancer production, has not been associated with leukoplakia. People who excessively use mouth rinses with alcohol content greater than 25% may have grayish buccal mucosal plaques, but these are not true leukoplakia. Alcohol causes dehydration of the oral mucosa and increases the ambient temperature of the oral cavity thereby making the oral mucosa more vulnerable to the carcinogenic effects of tobacco. Alcohol by itself contains known hydrocarbons and nitosamines.

Sanguinaria: This is a herbal extract used in the toothpaste and mouth rinse. It can cause true leukoplakia. This type of leukoplakia is called sanguinaria-associated keratosis and is usually located in the maxillary vestibule or on the alveolar mucosa of the maxilla.

Trauma: Continuous trauma or local irritation in the oral cavity is suspected as a causative agent for leukoplakia. The source of irritation may be malocclusion, ill-fitting denture, sharp broken teeth, hot or spicy food, root piece, etc. The usual site

to such irritation is the buccal mucosa and less often is the alveolar ridge. Chronic mechanical irritation can produce a white lesion with a roughened keratotic surface termed frictional keratosis.

Candidiasis: The presence of Candida albicans has been reported very frequently in association with leukoplakia, more commonly with nodular type. Candidalleukoplakiamay be associated with other local factors such as tobacco smoking, denture wearing or occlusal friction. Tobacco smoking may result in candidal colonization because of increased keratinization, reduced salivary IgA concentration or decreased PMNL function. There is a long standing discussion whether candida infection is a cause of leukoplakia or if it is a superimposed infection in a pre-existing lesion.

It has been shown that, upon treatment, non-homogenous candida-infected leukoplakia convert into a homogenous lesion, and some lesions even regressed.

Regional & Systemic Factors:

Tertiary Syphilis

White patches are seen on the tongue. Syphilitic glossitis is observed. Atrophy of the filiform and fungiform papillae occurs.

Deficiency of vitamin A,B complex, C,E beta-carotene.

- ***a.*** *Nutritional Deficiency:* Sideropenicanemia may be the disposing factor for the occurrence of leukoplakia.
- ***b.*** *Viral Infection:* The possible implication of human papilloma virus in the etiology and potential for the malignant transformation of oral premalignant lesion has been studied extensively and it was reported that the likelihood of detecting HPV was 2-3 times higher in precancerous oral mucosa and 4-5 times higher in squamous cell carcinoma than in normal oral epithelium. The possible viral etiology of oral leukoplakia had been first suggested by light microscopic examination of HPV suggestive changes. In a follow up study of 20 leukoplakias; Lind (1987) established a significant correlation between the prescence of HPV antigen and the degree of dysplasia and malignant transformation. Studies by Nielson (1996) in the

prevalence of HPV in oral premalignant lesions found an overall rate of HPV positive lesions to be 40.8% of which five of them were HPV 16. Laryngeal squamous cell papilloma and recurrent respiratory papillomatosis (RRP) are well-established HPV-induced tumours.

c. *Idiopathic Leukoplakia:* In a small proportion of cases, no underlying cause has been found. Such lesions are called idiopathic leukoplakia. They have higher potential for malignant transformation.

INCIDENCE:

The estimated prevalence of oral leukoplakia, worldwide, is approximately 2%. Petti, in a systematic review, summarized the world prevalence of leukoplakia based on 23 studies from 17 countries published between 1986 and 2002. Using statistical techniques, he calculated a global prevalence of 2.6%. In India, a striking variation has been observed with 0.2% in Bihar and 4.9% in Andhra Pradesh. Gujarat has shown a prevalence rate of 11.7% owing to the high prevalence of tobacco or guthka chewing practices. The systematic review by Petti also confirmed that oral PMD affects males at least three times as often as females.[24]

Brouns et al. found the prevalence of OL is approximately 2% with an annual malignant transformation of approximately 1%.

MALIGNANT TRANSFORMATION RATE: [25]

The possibility of malignant transformation of leukoplakias depends on multiple factors:

- Female gender
- Long duration of leukoplakia
- Leukoplakia in nonsmokers (idiopathic leukoplakia)
- Location on the tongue and/or floor of the mouth
- Size > 200 mm^2
- Nonhomogeneous type
- Presence of *Candida albicans*
- Presence of epithelial dysplasia.

The prognosis of leukoplakia varies. In a study conducted in Mumbai, 42.5% untreated leukoplakias diseappeared in 5 years and 45.3% in 10 years in the tobacco chewing group.

In Gujarat, 11% of leukoplakias re-examined after 2 years had increased in the size, 31.6% had decreased in size or disappeared and 57.3% had remained unchanged. In a study from developed world only 20.1% had disappeared, 17.8% had reduced in size and 3.3% had increased at 10 years follow up.

