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Malignant Potential of Oral Lichen Planus

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ABSTRACT:

Although these findings remain debatable, numerous research have revealed that a lesion initially identified as oral lichen planus (OLP) has a variety of possible malignant transformations over time. For instance, some studies have found varying OLP malignancy potential values. OLP is categorised by the World Health Organization (WHO) as a "possibly malignant condition" with an undetermined risk of malignant transformation, and it is advised that OLP patients be closely watched. The possibility of OLP undergoing malignant transformation has been investigated extensively. In the literature, there is ongoing discussion over the possibility of OLP developing malignant transformation. According to some experts, only OLLs (oral lichenoid lesions), not OLP, are premalignant in character and should be classified as "other dysplastic disorders" because of this. Furthermore, OLP patients have been observed to have a number of occurrences, such as multifocal dysplasia and/or oral squamous cell carcinoma, in the following years, raising the possibility of field cancerization in OLP.

Keywords: Oral lichen planus; Oral lichenoid lesions; Oral lichenoid reactions, oral cancer, Lichenoid, dysplasia, Malignant transformation.

INTRODUCTION

Oral lichen planus (OLP) has traditionally been seen as an autoimmune illness with chronic inflammation. It is a mucocutaneous condition that can simultaneously affect the scalp, skin, nail, and vaginal mucosa. All races and both sexes are affected by OLP, which has an incidence rate in the general population that ranges between 1 and 2% but is more prevalent in women. 70% of the affected females are between the ages of 30 and 60. Children can occasionally develop oral lichen planus [1]. Although new findings have demonstrated that immunological pathways may play a role in the etiopathogenesis, serve as a significant cause or contributing component. It is generally recognised that oral erythroplakia and leukoplakia are precancerous lesions[3].

Lesions in other sites are uncommon in the majority of OLP cases. OLP affects anywhere between 0.5% and 2.6% of people worldwide. The potential for OLP to develop into oral squamous cell carcinoma is one of the most crucial questions surrounding it (OSCC). The diagnostic criteria for OLP are part of this contentious topic and need more discussion. This article reviews OLP's differential diagnosis and malignant transformation[2].

Etiopathogenesis

1. Cell mediated Immunity

Although precise cause of OLP is still unknown, mounting evidence points to cell-mediated immunity as a crucial player in the disease's pathogenesis. A biological procedure is thought to be brought on by an antigen that changes the oral mucosa's basal keratinocytes. Systemic medicines, contact allergens in tooth restorative materials, mechanical trauma, bacterial or viral infection, or unexplained factors can all cause keratinocyte antigen expression[4]. Tumor necrosis factor (TNF)-alpha, which is secreted by activated CD8+ T lymphocytes and binds to the TNF-alpha receptor on keratinocytes, triggers keratinocyte apoptosis through the caspase cascade pathways[5].

The local response also involves mast cells and antigen-presenting Langerhans cells. In OLP, activated chymase, which is generated by mast cell degranulation, functions as a matrix metalloproteinase that breaks down the extracellular matrix of basement membrane and promotes lymphocyte migration to the connective tissues below the epithelial layer[6].

2. Association with hepatitis C virus

OLP and viral illnesses like the human papilloma virus, Epstein-Barr virus, and herpes simplex virus may be related, according to some reports[7]. HCV has received the greatest attention, yet there is still debate over its connection to OLP. While OLP and HCV have been linked in some groups, namely in the Mediterranean and Asia, this association has not been identified in other populations, such as those in Northern Europe, indicating geographic heterogeneity[8].

It is still unclear if HCV infection has a pathogenic role in OLP. The presence of HCV-specific CD4+ and CD8+ T lymphocytes in OLP lesions and the detection of HCV RNA in the mucosal lesions of individuals with the disease indicate that epithelial cells expressing HCV antigens may be targets for OLP's immunopathogenesis[9]. Clarifying the involvement of HCV in OLP pathogenesis will require additional research that takes into consideration parameters like HCV genotype, race, location, age, gender, treatment (before or after), and accessory co-infections such as candidiasis.

