

RECENT DATA ON IN THE INCIDENCE, PREVALENCE AND ETIOLOGY OF THE ORAL LEUKOPLAKIA

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REZUMAT

Leucoplazia este o leziune precanceroasă de mare relevanță în patologia orală. Articolul revizuire date recente din literatura de specialitate asupra leucoplaziei, cu accent asupra rolului etiologic al unor factori precum igiena orală, asocierea cu boli sistemice precum diabetul zaharat, asocierea cu hepatitele B și C. Prevalența transformării maligne a leucoplaziei orale este descrisă după date recente. Sunt incluse date epidemiologice și histopatologice asupra leucoplaziei păroase asociate cu SIDA. Recenzia este completată cu date epidemiologice recente asupra corelației leucoplaziei cu fumatul. Se subliniază rolul medicului dentist generalist în detectarea precoce a leucoplaziei orale și a tendinței de malignizare a afecțiunii.

Cuvinte cheie: leucoplazie orală, epidemiologie, etiologie

ABSTRACT

Oral leukoplakia is a precancerous lesion of great importance in oral pathology. The article reviews recent data from the literature on oral leukoplakia, with emphasis on the etiological role of the oral hygiene, the association with systemic disorders such as diabetes mellitus, viral infections like C and B hepatitis. The prevalence of the malignant transformation of oral leukoplakia as reflected in recent literature is described. Current epidemiological and histopathological data on AIDS-related oral hairy leukoplakia are included. The review is completed by recent epidemiological data on the correlation of leukoplakia with smoking habits. The role of the general dental practitioner in the early detection of oral leukoplakia and its malignant transformation tendency is underlined.

Key Words: oral leukoplakia, epidemiology, etiology

INTRODUCTION

Premalignant lesions of the oral mucosa are areas of morphologically altered tissue in which cancer can arise.¹ Oral leukoplakia (OL) has been defined as a white patch or plaque that cannot be characterized clinically or pathologically to belong to any other disease. Smoker's palate (leukokeratosis nicotina palati) cheek and lip biting, frictional white lesion and snuff dipper's lesion should not be considered leukoplakia.²⁻⁴

Various terms have been used to describe these lesions, and diagnosis is often made by exclusion. It is suggested that a proportion of lesions diagnosed as premalignant are actually reactive and for this reason the term "potentially premalignant" is often used when considering leukoplakia and erythroplakia.¹⁻⁵ Various definitions of OL have been proposed, but it is essentially a predominantly white lesion that cannot be characterized as any other definable lesion.^{1-4,6-9} It has been shown that most carcinomas develop from leukoplakias on the lateral borders of the tongue or in the floor of mouth, being referred to as "high-risk" sites.¹⁰⁻¹⁴

Leukoplakia is frequently found on the oral mucous membrane, and sometimes affects genital mucous membranes.

The etiology involves a series of general and local factors. General factors include: hormonal disorders, diabetes, the A hipovitaminosis, syphilis and malnutrition. Local factors include: smoking, alcohol,

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as well as a series of physical factors (biocurrents), mechanical factors (trauma, the incorrect prosthetic bridges, sharp edged teeth) and chemical factors (medicinal, irritant and toxic substances). Poor oral hygiene practices are also significantly associated with the development of OL.¹⁵ The studies have shown that poor oral hygiene habits seem to potentiate the effect of smoking tobacco in developing OL.

Among systemic associations of OL, it was found that its prevalence in diabetes mellitus patients was higher than the average ratios in Hungarian population samples, and OL showed the highest occurrence in the second year of established diabetes, with higher prevalence in insulin-treated patients.¹⁶ Concerning the association of OL with virus infections, a study on 73 Serbian patients with histologically proven OL and 90 controls showed that patients with OL do not have evidence of hepatitis C or B infections.¹⁷ According to other findings, the human papillomavirus may be a specific risk factor for the development of oral premalignant lesions, such as OL.¹⁸

OL is a precancerous or potentially malignant lesion, which means that in this morphologically altered tissue, cancer is more likely to occur than in its apparently normal counterpart.⁷⁻⁹ The frequency of malignant transformation in OL varies between 0 and 20%, during an observation period of 1 to 30 years.^{7,10,11} It is more or less accepted as an overall statement that approximately 5% of all leukoplakias will transform into cancer in an average period of 5 years. Recently, predictor gene sets to provide multigene classifiers for the diagnosis of precancerous to cancerous transition of oral malignancy in OL were identified.¹⁹ In limited case series, DNA-ploidy proved as effective as histopathology in predicting the site of transformation of proliferative verrucous leukoplakia towards squamous carcinoma.²⁰ OL patients who show p53 (tumor suppressor gene, one of the molecular targets of smoking-related carcinogens in oral cancer) expression have a higher risk of developing tongue cancer than those who don't show p53 expression.²¹ Heat shock proteins (HSP70 and HSP27) as objective markers of epithelial dysplasia in OL have been recently described.²²

A definitive clinical diagnosis of OL is made as a result of the identification, and - if possible - elimination of suspected etiologic factors and, in case of persistent lesions (no signs of regression within 2-4 weeks), histopathological examination.^{9,11}