The frequency of dysplastic or malignant alterations in oral leukoplakia has ranged from 15.6 to 39.2% in several studies. In Indian studies, the rate of malignant transformation ranges from 0.13% to 2.2% per year. In a Swedish study, 0.2% developed oral cancer in 2 years, 0.4% in 5 years in tobacco users while in non-tobacco users the transformation rate was 1.15 and 3.1% at 2 and 5 years respectively In systematic review, Petti has calculated a global transformation rate for oral leukoplakia of 1.36% per year. The lesions that are present in the floor of mouth, lateral tongue and lower lip are more likely to show dysplastic or malignant changes.

ERYTHROPLAKIA

Erythroplakia is defined as "A fiery red patch that cannot be characterized clinically or pathologically as any other definable disease". Tobacco and alcohol use are considered important etiologic factor. The possible role of C. albicans is at present still unclear.

Erythroplakia also may occur in conjunction with leukoplakia and has been found concurrently with a large proportion of early invasive oral carcinomas. Although erythroplakia is less common than leukoplakia, it has a much greater potential to be severely at the time of biopsy or to develop invasive malignancy at a later time.[25]

Fournier and Darier[20] first described erythroplasia as a malignant dyskeratosis with unknown etiology in 1893 and designated it as epitheliome papillaire.

According to Shafer and Waldron et al (1975)

Erythroplakia of the oral cavity is defined as a specific disease entity which must be differentiated from other specific or nonspecific inflammatory oral lesions, although this can only be done in most cases by biopsy. [26]

According to WHO Collaborating Centre for Oral Precancerous Lesions (1978)

"A fiery red patch that cannot be characterized clinically or pathologically as any other definable disease". [26]

According to Axell T, Pindborg JJ, Smith CJ, Vander Waal (1994)

The term Erythroplakia is used analogously to leukoplakia to designate lesions of the oral mucosa that present as red areas and cannot be diagnosed as any other definable lesion'.[26]

According to Bouquot, Ephros (1995) A chronic red mucosal macule which cannot be given another specific diagnostic name and cannot be attributed to traumatic, vascular, or inflammatory causes.[26]

Pindborg JJ, Reichart PA, Smith CJ, van der Waal (1997) A fiery red patch that cannot be characterized clinically or pathologically as any other definable lesion.[26]

According to Burket's 12th edition (2015) A red lesion of the oral mucosa that excludes other known pathologies.[27]

CLASSIfiCATION: [28]

(A) Clinical variations

a. Homogeneous erythroplakia
b. Erythroplakia interspersed with patches of leukoplakia
c. Granular or speckled erythroplakia (embracing the lesion described as speckled leukoplakia)

(B) Microscopic variations

(1) Neoplastic

(a) Squamous carcinoma
(b) Carcinoma in situ (intra-epithelial carcinoma) and less severe forms of epithelial atypia

(2) Inflammatory

(a) Candida albicans infections (including denture stomatitis)

(b) Tuberculosis

(c) Histoplasmosis

(d) Miscellaneous specific, non-specific and non-diagnosable lesions

CLINICAL FEATURES:

Erythroplakia mainly occurs in the middle age and the elderly with no significant gender predilection. Any site of the oral and oropharyngeal cavity may become involved, usually in a solitary fashion.

The floor of the mouth, tongue, and soft palate are the most common site and multiple lesions may be present. Prevalence figures of erythroplakia are only available from studies performed in south and southeast Asia and vary between 0.02% and 0.83%.

The clinical appearance may be flat or even depressed with a smooth or granular surface. In case of a mixture of red and white changes such lesion is usually categorized as non-homogenous leukoplakia (“erythroleukoplakia”).[29]

Etiology/Pathogenesis

Etiology and pathogenesis of oral erythroplakia are poorly understood. Predisposing factors are widely unknown, but it was suggested that tobacco and alcohol use are probably involved in most cases. A recently published series of papers based on a large case control study in Kerala, India, shed more light on some of the factors involved in the etiology of oral erythroplakia.

One of these studies evaluated the risk of oral erythroplakia in relation to chewing tobacco, smoking, alcohol drinking, body mass index (BMI), and vegetable, fruit, and vitamin/iron intake. The adjusted odds ratio (OR) for OE was 19.8 (95% CI, 9.8–40.0) for individuals who had ever chewed tobacco, after controlling for age, gender, education, BMI, smoking and drinking. The adjusted OR for ever-alcohol drinkers was 3.0 (95% CI, 1.6–5.7) after controlling for age, gender, education, BMI, chewing tobacco and smoking. For forever smokers, the adjusted where the epithelium is fairly thick. Shear assumed that the poorly differentiated epithelium might be more translucent than normal, an assumption which has never been substantiated.

