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MALIGNANT TRANSFORMATION OF ORAL LEUKOPLAKIA – A REVIEW

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ABSTRACT Oral Leukoplakia is one of the most common oral premalignant lesions and defined as white patch or plaque that does not rub off clinically identified as another entity. Etiological factors are smoking, viral and fungal agent and specific nutrients and deficiency may have role in the development and progression. Clinically it can be classified as homogenous and non-homogenous. It most seen on buccal mucosa and lateral border of tongue. Malignant transformation of oral leukoplakia is about 5-18%. A higher chance of it transformation has been seen in non-homogeneous, high risk anatomic structures such as the floor of the mouth or the tongue, as well as a history of non-smoking. It can be diagnosed by biopsy, toluidine blue staining or lugol s iodine and exfoliative cytology. Management is surgical excision, cryosurgery, CO2 laser, retinoids, photodynamic therapy.

KEYWORDS : Oral Leukoplakia, malignant, smoking, cytology, surgical exicison.

INTRODUCTION

Precancerous lesion is a benign morphologically altered tissue that has a greater than normal risk of malignant transformation. Precancerous lesions can grow into some forms of cancer, but early detection and prompt treatment of these lesions can save them from becoming cancerous. Oral leukoplakia is noted to be the most common premalignant lesion of the oral mucosa [1] and it is crucial to describe its histological and clinical features. However, the mechanism of malignant transformation remains unknown. In this review, we concentrate on the connection between oral leukoplakia's clinical and histological traits and its malignant development. Leukoplakia is recognized by two forms: Homogeneous and the non-homogeneous type. In contrast to non-homogeneous leukoplakia, which is a mixture of white and red lesions that may be irregularly flat, nodular, or verrucous, homogeneous leukoplakia has a predominately white lesion that is uniform flat, thin, and smooth across the lesion. [2] Typical histologic findings in leukoplakia include epithelial hyperplasia, hyperkeratosis, and epithelial dysplasia or carcinoma.[3] The pooled estimate of the annual rate of OL malignant transformation is 5-18%. Some clinical traits, such as lesion shape, size, and placement, dysplasia, and cigarette use, may be linked to increased malignant potential.

Terminologies

Axéll (1996) states leukoplakia as a white patch measuring 5 mm or more which cannot be scrapped off and cannot be attributed to any other diagnostic disease.[4] As per the International Symposium, Uppsala, Sweden (1996): It is "a predominantly white lesion of the oral mucosa that cannot be characterized as any other definable disease." The WHO (1997) described leukoplakia as "a predominantly white lesion of the oral mucosa that cannot be characterized as any other definable lesion."[5] 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"[6]

Epidemiology

In a 10-year prospective research in India of large random samples from diverse geographic locations with varying types of tobacco use, the yearly incidence rates of leukoplakia were one thousand population per year varied from 1.1 to 2.4 among men and from 0.2 to 1.3 among women; the prevalence varied from 0.2 to 4.9%. [7] In an adult Swedish population, a 3.6% prevalence rate was recorded[7]. Leukoplakia typically develops after the age of 30, with a peak incidence occurring over the age of 50[8].

Etiopathogenesis

According to epidemiological research, smokers have a 5-9 times higher chance of acquiring oral cancer than non-smokers.[9-11] Roed-Petersen et al. and Daftary et al. (1972) found that the role of Candida in correlation with the clinical types and histological dysplasia's[12] and the concurrent existence seemed to play a role in malignant transformation (25.9%).[13] Bánóczy observed statistically significant decrease in serum levels of Vitamin A, B12, C, beta carotene, and folic acid in patients with oral leukoplakia. Mutations of p53 in the cells from dysplastic areas of leukoplakia who smoke and drink heavily.[14] Caldera et al. found a high-risk factor of leukoplakia for malignant transformation is the infection with human papilloma viruses as oncogenic proteins such as HPV-16L1 can promote carcinogenesis.[15]

Clinical Features

Leukoplakia usually presents as a single or multiple lesions, localized change of the oral mucosa. Clinically leukoplakia can be classified homogeneous and the non-homogeneous type.[2] Axéll et al. (1996) found that leukoplakia was commonly present in buccal mucosa (76%), alveolar sulcus (19%), and tongue (5%).[4] Brouns et al. found the location of the Oral leukoplakia were present on Tongue, Floor of the mouth, lower

lip, hard palate, buccal mucosa, upper alveolus and gingiva, lower alveolus, and gingiva and finally in multiples sites.[16]

Malignant Transformation Of Leukoplakia

The lesions and conditions that are considered precancerous or pre-malignant are now referred as oral potentially malignant disorders – OPMD. Of these conditions, most encountered OPMD is oral leukoplakia. Warnakulasuriya et al. were listed as a risk for malignant transformation in PMD.[6]

1. Female gender
2. Long duration of leukoplakia
3. Leukoplakia in non-smokers (idiopathic leukoplakia)
4. Location on the tongue and/or floor of the mouth
5. Size >200 mm2
6. Non-homogeneous type
7. Presence of C. albicans
8. Presence of epithelial dysplasia

