

Case Study

**ORAL PREMALIGNANT LESIONS INDUCED  
BY SMOKELESS TOBACCO- A CASE SERIES**

**ABSTRACT**

Tobacco in any form can cause wide spectrum of oral mucosal lesions. Tobacco use causes an array of changes in the oral cavity, from mucosal pigmentation to thickening, ulceration of the epithelium. Oral cancer and other oral mucosal lesions such as tobacco induced keratosis, leukoplakia, and submucous fibrosis are strongly associated with tobacco consumption. The prevalence and severity of lesions demonstrate a dose-response relationship, which is best predicted by the amount, frequency and duration of smokeless tobacco use.

**KEYWORDS-** tobacco induced keratosis, leukoplakia, erythroplakia, submucous fibrosis

**INTRODUCTION**

Tobacco use is one of the most common habit seen in India.<sup>1</sup> India is the second largest producer and consumer of tobacco next only to China. <sup>2</sup>The prevalence of tobacco use among Indian adults is 35%.<sup>3</sup> Tobacco is used in chewable as well as smokable forms. Smokeless tobacco is used in various forms like betel quid which is a mixture of areca nut, slaked lime, and flavoring agent wrapped in betel leaf and tobacco commercial preparations such as gutka, zarda, khaini, mishri, etc., contain the pieces of areca nut coated with powdered tobacco, sweetening and flavoring ingredients in addition to other spices such as saffron, cardamom, etc. which are very popular and highly addictive.<sup>4,5</sup>

23 Tobacco in any form can cause wide spectrum of oral mucosal lesions. The type  
 24 and location of these lesions in turn depends on the type, duration of frequency of use.  
 25 Tobacco use causes an array of changes in the oral cavity, from mucosal pigmentation to  
 26 thickening, ulceration of the epithelium. Oral cancer and other oral mucosal lesions such as  
 27 tobacco induced keratosis, leukoplakia, and submucous fibrosis (SMF) are strongly  
 28 associated with tobacco consumption. In comparison to Western populations, in which oral  
 29 cancer represents about 3% of malignancies, it accounts for over 30% of all cancers in India;  
 30 this difference can be attributed to regional variation in the prevalence and pattern of tobacco  
 31 habits.

### 32 **Carcinogens in commonly used smokeless tobacco forms- pan masala and gutkha:**

33 The main carcinogens in pan masala and gutkha are derived from their ingredients areca  
 34 nut, lime, catechu and tobacco. Several carcinogens are derived from tobacco but also from  
 35 areca nut . Carcinogenic nitrosamines that could be derived from major ingredients of pan  
 36 masala (areca nut) and gutkha. The carcinogenic TSNAs(Tobacco-specific nitrosamines) ,  
 37 N<sup>o</sup>-nitrosonornicotine (NNN), 4-(N-methyl-N-nitrosamino)-1-(3-pyridyl)-1-butanone (NNK)  
 38 and N-nitrosoanabasine (NAB), as well as the volatile nitrosamines N- nitrosodimethylamine  
 39 and N-nitrosodiethylamine, have been detected in the saliva of chewers of BQ with tobacco.  
 40 Chemical products of smokeless tobacco is nicotine, nitrosamines, nitrosamine acids  
 41 ,polycyclic aromatic hydrocarbons(PAHS), aldehydes and metals.Tobacco specific  
 42 nitrosamines are formed from alkaloids during the processing of tobacco leaves. The average  
 43 consumption in regular users of snuff is about 10-15 g per day. In general the snuff is kept in  
 44 the oral cavity for several hours per day.<sup>6</sup>

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## 47 **Terminology and Definitions-**

48 Precancerous Lesion can be defined as a benign lesion with morphologically altered clinical  
49 or histopathological tissue which has greater than normal risk of containing microscopic  
50 focus of cancer or of transforming into malignant lesion after diagnosis at a later date.

51 Precancerous Condition can be defined as a disease or patient habit which does not  
52 necessarily alter the clinical appearance of local tissue but is known to have a greater than  
53 normal risk of precancerous lesion or cancer development.<sup>7</sup>

54 Following are the smokeless tobacco induced oral premalignant lesions-

## 55 **TOBACCO POUCH KERATOSIS:**

56 Tobacco pouch keratosis is a „“white keratotic oral mucosal changes „“ resulting from  
57 chronic use of smokeless tobacco. It is only seen where the mucosa is in direct contact with  
58 snuff or chewing tobacco and it is also called as snuff dippers keratosis and smokeless  
59 tobacco keratosis. Most common area of involvement is the anterior mandibular vestibules  
60 followed by the posterior vestibules. The surface of mucosa appears white corrugated or  
61 wrinkled area where the tobacco has been placed.<sup>8</sup> The white tobacco pouch may become  
62 leathery or nodular in long-term heavy users. The histopathologic appearance of smokeless  
63 tobacco keratosis is not specific. Squamous epithelium is hyperkeratinized and acanthotic  
64 (Thickened spinous layer with or without intracellular vacuolization or “edema” of glycogen-  
65 rich superficial layer.<sup>9</sup>