Another aspect, which may have a role in the pathogenesis of OE, is infection with Candida. Candida albicans has often been demonstrated in

erythroleukoplakia as secondary infection. After antifungal therapy the red component of these lesions and often the white component as well, diminishes or disappears. Unfortunately, it is not yet known whether the red surface change in oral erythroleukoplakia (and nodular leukoplakia) is the result of inflammation, dysplasia, or both. No study has yet shown a positive correlation between the presence of dysplastic epithelium and candidal hyphae in homogeneous OE or carcinoma in situ.[30]

HISTOPATHOLOGY:

Erythroplakia as a clinical term does not carry any histological suggestion; however, histological biopsy of Oral Erythroplakia.

- Epithelial Dysplasia – mild to moderate
- Carcinoma in Situ – moderate to severe dysplasia

According to Reichart and Philipsen (2005) , all Erythroplakia showed some degree of epithelial dysplasia: 51% showed invasive squamous cell carcinoma, 40% Carcinoma in situ or severe dysplasia and the remaining 9% demonstrated mild to moderate dysplasia.[31]

Differential diagnosis

Oral erythroplakia is a diagnosis of exclusion. Therefore, from the clinical point of view some diseases of the oral mucosa with red (erythematous) changes should be considered as differential diagnoses. Some of the red lesions of the oral mucosa that may be confused with OE. Of these erythematous candidiasis and atrophic oral lichen planus are the most important. As has been stated by numerous experts in the field, biopsy is mandatory in cases of doubt. [32]

Red lesions resembling oral erythroplakia:

(A) Mycotic infections:

i. Oral candidiasis
ii. Erythematous candidiasis
iii. Generalized candidal erythema

iv. Denture-induced stomatitis

v. Histoplasmosis

(B) Bacterial infections:

i. Tuberculosis

(C) Mucosal diseases:

ii. Atrophic oral lichen planus

iii. Lupus erythematosus

iv. Pemphigus, Pemphigoids

(D) Others:

i. Amelanotic melanoma

ii. Haemangioma

iii. Telangiectasia, lingual varices

iv. Kaposi's sarcoma

v. Oral purpura

MALIGNANT TRANSFORMATION RATE

Oral erythroplakia has the highest risk of malignant transformation compared to all other oral mucosal lesions at risk for transformation. Erythroplakias are considered most severe because microscopically 91% of them show either squamous cell carcinoma, carcinoma-in-situ or moderate to severe epithelial dysplasia. Information on malignant transformation is available from reverse smoking associated red areas. These demonstrated a malignant transformation rate of 118 per 1000 red areas. Among all palatal components red area are nearly 10 times more dangerous than white patches.Generally, transformation rates, including those with invasive carcinoma already at biopsy, vary from 14% to 50%.[26]

PALATAL LESIONS IN REVERSE SMOKERS

In some southeast Asian and South American countries, individuals practice a habit known as reverse smoking in which the lit end of the cigarette or cigar is placed inside the mouth. This habit creates a more severe heat-related alteration of the palatal mucosa known as reverse smokers palate, which has been associated with a significant risk of malignant transformation.[33]

EPIDEMIOLOGY:

The annual age- adjusted incidence rates of palatal changes (encompassing all components) was 249 per 1000 among men and 39.6 per 1000 among women and incidence was in the 55-64year age group (srikakulum data).[33]

CLINICAL ASPECT: [33]

Palatal changes comprise several components:

- Keratosis- diffuse whitening of entire palatal mucosa.
- Excrescences- 1-3mm elevated nodules, often with central red spots;
- Patches- well defined, elevated white plaques.
- Red areas- well defined reddening of the palatal mucosa,
- Ulcerated area- creater-like area covered by fibrin, and
- pigmented areas- Area of palatal mucosa that are devoid of pigmentation.

Oral Lichen planus

It is a mucocutaneous condition in which involves various mucosal surfaces either alone or along with involvement of skin. It most commonly involves the oral mucosa when compared with other mucosal sites. Oral lichen planus is a disease of unknown etiology affecting stratified squamous epithelia. In isolated Oral lichen planus, only oral lesions will exist. The disease affects 0.5%-2% of the general population. This disease most commonly involves middle aged patients of 30-60 years age group and females are more prone than males with a ratio of 1.4:1. Oral lichen planus can be seen rarely in children and young adults. Oral lichen planus should be considered as a potentially malignant disorder because there is a relationship between oral cancer and Oral lichen planus, although the degree of risk involved is variable.[34]

TYPE OF LICHEN PLANUS:[35]

Reticular Lichen Planus

Reticular lichen planus is the most common type and is often found incidentally. Lesions are asymptomatic and located on the buccal mucosa, tongue, gingivae, or in the vestibule. The lesions present as white, slightly raised plaques or papules with interlacing white lines described as Wickham striae on an erythematous background.