Lind et al reported that females were more prone to endure malignant transformation and epithelial dysplasia .[17] Yet, some studies discovered a higher risk of malignant transformation among males in India, particularly in connection with smoking and chewing tobacco use [18] the incidence of malignant transformation from leukoplakia increases with time. The Mean malignant transformation rate increased by 7-fold from 5th year of leukoplakia when compared to first 5 years. Patients with a higher number of lesions were at greater risk of developing carcinomas [19]. Martorell-Calatayud et al. found that leukoplakia situated in the ventrolateral area of the tongue and on the floor of the mouth, with a 43% average transformation rate. This is attributed to the fact that these areas are more exposed to carcinogens in Salivary secretions and that the epithelium is more permeable in this area.[20] some studies identified the buccal mucosa and the Labial commissure as the locations with the highest malignant transformation rate,[21,] but this is particularly true of patients with Tobacco chewing and smoking habits. Increase in the risk of malignant transformation in non-homogenous leukoplakia as compared to homogenous leukoplakia.[22] Among the three clinical manifestations of non-homogeneous leukoplakia, erythroleukoplakia had a much greater rate of malignant development. On study noted that dysplasia was higher in Oral Leukoplakia lesions infected with Candida (55.9%)[23]. An aggressive kind of leukoplakia known as proliferative verrucous leukoplakia carries a significant chance of developing into verrucous or OSCC. The severity of oral epithelial dysplasia is currently used as the gold standard for predicting malignant transformation in oral leukoplakia. In a Dutch study [24] Oral Leukoplakia diagnosed with moderate or severe epithelial dysplasia had a significantly higher risk of malignant development. HPV is detected frequently in oral dysplasia lesions and carcinoma, and is well known to be an independent risk factor for oral cancer[25]. A correlation between high macrophage infiltration and M2 polarization with histomorphology parameters of tumour progression and inferior outcome in early stage OSCC was already shown [26].

Histopathology

The various cellular changes that may occur in epithelial dysplasia are Kramer et al. 1. Loss of polarity of the basal cells 2. Presence of more than one layer of cells having a basaloid appearance 3. Increased nuclear-cytoplasmic ratio 4. Drop-shaped rete processes 5. Irregular epithelial stratification 6. Increased number of mitotic figures 7. Presence of mitotic figures in the superficial half of the epithelium 8. Cellular pleomorphism 9. Nuclear hyperchromatism 10. Enlarged nucleoli 11. Reduction of cellular cohesion 12. Keratinisation of single cells or cell groups in the prickle layer[27.] A change in the micro vascularization, a rise in the quantity of subepithelial lymphocytes, plasma cells, Langerhans cells, and interepithelial cells, as well as the presence of Candida organisms, are some of the additional dysplasia indications. Epithelial dysplasia is typically categorised into three ranges based on the presence of dysplastic features: mild, moderate, and severe [28]. it is recommended that the histological report of a leukoplakia should include absence or presence of epithelial dysplasia and an assessment of its severity.[29] The location of oral leukoplakia has a correlation with the dysplastic or malignant changes at biopsy. In the study by Waldron and Shafer, the floor of mouth was the highest-risk site (42.9%), followed by the tongue (24.2%) and lip (24.0%) [30] the thicker leukoplakia, the greater the chance of locating dysplastic changes; therefore, verrucous leukoplakia show more dysplasia.[29]

Diagnosis

Before accepting a firm clinical diagnosis of leukoplakia in a patient with a white lesion of the oral mucosa, the clinician will first attempt to rule out any other clearly identifiable white lesions. If symptoms are evident, the biopsy should be performed at the site of redness or induration. Biopsies of exophytic, verrucous or papillary lesions should be taken deep enough to include enough underlying connective tissue, and preferably from the margins. Diagnostic methods other than histological examination, such as the use of toluidine blue staining or Lugol's iodine, and exfoliative cytology [2]. Precancerous lesions and early oral malignancies are frequently inconspicuous and asymptomatic. Consequently, it's crucial for the physician to keep a high level of scepticism, particularly if there are risk factors like tobacco use or alcohol misuse. Clinically discernible premalignant alterations of the oral mucosa frequently precede invasive oral squamous cell carcinoma. These lesions present as either white or red patches. The patient can detect a non-healing ulcer as the cancer progresses. Bleeding, loosening of the teeth, dysphagia, dysarthria, odynophagia, and the formation of a neck mass are later-stage symptoms. The best and most reliable way to diagnose a suspicious lesion is still with a traditional biopsy using a scalpel or small biopsy forceps. PET scans are also becoming an increasingly popular tool for the identification of primary, recurrent, and metastatic disease.

Treatment Plan

The primary goal of treating white oral lesions is to eradicate any potential contributing factors, e.g. friction, C. albicans, thus ruling out other definable lesions. Apart from the surgical excision, various treatment modalities are available, such as cryosurgery, CO2-1aser surgery, retinoids and other drugs, and recently photodynamic therapy Surgical excision. surgical removal has been advised as the best course of treatment for oral leukoplakia. Oral leukoplakia can be effectively treated with vitamin A. Disadvantage of vitamin A and its derivates is its toxicity, necessitating reduction of the dose or temporary abstinence of the drug. Beta-carotene and vitamin E are considerably less toxic than 13- cis-retinoid acid. The major drawback for most current agents is the recurrence of lesions when treatment is discontinued.[2] Ramanathan et al. suggested that the candida-associated leukoplakia may respond to topical antifungal agents including imidazoles.[31] Lamey et al. (1994) reported an OL with epithelial dysplasia that resolved within 11 days of systemic treatment with fluconazole antifungal agent.[32] Lodi and Porter showed that CO2 LASER vaporization showed maximal while CO2 LASER evaporation showed minimal recurrence of leukoplakia. However, cryosurgery and conventional blade surgery showed up to 22% and 13% recurrence rates, respectively.

CONCLUSION

The chance of malignant transformation is higher in oral leukoplakia, when compared to other OMPDs. To avoid these complications, the treatment phase should be started in the initial stage.

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