Tobacco role in the etiology of precancerous lesions

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Abstract

The use of tobacco and tobacco smokeless has increased and has been associated with oral leukoplakia and other precancerous oral lesions. The presence of leukoplakia in adolescent users of smokeless tobacco is related to years of use, frequency of use, and amount used. Malignant transformation may occur in 0,5% to 6,2% of individuals and is expected to increase with years of use.

Key words: tobacco, oral premalignant lesions.

Introduction

American aborigines used Tobacco mixed with spices and other plants; this mixture was inserted into a primitive pipe that they called tobaga and then smoked.

These aborigines used tobacco for medicinal and religious purposes. Aztecs chewed tobacco leaves to treat toothaches and aborigines of North America mixed tobacco leaves with seashells and lime for the same purpose. Inhaled tobacco was also used to induce hallucinations. Apparently these Indians used the tobacco species nicotiana rustica, which has a high content of nicotine as well as other alkaloids as opposed to the species, used presently, nicotiana tabacum, in the production of cigarettes and other forms of tobacco. According to some historians the aborigines also believed that tobacco could cure stomach ailments as well as headaches. American Indians rubbed tobacco juice on the wound produced by snakebite in order to treat it. Historical reports are not in agreement as to who was the first to introduce tobacco to Europe. Some maintain that Columbus brought seeds back after his first trip while others assume that Juan Ponce de Leon was the first to bring tobacco seeds to Europe in 1496 at his return from America on the second trip of Columbus. It is also stated that Columbus might have been the first European to oppose the use of tobacco because it is said that he admonished his sailors for engaging in the practice of inhaling tobacco smoke imitating the American Natives. Posterior explorers, especially the Portuguese, possibly recognized the potential of this "holy herb" and tobacco was fully introduced to Europe as a medicinal plant. Sir Walter Raleigh brought tobacco seeds to England after his second trip to America in 1565.

General statistic

Thirty percent of all cancer deaths and over 80% of lung cancer deaths are caused by tobacco.

The same report states that 48 million US adults smoke cigarettes and half of those will die of smoking related disease if they continue smoking. Hoffmann and Djordjevic in 1997 reported that the habit of chewing tobacco had declined by 30.6%, but that snuff use had increased, by almost 52%. The increase was due, primarily, to the use of oral snuff by teenage and adolescent males. Chewing of tobacco represents a risk of oral cancer. Snuff dipping is considered as one of the etiological factors of OSCC of the cheek, gingiva, and pharynx.

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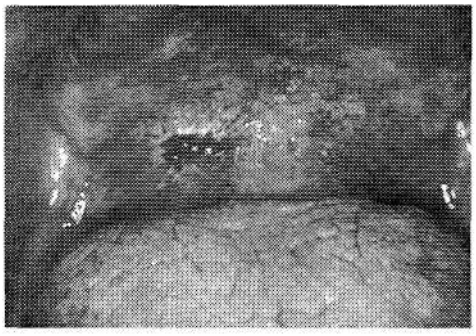
Tobacco and premalignant lesions

WHO defines a precancerous lesion as "a morphologically altered tissue in which cancer is more likely to occur than in its apparently normal counterpart". It may precede or co-exist with the carcinoma. It is more correct to consider it as a "lesion with malignant potential", because its evolution is not always to cancer, but the high degenerative risk impose a long and careful follow-up. The most common precancerous lesions of the oral mucosa are leukoplakia (white plaque) and erythroplasia (red patch). It should be stated that not all white or red oral mucosal lesions are precancerous but because of the possibility of having a premalignant potential, all of them should be carefully evaluated and if deemed necessary, a biopsy should be performed.

1. Erythroplasia (Bowen's Disease, Erythroplakia, Carcinoma in situ, Red, macular squamous cell carcinoma). It is considered a premalignant process that ultimately leads to carcinoma of the oral mucosa. The etiology is unknown and the lesion probably has the same causative factors as cancer does. Shafer and Waldron (1975) reported that the peak age of occurrence fell in the 50s and 60s. It is seen more frequently to the great smokers and alcohol drinkers.

Figure 1. Area of ulceration that is surrounded by areas of white coloration (reverse smoking)



Erythroplasia is a red lesion of the oral mucosa with no apparent cause. Erythroplasia also should be carefully evaluated especially if there is history of tobacco usage.

Erythroleukoplakia is a frequent combination of white and red lesions. These combined lesions have four times the potential for malignant transformation than that of a plain white or red lesion and because of this increased risk invariably they should be biopsied.

Erythroplasia appears as velvety red or granular red maculae (patch) that may be slightly raised. The lesion is painless and varies greatly in size; the borders may be either well circumscribed or may blend imperceptibly with the surrounding, normal mucosa. The small lesions are easily overlooked, but the chances for their detection are greatly enhanced by first drying the mucosa with a gauze since this intensifies the red color. Two different clinical appearances have been described:
atrophic (homogenous) form which is completely red in appearance;
hypertrophic form in which small leukoplakic specks are scattered over an area of erythroplasia. Numerous white spots or plaques are noted in or peripheral to the erythematous lesion (speckled erythroplasia).

The floor of the mouth, retromolar area, mandibular alveolar mucosa, and mucobucal fold are the most common sites of involvement.