Erosive Lichen Planus:

Erosive lichen planus appears atrophic, with areas of ulceration, erythema, and keratotic white striae. There can be pseudomembranes, and in the gingival region it often appears similar to desquamative gingivitis. There is a range of symptoms, from a mild burning sensation to debilitating pain. Lesions can interfere with speech, chewing, and swallowing. These lesions can be mixed with reticular lesions, which are not seen in other vesiculoerosive diseases, such as pemphigus, pemphigoid, and linear immunoglobulin A (IgA) disease.

Two additional presentations are the atrophic and bullous forms, which are considered variants of the erosive type. Atrophic OLP appears as diffuse, erythematous patches surrounded by fine white striae. This form can cause significant discomfort. In the bullous form, intraoral bullae are present on the buccal mucosa and the lateral borders of the tongue; the bullae rupture soon after they appear, which results in the classic appearance of erosive Oral lichen planus.[36]

Erythematous, Atrophic Lichen Planus:

This form of lichen planus presents as a red, diffuse lesion with mucosal atrophy.

Plaque like Lichen Planus:

Solitary, slightly raised, or flat white lesions appear similar to leukoplakia; a common oral location is on the tongue

Bullous Form:

This rare form of OLP exhibits bullae that rupture, progressing to erosive lichen planus.

Annular and linear form:

These consist of striae that occur in a circular and linear fushion.

CLINICAL FEATURES:

Oral lichen planus predominately affects females, with most patients aged between 30 and 70 years. It is a rare occurrence in children; but in men, lesions often develop at an earlier age. The presentation is varied in clinical appearance, with most lesions being bilateral and located on the buccal mucosa. Lesions can appear, however, on the tongue, in the vestibule, and on the gingivae. Isolated gingival lichen planus may be seen in up to 8.6% of patients. Lesion occur in various clinical forms, and those showing ulcerated, erosive, or atrophic areas generally considered as greater risk for malignant transformation. It can also co-exist with oral submucous fibrosis, leukoplakia. Lesions are generally asymptomatic but, when erosive or ulcerated, there may be burning sensation, pain or other symptom.[37]

ETIOLOGY:

The etiology of oral lichen planus appears to be multifactorial and complicated. Earlier studies have implicated stress, anxiety, depression as the causes for OLP. However, whether stress is the cause or the consequence, was left undetermined. Familial cases of OLP have been reported and role of genetic predisposition was considered.[38]

Pathogenesis:

Pathogenesis of oral lichen planus may be antigen-specific and non-specific. Antigen-specific mechanisms include antigen presentation by basal keratinocytes and non-specific mechanisms include mast cell degranulation and matrix metalloproteinase (MMP) activation in OLP lesions. Both these mechanisms may combine which results in CD8+ cytotoxic T-cell accumulation in the superficial lamina propria followed by basement membrane disruption, intraepithelial T-cell migration, and keratinocyte apoptosis. OLP chronicity may be due to deficient antigen-specific TGF-b1-mediated immunosuppression. This breakdown of normal oral mucosa could result in OLP.

Both endogenous and exogenous factors may cause cell-mediated immunity in a genetically susceptible patient and appears to play a major role in the pathogenesis of OLP. The nature of the antigen implicated in OLP is uncertain, however numerous predisposing factors are known to induce OLP are identified. These are systemic medications, dental materials, chronic liver disease and hepatitis C virus, stress, genetics, tobacco chewing, Graft versus Host disease.

Systemic medications such as antimalarial drugs, non-steroidal anti-inflammatory drugs, antihypertensive agents, diuretics, oral hypoglycemic agents, beta blockers, pencilllins, sulfonamides, tetracyclines, heavy metals, thyroid preparations, antiretroviral medication have been reported to cause OLP.

The association of OLP with chronic liver disease was first suggested by Mokni et al in 1991. Epidemiological evidences strongly suggest that Hepatitis C Virus may be an etiologic factor in OLP. Association of OLP with several different autoimmune diseases such as alopecia areata, dermatitis herpetiformis, myasthenia gravis, etc. has been documented.

Periods of psychological stress and anxiety are associated with aggravation of OLP in most of the studies conducted so far. Genetic predisposition also play a role in OLP pathogenesis. Koebner phenomenon is a characteristic feature of cutaneous LP and is also observed in oral cavity. The erosive OLP lesions are most commonly seen in areas of trauma such as buccal mucosa and lateral surfaces of the tongue. These lesions may decrease in severity with the elimination of trauma. Smoking, tobacco chewing, and betel nut chewing has been associated with the development of OLP in studies conducted in indian population. Grinspan in 1963 found an interesting association between oral lichen planus, diabetes mellitus and hypertension, which he termed as Grinspan syndrome.