Clinical features

Clinically, OLP has distinct and easily distinguishable characteristics. OLPs typically have many foci and almost always have a bilateral symmetric pattern. They are a mixture of white and red lesions. The buccal mucosa is the most often impacted area, while some cases also involve the tongue, gingivae, and lower lip (in decreasing order of frequency). Palate, oral floor, and upper lip lesions are uncommon[10]. Red lesions can have an atrophic appearance, whereas white lesions have a reticular, papule, plaque-like appearance bullous-like, erosive (ulcerated), or (erythematous). The aforementioned six forms of OLP are subdivided into them: Bullous, Papule-like, Reticular, Atrophic, Erosive.

Typically, white lesions develop against a background of widespread erythema. The most frequent form of OLP, known as the reticular form, exhibits Wickham's striae, a network of thin white lines that resembles lace.

Leukoplakia-like, uniformly white spots are how plaques manifest. The buccal mucosa and the dorsum of the tongue are frequent locations for this morphology to be seen.

The next most typical type is the erosive form, which is equally important for OLP. This variety manifests as partly ulcerated, atrophic, and erythematous patches that are frequently bordered by tiny white lines. The epithelium tears when erosion is severe, as seen in the benign mucous membrane pemphigoid instance. The bullous form of this kind is quite uncommon.

The atrophic variant presents as a mucosal atrophy and a diffuse red lesion. Red lesions of both the atrophic (erythematous) and erosive (ulcerated) kinds sometimes exhibit burning or painful etching symptoms[11].

Histological characteristics

Dubreuill first reported the histology of OLP in 1906, and Shklar refined it in 1972. Shklar identified three distinguishing characteristics: (1) overlaying keratinization; (2) liquefaction degeneration of the basal cell layer; and (3) a thick subepithelial band of lymphocytes[12].

The following three discoveries were supported by the WHO diagnostic criteria from 1978.

(1) Hyperparakeratosis or hyperorthokeratosis are typically present in the keratinized layers, and they are frequently accompanied with thickening of the granular cell layer and a saw-toothed appearance of the rete pegs. In skin lesions, the saw-toothed appearance is typical; it is less common in mouth lesions. Although the epithelium's thickness fluctuates, atrophy and erosive epithelium are sometimes visible.

(2) An eosinophilic ring may frequently replace basal cell layer liquefaction degeneration.

(3) T cells make up the majority of a thick, band-like lymphocyte infiltration that is present in the lamina propria's superficial region and close to the epithelium[13].

Malignant transformation of OLP

The potential for OLP to develop into OSCC in a malignant state is one of the most significant difficulties with this condition. OLP is a precancerous condition according to the WHO, however the likelihood that it will develop into cancer is still up for debate in the literature. While some authors agree that OLP may have malignant potential, others disagree with this assertion. The premalignant potential of OLP was examined in papers from 1950 to 1978 by Krutchkoff et al. [14], but not enough recorded data was discovered to clearly support the claim that OLP is a premalignant condition.

The WHO criteria released in 2003[15] have been modified due to a lack of data to support the initial diagnosis of OLP in patients who later developed OSCC. van der Meij et al. reported that a subgroup of OLL patients with a high likelihood of developing cancer may be found by using stringent clinical and histological diagnostic criteria adopted by the WHO. Subsequent follow-up investigations have largely used strict clinical and histological diagnostic criteria, and some of these have revealed the possibility of malignancy[16].

Nonetheless, the majority of cases of OSCC linked with OLP are detected on the lateral side of the tongue, as is normal for OSCC[17]. It is interesting to note that in certain cases, OSCC has apparently developed from the plaque form of OLP on the dorsum of the tongue, which is a rare position for OSCC[18]. What mechanisms might lead to OLP's malignant transformation is unknown. Chronic OLP inflammation may result in a cytokine-based milieu that causes genetic changes in epithelial cells to develop to malignancy. These modifications include an increase in aneuploidy and loss of heterozygosity (LOH) at tumour suppressor gene loci[19].