The clinical diagnosis of OL is based on the criteria issued by the WHO and modified by Axell, including the clinical distinction between the homogeneous and

non-homogeneous type of leukoplakia.^{6,7} Recently, oral lumenoscopy (ViziLite) has proved effective in visualizing oral mucosal lesions – white lesions and lesions that were both red and white showed enhanced brightness and sharpness.²³ Advances in techniques for detecting premalignant lesions and predicting their progression or recurrence include vital tissue staining with toluidin blue and exfoliative cytology.²⁴ One must remember that leukoplakia is a diagnosis by exclusion and the term should be used as a clinical diagnosis only, as about 5% of the cases progress to cancer in a mean observation period of 5 years.²⁵

The value of the oral cancer screenings has become important as a consequence of the lack of improvement in the long-term outcomes associated with oral carcinoma over the past decades. The dentist must mark the distinction between reactive lesions (usually change over one- to two weeks) and malignant and premalignant lesions, which do not change, so that biopsy of the lesion must be undertaken as a standard procedure in the evaluation of a lesion of a latter kind.²⁶

CURRENT DATA ON AIDS-RELATED ORAL HAIRY LEUKOPLAKIA

Oral hairy leukoplakia (OHL) is one of the most common oral manifestations in AIDS, with an important diagnostic and prognostic value. The disease was first observed in 1981 and reported in 1984 and initially the entity was restricted only to seropositive HIV-male homosexual patients, but the risk group has been expanded since 1986 to all patients infected with HIV.²⁷ The typical OHL lesions are caused by the Epstein-Barr virus and are highly predictive for the development of AIDS. The co-infection with multiple strains of replicating Epstein-Barr virus was recently documented in OHL.²⁷ The prevalence of clinical OHL in 120 pediatric patients infected with HIV-1 was 1.67%, while the cytopathology revealed subclinical cases of OHL in 16.7% of the cases, suggesting that in pediatric patients the prevalence of OHL may be larger than described in the literature.²⁸ The histopathological characterization of subclinical OHL was made in a study from 2001, which found the absence of parakeratosis and papillomatosis, mild acanthosis, ballooning cells and nuclear alterations.²⁹ Data on the prevalence of OHL in adults were collected for the first time in Southern Australia in a study from 2001.³⁰ According to the study, the prevalence of OHL in South Australian HIV-infected patients was 45.2%, comparable with the results of other studies.

RECENT EPIDEMIOLOGICAL DATA ON CORRELATIONS OF LEUKOPLAKIA WITH SMOKING HABITS

Numerous recent studies attempted epidemiological approaches in various communities around the globe. In a retrospective study, the charts of 91 patients with OL registered at the Department of Oral Surgery and Stomatology of the University of Berne from August 1995 to December 2001 were analyzed.³¹ The 91 patients included had a total of 145 leukoplakia lesions. The gender distribution corresponded to 39F/52 M, with an age peak range of 50-59 years, and 66 patients were smokers. Of 52 biopsies, 3 were histologically confirmed to be a carcinoma in situ. In the same service, a study on 258 new patients with oral soft tissue lesions, undertaken in 2003, identified 41 cases of precancerous lesions, out of which 11 were OL, and ten patients had oral malignancies.³²

From 1995 to 1998, an annual screening for cancer and precancer took place in Municipal Health Centers in Tokoname, Japan.³³ The screening engaged 9,536 volunteers aged 45-90 years. In this study, the age-adjusted incidence rate for leukoplakia was 409.2 in male and 70.0 in female per 100,000 person-years observations. The prevalence of smoking in positive OL diagnoses (39.8%) was higher compared with the negative diagnoses (n.s.).

A comparative study of oral lichen planus and OL in two Argentine populations revealed an incidence of 418 leukoplakia cases out of 4,838 patients investigated in both populations.³⁴ The population with a larger percent of smokers presented a larger amount of OL.

In a cross-sectional study assessing a total of Iranian 1,167 textile factory workers randomly selected from a total of 6,947, 43 positive detections (3.7%) had leukoplakia, and a statistically significant positive correlation between tobacco smoking and OL was found ($p < 0.001$), even in the relatively young cohort with generally mild tobacco use that was investigated.³⁵ The possible clinicopathologic differences between OL in current smokers and never-smokers were evaluated in a study carried out in the Department of Oral Surgery and Oral Medicine of the University of Santiago de Compostella, Spain.³⁶ This retrospective study compared 41 current-smoking patients with 11 never-smoking patients and found that nonsmoking-related leukoplakia lesions are more frequent among women than among men, and they are more likely to be located on the tongue than smoking-related lesions. Interestingly, dysplastic lesions were observed most frequently in the never-smoking patients ($p = 0.026$).

When the tobacco usage was analyzed in relation to the anatomical site of OL, clinical data collected in a study carried out at ACTA showed that leukoplakias in the floor of the mouth appeared to be statistically significantly more often present in smokers than in non-smokers, compared to all other oral sites.³⁷ By contrast, leukoplakias on the borders of the tongue were found to be statistically more common among non-smokers than smokers, when compared to all other sites in the mouth.

There is evidence to suggest that smoking cessation in leukoplakia reduces the malignant transformation risk, and appropriate intervention is advised.⁵⁻⁷

CONCLUSIONS

The role of the dentist in detecting and diagnosing leukoplakic lesions is fundamental, as leukoplakia has a high potential of malignant transformation and may develop carcinomas with a severe evolution.

Spending a few moments discussing with the patients the overall benefits of giving up smoking might be considered as efficient anti-smoking interventions.

The ability to identify OL in patients with increased risk of cancer development is critical for improving control of the oral cancer. Once identified, the highest risk individuals could be offered more aggressive treatment options and more intensive follow-up.^{13,14}

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