OLP is a T-cell mediated autoimmune disease in which the auto-cytotoxic CD8+ T cells trigger apoptosis of the basal cells of the oral epithelium. Initially keratinocyte antigen expression or unmasking of an antigen may occur followed by migration of T cells (mostly CD8+, and some CD4+ cells) into the epithelium. These migrated T cells are activated directly by antigen binding to major histocompatibility complex (MHC)-1 on keratinocyte or through activated CD4+ lymphocytes. In OLP, there will be up regulation of MHC-II expression along with increased number of Langerhan cells facilitating the antigen presentation to CD4+ cells, which activate CD8+ T cells through receptor interaction, interferon γ and IL-2. The activated CD8+ T cells trigger the apoptosis of basal keratinocytes by releasing tumor necrosis factor-α, granzyme B and by Fas–FasL mediated apoptosis. This results in loss of integrity of basement membrane. The MMP are principally involved in connective tissue matrix protein degradation.[39]

DIAGNOSIS

The diagnosis can be made depending on the history, clinical and histopathological examination. However, in classical lesions, the diagnosis can be arrived based on clinical appearances (Wickham's striae, erythematous area) only. When skin lesions are also present, the accuracy of diagnosis is strengthened.

Differential diagnosis of reticular OLP includes leukoplakia, lichenoid reactions, lupus erythematosus and graft vs host disease. The differential diagnosis of erosive OLP includes chronic cheek chewing, hypersensitivity mucositis, chronic candidiasis, discoid lupus erythematosus, squamous cell carcinoma, benign mucous membrane pemphigoid, pemphigus vulgaris and erythema multiforme.

It is sometimes difficult to clinically diagnose "desquamative gingivitis" when lesions in other sites are absent. Mucous membrane pemphigoid, pemphigus vulgaris and OLP may present as desquamative gingivitis of very similar clinical aspect. Biopsy is the gold standard for the diagnosis of OLP. The biopsy should include marginal tissue containing both lesional and normal-appearing areas. OLP can be distinguished from other chronic white or ulcerative oral lesions including reactive keratoses, chronic hyperplastic candidosis, epithelial dysplasia, discoid lupus erythematosus, gastrointestinal disease or anemic states with the help of histopathological examination.

Direct and indirect immunofluorescent studies, direct oral microscopy and enzyme linked immunosorbent assays can be helpful in reaching a diagnosis for problematic cases and to exclude malignancy. Among these, the most important being the Immunofluorescent studies which are helpful in making a diagnosis in cases of OLP that may resemble other diseases.[40]

Differential Diagnosis:

The diagnosis of OLP can be rendered more confidently when characteristic cutaneous lesions are present. Except for the pathognomonic appearance of reticular OLP (white striae occurring bilaterally on the buccal mucosa), in most cases histopathologic evaluation of lesional tissue is required to obtain a definitive diagnosis. Even classic cases of lichen planus may be worthy of biopsy so as to establish baseline histopathologic features. The differential diagnosis of erosive OLP includes squamous cell carcinoma, discoid lupus erythematosus, chronic candidiasis, benign mucous membrane pemphigoid, pemphigus vulgaris, chronic cheek chewing, lichenoid reaction to dental amalgam or drugs, graft-versus-host disease (GVHD), hypersensitivity mucositis and erythema multiforme.8 The plaque form of reticular OLP can resemble oral leukoplakia.[41]

Biopsy Procedures:

The definitive diagnosis of OLP depends on histopathologic examination of the affected tissue. However, performing a biopsy of lesional tissue, particularly if the OLP is of the erosive form, can be challenging. It is important to obtain an elliptical wedge of mucosa extending beyond the affected area, to avoid stripping the superficial epithelial layer from the underlying connective tissue.

Histopathologic Features:

The classic histopathologic features of OLP include liquefaction of the basal cell layer accompanied by apoptosis of the keratinocytes, a dense band-like lymphocytic infiltrate at the interface between the epithelium and the connective tissue, focal areas of hyperkeratinized epithelium (which give rise to the clinically apparent Wickham's striae) and occasional areas of atrophic epithelium where the rete pegs may be shortened and pointed (a characteristic known as sawtooth rete pegs). Eosinophilic colloid bodies (Civatte bodies), which represent degenerating keratinocytes, are often visible in the lower half of the surface epithelium.

Although the histopathologic features of OLP are characteristic, other conditions, such as lichenoid reaction to dental amalgam and drugs, may exhibit a similar histologic pattern.

The histopathologic diagnosis of OLP can be complicated by the presence of superimposed candidiasis; diagnosis can also be more difficult if the biopsy exhibits an ulcerated surface. In these situations, the biopsy findings are sometimes interpreted as representing a nonspecific chronic inflammatory process.

On occasion, the histopathologic features are equivocal, and the oral pathologist examining the submitted tissue may recommend that a second biopsy be performed to obtain fresh tissue for immunofluorescence. Immunofluorescent examination of OLP lesional tissue usually demonstrates deposition of fibrinogen along the basement membrane zone. Chronic ulcerative stomatitis is a relatively recently described condition that has light microscopic features similar to OLP but possesses a characteristic immunofluorescent pattern. It is reportedly less responsive to corticosteroid therapy than OLP.