66

67 **Fig. 1-** Tobacco pouch keratosis on lower labial vestibule

## 68 **LEUKOPLAKIA**

69 Leukoplakia is defined as “A white plaque of questionable risk having excluded (other)  
70 known diseases or disorders that carry no increased risk for cancer”. It should be realized that  
71 there are several white lesions, including amalgam associated leukoplakic or lichenoid  
72 lesions, that cannot always be clearly distinguished from leukoplakia and yet may carry an  
73 increased risk of malignant transformation.<sup>10,11</sup>

74 Clinically, leukoplakia can be subdivided in a homogeneous type (flat, thin, uniform  
75 white in colour) and a non-homogeneous type. The non-homogeneous type has been defined  
76 as a white-and-red lesion (“erythroleukoplakia”), that may be either irregularly flat  
77 (speckled) or nodular. Verrucous leukoplakia is yet another type of non-homogeneous  
78 leukoplakia. Although verrucous leukoplakia usually has a uniform white appearance, its  
79 verrucous texture is the distinguishing feature from homogeneous (flat) leukoplakia.

80 Proliferative verrucous leukoplakia (PVL) is a subtype of verrucous leukoplakia, being  
81 characterized by multifocal presentation, resistance to treatment and a high rate of malignant  
82 transformation.<sup>7</sup>

83 Histopathologically, a distinction can be made between dysplastic and non-dysplastic  
84 leukoplakia. There may be considerable intra- and interobserver variation among pathologists  
85 in the assessment of the presence and the degree of epithelial dysplasia. Verrucous  
86 leukoplakia may show a spectrum of histopathological changes, ranging from hyperkeratosis  
87 without dysplasia to verrucous hyperplasia and verrucous carcinoma.  
88 An annual malignant transformation rate of approximately 1% is probably a realistic figure  
89 for all types of leukoplakia together.<sup>7</sup>

## 90 **ERYTHROPLAKIA**

91 Erythroplakia is defined in a similar way as leukoplakia, being a “A fiery red patch that  
92 cannot be characterized clinically or pathologically as any other definable disease”.<sup>10</sup> Instead  
93 of a patch, the clinical appearance is often a flat or even depressed erythematous change of  
94 the mucosa; for that reason the term ‘erythroplasia’ may be more appropriate. In case of a  
95 mixture of red and white changes such lesion is categorized as non-homogeneous leukoplakia  
96 (‘erythroleukoplakia’). Tobacco and alcohol use are considered important aetiologic factors.  
97 Reported prevalence figures vary between 0.02% and 0.83%.<sup>12</sup> Erythroplakia mainly occurs  
98 in the middle aged and the elderly, usually in a solitary fashion. This solitary presentation is  
99 often helpful in clinically distinguishing erythroplakia from erosive lichen planus and  
100 erythematous candidiasis, since these lesions occur almost always in a bilateral, more or less  
101 symmetrical pattern. Histopathologically, erythroplakia commonly shows at least moderate or  
102 severe dysplasia. Probably by far the majority of erythroplakias will undergo malignant  
103 transformation.

**ORAL SUBMUCOUS FIBROSIS:**

OSF is predominantly caused by the use of areca nut and also occurs in association with smokeless tobacco habit. Besides being regarded as a precancerous condition; it is a seriously debilitating and progressive disease. Marked by stiffening of the oral mucosa and development of fibrous bands, loss of elasticity of the mucosa results in a progressive restriction of mouth opening. Affected users experience a burning sensation of the oral mucosa, occasional mucosal ulceration, a peculiar marble-like blanching of the mucosa and palpable fibrous bands of the buccal mucosa, soft palate. Oesophageal subepithelial fibrosis, an extension of oral submucosal fibrosis, was seen more frequently in patients who had consumed pan masala, gutka, areca nut, tobacco or a combination of some or all of these, with or without betel leaf. Characteristics of Oral Submucous Fibrosis are palpable fibrous bands in buccal mucosa and soft palate, tough, leathery texture of the mucosa, blanching of the mucosa (defined as a persistent, white, marblelike appearance of the oral mucosa, which may be localized, diffuse or reticular), accompanied by histopathologic features characteristic of OSF (atrophic epithelium with loss of rete ridges and juxta-epithelial hyalinization of the lamina propria and the underlying muscle).<sup>6</sup>



122 Fig 2- Oral Submucous fibrosis with reduced mouth opening and blanching on palate and  
123 buccal mucosa

## 124 **Conclusion:**

125 The oral mucosal lesion is generally influenced by the person's specific quid habits, and there  
126 seems to be a significant relationship between quid cessation and a decrease in the incidence  
127 rate of white lesions. No specific test is available to confirm whether a particular oral lesion  
128 was caused by the patient's quid habit. The diagnosis must be made on the basis of a history  
129 of repeated exposure to betel quid containing certain ingredients, the clinical appearance and  
130 the texture of the tissue. Incisional biopsy is recommended, specifically biopsy of the most  
131 severely affected area to rule out squamous cell carcinoma.

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