Gonzales-Moles et al. hypothesised that incorrect OLP classification might be to blame for the high prevalence of malignant transformation seen in numerous investigations. Hence, 1% or fewer of OLP may develop into cancer[20]. According to Iocca et al., OLP had the lowest rate of malignant transformation among Oral Malignant Potential Disorders (OMPDs), which suggests that OLP does not have epithelial dysplasia. 3 (3.7%) of the 81Oral

Epithelial Dysplasia (OED) patients in this research went on to develop SCC. This incidence was significantly greater than the rate in OLP patients, indicating that OLP has a low malignant potential[21]. Lodi et al. pointed out that lesions with OLP-like clinical characteristics but dysplasia may be the first stage of OLP's malignant development. As a result, OLP with epithelial dysplasia is not included in these studies is still up for debate [22].

Michele Giuliani et al. screened 21 out of 7429 patients and included them in his review. On average, 92 out of 6,559 patients (1.40% for OLP and 2.43% for OLL) had oral squamous cell carcinoma, with an annual TR of 0.20%. The probability of transformation appears to be slightly increased by female gender, red clinical forms, and tongue site[23].

Moreover, Gonzales-Moles et al. discovered a noticeably increased incidence in participants above the age of 50 or 60. Demographics were thus indicated to be linked to the age and sex associated with the probability of malignant transformation[24]. Aghbari et al. observed that rates of malignant transformation were 1.7%, 1.3%, and 0.1% in erosive, atrophic, and reticular patterns, respectively, depending on the clinical type some studies showed that the expression of p53 and metalloproteinases (MMPs) in atrophic OLP were upregulated compared to nonatrophic OLP. Therefore, red-type OLP was suggested to have a higher malignant potential than white-type OLP[25]. The tongue (1.05%) and buccal mucosa (0.7%) were the most frequent sites, followed by the gingiva and lips (0.6%) and the floor of the mouth (0.5%).

According to Rhodus et al., OLP patients saliva included high levels of TNF-, IL-1, IL-6, and IL-8. Except from that atrophic OLP had higher levels of p53 and metalloproteinases (MMPs) than nonatrophic OLP, according to certain research. As a result, it was hypothesised that red-type OLP had a larger malignant potential than white-type OLP.

18 of the investigations by Richards, D., twenty-one patients were retrospective, and 3 were prospective. There were 6559 patients in all, 6353 of whom had OLP and 206 had OLL. The follow-up intervals were 18 to 300 months long. Throughout the monitoring period, 92 cases of oral squamous cell carcinoma appeared. The total transformation rate (TR) was 1.4%; OLP had a TR of 1.37%, and OLL had a TR of 2.43%[26].

In a case-control research by Yu-Wei Chiu, 45 normal controls and 42 dysplasia, 90 OSCC, and 43 OLP patients had ZNF582m examined at one mucosal location whereas 45 normal controls had ZNF582m evaluated at both the lesion and neighbouring normal sites. In those groups, high-risk behaviours such as smoking cigarettes and consuming betel nuts were also compared.

ZNF582m was substantially lower in OLP lesions compared to dysplasia and OSCC. ZNF582m increased at the nearby normal mucosa in OSCC patients with OLP and dysplasia. Moreover, ZNF582m was comparable to normal mucosa in the control group at places nearby that were normal in OLP patients. Based on ZNF582m levels, OLP is unlikely to be possibly cancerous. Moreover, ZNF582m might be a useful biomarker for differentiating OLP from real potentially malignant illnesses with dysplastic characteristics and OSCC, as well as for monitoring the malignant transformation of OLP[27].

Conclusion

Although the prevalence of OLP malignancy is still debatable, it is necessary to carefully monitor OLP patients over an extended period of time in order to discover malignancy from OLP early on. The follow-up period can be anywhere between two months to a year. Individuals with the reticular form of OLP may undergo annual evaluations, however those with dysplasia should undergo more frequent testing, such as every two to three months.

To clarify the malignant potential of OLP, a prospective, lengthy follow-up study with exact diagnostic criteria will be needed.

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