If the biopsy report is equivocal, or does not agree with the clinical picture, it may be prudent to perform another biopsy, especially when dealing with isolated lesions occurring in locations where the risk of development of squamous cell carcinoma is higher, such as the lateral and ventral surfaces of the tongue and the floor of the mouth.[41]

MALIGNANT TRANSFORMATION RATE:

It has been reported to be 0.3% (Gupta et al 1980) to 10% (Dechaume et 1957). Clinically atrophic, erosive and ulcerative forms of LP and lesions showing erythroplakia components are indicated to be more cancer prone. it was suggested that cancer development in this condition could be due to interplay of factors such as presence of erosive components, atrophic epithelium, and superimposed tobacco habits (Murti et al 1986). The malignant transformation rate for erosive from is 0.4-2.[42]

Oral submucous fibrosis

Oral submucous fibrosis is defined as “an insidious chronic disease affecting any part of the oral cavity and sometimes pharynx. It is associated with juxta-epithelial inflammatory reaction followed by fibroelastic changes in the lamina propria layer, along with epithelial atrophy which leads to rigidity of the oral mucosa proceeding to trismus and difficulty in mouth opening.” Other terms used to describe this condition are juxta-epithelial fibrosis, idiopathic scleroderma of the mouth, idiopathic palatal fibrosis, submucous fibrosis of the palate and pillars, sclerosing stomatitis, and diffuse OSMF.[43]

Oral submucous fibrosis (OSMF) precancerous condition and is chronic, resistant disease characterized by juxta-epithelial inflammatory reaction and progressive fibrosis of the submucosal tissues. It occurs at any age but most commonly seen in young and adults between 25 and 35 years (2nd–4th decade). Onset of this disease is insidious and is often 2–5 years of duration. It is commonly prevalent in Southeast Asia and Indian subcontinent. The prevalence rate of OSMF in India is about 0.2%–0.5%. This increased prevalence is due to increased use and popularity of commercially prepared areca nut and tobacco product - gutkha, pan masala, flavored supari, etc. The malignant transformation rate of OSMF was found to be 7.6%.[44]

Classification system[44]

Recent classification system:

Kerr et al. gave the following grading system for OSMF as:

- Grade 1: Mild: Any features of the disease triad for OSMF (burning, depapillation, blanching or leathery mucosa) may be reported inter-incisal opening >35 mm
- Grade 2: Moderate: Above features of OSMF and inter-incisal limitation of opening between 20–35 mm

- Grade 3: Severe: Above features of OSF and inter-incisal opening <20 mm
- Grade 4: Above features of OSMF with other potentially malignant disorders on clinical examination Grade 4B: Above features of OSMF with any grade of oral epithelial dysplasia on biopsy
- Grade 5: Above features of OSMF with oral squamous cell carcinoma.

More et al. gave the following classification based on clinical and functional parameters as:

I: Clinical staging:

- Stage 1 (S1): Stomatitis and/or blanching of oral mucosa.
- Stage 2 (S2): Presence of palpable fibrous bands inbuccal mucosa and/or oropharynx, with/without stomatitis.
- Stage 3 (S3): Presence of palpable fibrous bands in buccal mucosa and/or oropharynx, and in any other parts of oral cavity, with/without stomatitis.
- Stage 4 (S4): A: Any one of the above stage along with other potentially malignant disorders, e.g., oral leukoplakiaand oral erythroplakia.

  B: Any one of the above stage along with oral carcinoma.

II: Functional staging:

M1: Inter-incisal mouth opening up to or >35 mm

M2: Inter-incisal mouth opening between 25 to 35 mm

M3: Inter-incisal mouth opening between 15 to 25 mm

M4: Inter-incisal mouth opening <15 mm.

Prakash et al. assessed the morphologic variants of soft palate by conducting a clinic-radiological study. The authors based on these variants assessed the severity of OSMF to establish it as a basis for staging of OSMF.

Six morphologic variants were delineated as follows:

Type 1: Leaf shaped Type

Type 2: Rat tail shaped Type

Type 3: Butt shaped Type

Type 4: Straight line Type

Type 5: Deformed S Type

Type 6: Crook shaped.

Patil and Maheshwari suggested a new classification based on cheek flexibility. Here, cheek flexibility was measured as a distance in millimetres from maxillary incisal midline to the cheek retractor during retraction.

- Normal cheek flexibility observed was: males 35–45 mm and females 30–40 mm.
- Grade 1 (Early): Cheek flexibility of 30 mm and above
- Grade 2 (Mild): Cheek flexibility between 20 to 30 mm
- Grade 3 (Moderate): Cheek flexibility less than 20 mm
- Grade 4 (Severe): Any of the above condition without concurrent presence of potential malignant lesions.
- Grade 5 (Advanced): Any of the above condition with concurrent presence of oral carcinoma.