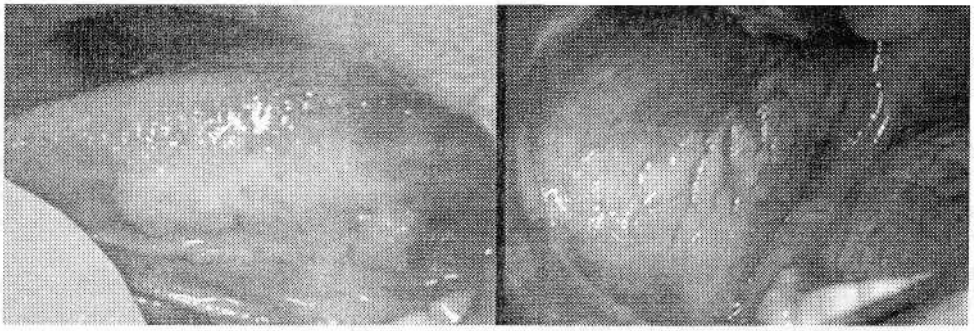
2. Leukoplakia

Is the most common and best-studied precancerous lesion. Leukoplakia is a diagnosis by exclusion, and the term is now used in a clinical descriptive sense. Pindborg defines it as "a white patch or plaque, not smaller then 5 mm, firmly attached to the oral mucosa (cannot be scrapped off with a tongue blade), that cannot be classified clinically and pathologically in any other disease entity. Some of these white lesions can be a consequence to trauma and histologically are diagnosed as hyperkeratosis. In such cases there is a history of trauma or a direct relationship of the white lesion with a broken denture or a broken tooth. Leukoplakia is also found in the oral mucosa of some heavy smokers. The direct relationship of leukoplakia and tobacco smoking has not been proved but it is most certainly a by-product of chewing tobacco *(Figure 2).*

A particular form of leukoplakia known as proliferative verrucous leukoplakia (PVL) also can be associated to tobacco usage *(Figure 3).* Around 1/3 of PLV are diagnosed in heavy smokers. PVL has a higher risk of malignant transformation than the most common non-verrucous leukoplakias. The hystologic form of speckled leukoplakia is four to five times more likely to result in malignant transformation than homogenous leukoplakia.

Snuff Pouch (SP) is a form of hyperkeratosis with various degrees of clinical manifestation. SP develops on those mucosal sites where the tobacco is held. The causal agents of SP are considered to be the nitrosamines and hydrocarbons contained in tobacco. Prolonged use of this habit

Figure 2. Leukopiakia on a non-smoker patient and Leukopiakia on a heavy-smoker patient. Note the elevated and nodular appearance of the buccal mucosa lesion



may conduce to the development of a squamous cell carcinoma (see above) due to the carcinogenic potential of those components. SP has been classified clinically into three different degrees. Degree 1 SP has the color of normal mucosa presenting a minor degree of superficial early wrinkling, the wrinkles disappear when the lesion is stretched. Degree 2 SP is a combination of white-gray and reddish areas with moderate wrinkles, neither wrinkles nor colors disappear when the lesion is stretched *(Figure 4).*

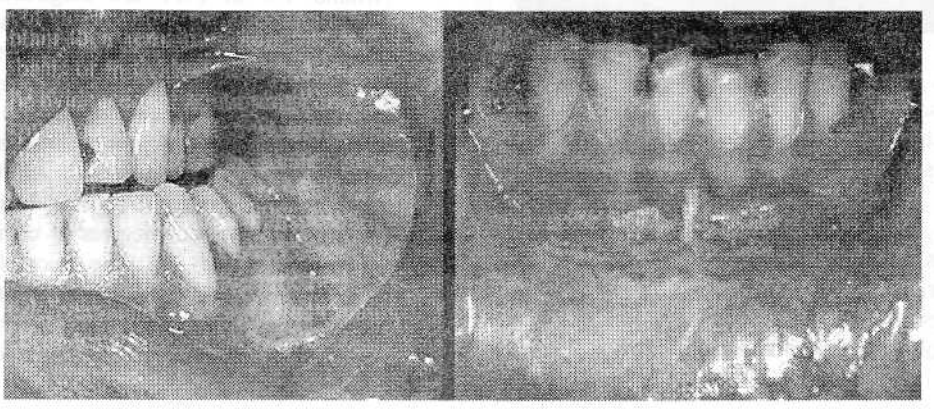
Figure 3. Proliferative verrucous leukoplakia also on the bucal mucosa of a heavy smoker

Conclusions

As a summary it can be said that any of the following statements have been proven to be true in relationship to tobacco usage and oral lesions, and that any one of them should be more than reason enough to stop smoking:

- Tobacco can induce the development of oral leukopiakia and erythroleukoplakia, which have a potential risk for malignant transformation.
- Tobacco can induce cellular changes and atypia typical of pre-malignant and frankly malignant transformation.
- » Tobacco contains carcinogenic agents.
- Patients with oral cancer use tobacco more than persons in control groups.
- Tobacco used in any form induces a high prevalence of cancer in various oral sites.

Figure 4, Thse are two examples of snuff pouches. To the left a Degree 1 and to the right a Degree 2.



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