ETIOPATHOGENESIS[46]

OSMF was first described by Schwartz in 1952, where it was classified as an idiopathic disorder by the term atrophia idiopathica (tropica) mucosae oris. Since then, many hypotheses are being suggested that OSMF is multifactorial in origin with etiological factors are areca nut, capsaicin in chilies, micronutrient deficiencies of iron, zinc, and essential vitamins. Autoimmune etiological basis of disease with demonstration of various autoantibodies with a strong association with specific human leukocyte antigen (HLA) antigens has also been suggested.

Areca nut (betel nut) chewing is one of the most common causes of OMSF which contains tannins (11%–12%) and alkaloids such as arecoline, arecaidine, guvacine, and guvacoline (0.15%–0.67%). Out of all arecoline is the main agent. Arecaidine is an active metabolite in fibroblast stimulation and proliferation, thereby inducing collagen synthesis. With the addition of slaked lime (Ca[OH] 2) to areca nut, it causes hydrolysis of arecoline to arecaidine making this agent available in the oral environment. Tannin present in areca nut reduces collagen degradation by inhibiting collagenases. OSMF is induced as a combined effect of tannin and arecoline by the mechanism of reducing degradation and increased production of collagen, respectively.

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Areca nut :

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Tobacco & lime:

These are known irritants and causative factors in oral malignancy. They may act as local irritants. The commercially freeze dried products such as pan masala, Gutkha and Mawa (areca, tobacco and lime) have high concentrates of areca nut per chew and appear to cause OSF more rapidly than by self-prepared conventional betel quid which contain smaller amount of areca nut. (Shah & Sharma, 1998; Sinor et al, 1990).

Chillies:

The use of chillies *(Capsicum annum and Capsicum frutescence)* has been thought to play an etiological role in oral submucous fibrosis. Capsaicin, which is vanillymide of 8-methyl-6-nonenic acid, is the active ingredient of chillies, play an etiological role in oral submucous fibrosis (Rajendran, 1994).

Nutritional deficiency:

Deficiency of iron (anemia), Vitamin B complex, minerals, and malnutrition are promoting factors that disturbs the repair process of the inflamed oral mucosa, thus leads to deranged healing and resultant scarring and fibrosis. The resulting atrophic oral mucosa is more susceptible to the effects of chilies, betel nuts, and other irritants.

Defective iron metabolism:

Microcytic hypochromic anemia with high serum iron has been reported in submucous fibrosis (Rajendran, 1994).

Collagen disorders:

Oral submucous fibrosis is thought to be a localized collagen disease of oral cavity. It is linked to scleroderma, rheumatoid arthritis, Duputreyen's contracture and intestinal fibrosis. A link between scleroderma and oral submucous fibrosis has also been suspected on the basis of similarity of histological characteristics (Tsai et al, 1999; Tilakratne et al, 2005).

CLINICAL FINDING:

Clinically, OSMF is characterised by a burning sensation, blanching and stiffening of the oral mucosa and oropharynx, and trismus. The most characteristic feature is the marked verticle fibrous ridge formation within the cheeks and board like stiffness of the buccal mucosa. The fibrosis in the soft tissue leads to trismus, difficulty in eating, and even dysphagia. In advanced stages vertical fibrous bands appear in the cheeks, faucial pillars, and encircle the the lips. Through an as yet unknown process, fibrosis and hyalinization occur in the lamina propria, which results in atrophy of the overlying epithelium.

The atrophic epithelium apparently predisposes to the development of a squamous cell carcinoma in the presence of carcinogene. Biopsy of the tissue is rarely performed due to the observation that such investigation results in further fibrous scar formation and worsening of the symptoms.[25]

The clinical presentation can be summarized into early and late forms:

- Early forms are characterized by burning sensation exacerbated by spicy foods, vesiculation, blanching of mucosa, and leathery mucosa.
- Late forms are characterized by fibrous bands within the mucosa, limitation of mouth opening, narrowing of the oropharyngeal orifice with distortion of uvula and woody changes of the mucosa and tongue.[6]

INCIDENCE:

In india, OSMF affects between 0-2% and 1.2% of an urban population attending dental clinics. There is a positive association between the incidence of leukoplakia and oral cancer with OSMF. The frequency of malignant change has been reported from paymaster, who observed the occurrence of squamous cell carcinoma in one third of his patient with OSMF. In a long-term follow-up study over a period of 17 year by Murti *et al.,* the annual malignant transformation rate was approximately 0.5% to 7.6% over 17 years.[6]

MALIGNANT TRANSFORMATION RATE

Malignant transformation rate was found to be in the range of 7-13%. Frequent evaluation for development of oral squamous cell carcinoma is essential because a 17year malignant transformation rate of 8% has been determined for betel quid users in India. Overall, person with oral . submucous fibrosis are at least 19 times more likely to develop oral cancer than cancer without the disease.[49]

DISCOID LUPUS ERYTHEMATOSUS:

Lupus erythematosus is a rather common disease of unknown etiology. One of its form is form is the discoid lupus erythematosus. The disease is characteristically classified as an auto-immune disease. It is thought to be a pre malignant condition.[50]

Discoid lupus erythematosus (DLE) is a chronic, scarring, atrophy producing photosensitive dermatosis. DLE may occur in patients with systemic lupus erythematosus (SLE) and in some patients (<5%) with DLE, progress to SLE.

Worldwide, the prevalence of lupus erythematosus (LE) ranges from 17 to 48 cases per 100,000 populations. The highest prevalence of LE occurs in persons aged 4060 years and is approximately 10 times higher in women than in men.

Malignant degeneration of chronic lesions of LE is possible, leading to non-melanoma skin cancer. Oral mucosal lesions are considered to be a pre-malignant condition.

Clinical Features

Discoid lupus is by far the most common manifestation of LE. It commonly presents with erythematous, scaly papules and plaques occurring on sun-exposed areas, although 50% of discoid lupus lesions are found on areas of hair-bearing scalp that are presumably protected from the sun. In the localized variety of discoid lupus the lesions tend to be confined to the head and neck and in the generalized variety they occur both above and below the neck. Patients with generalized discoid have significantly greater chances of having laboratory abnormalities and of progressing to systemic LE. Most people with DLE do not have any systemic or serologic abnormality although antinuclear antibodies may be present.

Discoid lupus occurs at all ages and among all ethnic groups; it occurs more frequently in women than in men, but the predilection among women is not as marked as in systemic lupus. Discoid lupus starts as an erythematous papule or plaque, usually on the head or neck, with an adherent scale. The lesion tends to spread centrifugally and as it progresses there is follicular plugging and pigmentary changes, generally hyperpigmentation at the periphery, and hypopigmentation with atrophy, scarring, and telengiectasia at the center of the lesion.

Involvement of the scalp commonly produces a scarring alopecia, but there has been an increase in incidence of alopecia areata among patients with LE. Scarring alopecia was present in 34% of 89 patients with DLE and was associated with a prolonged disease course. More than half of those patients had scalp disease at the onset. There are no reliable predictors of scalp involvement. Histologically there is a perifollicular lymphocytic inflammation maximal around mid-follicle. The mid-follicle is in fact a very important structure becuase it contains the bulge that contains the follicular stem cells.[51]

Treatment of Discoid Lupus Erythematosus

DLE is a scarring autoimmune disease that can linger on for a prolonged period, not surprisingly, the psychological impact is considerable. Consequently there is a need for treatment, often prolonged, that incurs considerable expenditure for health facilities.

Early effective treatment may lead to total clearing of skin lesions, but failure of treatment results in permanent scarring; the depressed scars, hair loss, and pigmentary changes are often extremely disfiguring, particularly in darker-skinned people. According to a 2004 systematic review of treatment of discoid lupus by Jessop et al only 30 trials were identified through a search of the Cochrane Clinical Trials Register (December 1999); Medline (January 1966 to December 1999);

Embase (January 1980 to January 2000); and Index Medicus (1956 to 1966). Only 4 of these were controlled trials and only 2 of the latter were randomized (A, level 2). Accordingly, more evidence is needed to guide clinicians to the best treatment options for DLE, particularly for the severe type.

The treatment of DLE would in most instances be initiated at a dermatology department, but before instituting treatment for discoid lupus patients should be assessed for systemic involvement. This should include a full history and physical examination, full blood count, erythrocyte sedimentation rate, midstream urine, and antinuclear antibody. If SLE is suspected, anti-double stranded DNA, extractable nuclear antigen, C3/C4, and renal review should also be included.[52]

Conclusion:

It is estimated that most of all cancers and cancer mortality worldwide are preventable through early detection, as it provides a greater chance of initiating early and successful treatment. Only sure way to avoid cancer is not to be born, but we can reduce our chances for cancer by a balanced approach to cancer prevention, early detection, and effective early treatment. The main objective of secondary prevention is early detection of PMDs when they can be treated most effectively. PMDs are often undiagnosed due to lack of public awareness and due to lack of knowledge among medical professionals. Clinical appearance and diagnosis of a lesion is not adequate to determine its premalignant nature as not all white lesions turn malignant. Diagnostic biopsy and histopathological examination should be considered for any mucosal lesion that persists for more than 14 days after obvious irritants have been removed. Prognosis and patient survival is directly related to stage and grade of cancer at initial diagnosis.

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