ORAL LICHEN PLANUS – REVIEW ARTICLE

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Abstract:
It is a chronic inflammatory illness that affects the mucous lining of oral cavity. OLP is an autoimmune disorder in which the oral epithelium's basal cells apoptosis is brought on by T- lymphocytes. Several antigen-specific and non-specific inflammatory mechanisms have been proposed to explain why CD8+ T cells homing and sub-epithelially concentrating lead to keratinocyte death. There are several different therapeutic alternatives, such as topical corticosteroids and laser ablation of the lesion. In this work, we examine several hypotheses on the pathogenesis of OLP as well as potential therapeutic approaches.

Keyword: Autoimmune disorder, Premalignant Lesion, Corticosteroids, Oral lichen planus, Psychosomatic disorder.

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Introduction:
It is a skin condition and chronic inflammatory illness that affects mucous membranes. Women are affected by it 1:4 as commonly as men, and it frequently shows up in the fourth decade of life. [1] About 1% to 2% of the population are afflicted by the condition. [2,3] Some examples of clinical signs include reticular, papular, plaque-like, erosive, atrophic, or bullous forms. The areas that are most frequently affected intraorally include the buccal mucosa, tongue, and gingiva, while other areas may occasionally be involved. [4]. In this review article, we discuss the most recent hypothesis about the pathogenesis and OLP treatment modalities.[5]

PATHOGENESIS
Hepatitis C virus (HCV) may be the etiologic factor in OLP, according to epidemiological data from more than 90 well-controlled research done internationally. The association seems to be more prevalent in Southern Europe, Japan, and the United States. The fact that countries with the greatest prevalence of HCV show little or modest correlations suggesting that the LP-HCV relationship cannot be explained just by population. They most likely suggest that the HCV-specific T lymphocyte may be involved in the pathogenesis of oral lichen planus. The lymphocytic invasion band, for example, could target cells that are HCV-infected. The likelihood that someone with OLP will get HCV infection is yet uncertain, as is the likelihood that someone with OLP will develop HCV infection. [6-10]To properly appreciate the hypothesized pathogenetic relationship between OLP and HCV, which is currently under dispute, further prospective and interventional investigations are necessary. [11]

DIFFERENTIAL DIAGNOSIS
The diagnosis of reticular lichen planus is based on the clinical features. Pathognomonic white striae that grow bilaterally and interlace on the posterior buccal mucosa. When evoking the erosive and erythematous forms of OLP, as well as when a super-imposed candidal infection masquerading as a normal reticular pattern, problems frequently occur. There are several probable diagnosis, including chronic ulcerative stomatitis, leukoplakia, lichenoid reactions, pemphigus, lupus erythematosus, pemphigus, mucous membrane pemphigoid, and erythematous candidiasis. Clinically, lichenoid drug reactions often present as unilateral symptoms, and taking new drugs is frequently present. The easiest way to tell if a patient has lichenoid drug reactions is to see if the reaction goes away when the offending medicine is taken away but comes back when the patient is challenged again. When OLP-like lesions are restricted to areas of the oral mucosa in close contact or proximity to restorative materials, typically amalgam, lichenoid reactions generated by these materials may be seen. The diagnosis of oral lichenoid response is supported by a positive patch test, a significant clinical correlate of restorative proximity, and a biopsy that demonstrates a significant lymphocytic infiltration rather than a sub-epithelial band. Lupus erythematosus (LE) lesions seem similar to erosive lichen planus, however they are less regularly distributed. Whereas LE's keratotic striae radiate from the centre core in a distinctive way, Wickham's striae are noticeably coarser and more prominent. There is evidence of perivascular infiltration in LE biopsies.

Although both the disorders have a desquamative clinical appearance, it is crucial to differentiate pemphigoid and erosive or atrophic gingivitis. Erythematous lesions that show as distinct lesions without white striae include pemphigus and pemphigoid. This can assist in the clinical separation of erosive and atrophic kinds of OLP since they typically display a reticular appearance. Using Nikolsky's sign, which is the peeling of the epithelium from the epithelial junction and connective tissue in the unaffected area, it may be recognized from the erosive and erythematous types of lichen planus. Pemphigus or pemphigoid can be determined using a sample of the perilesional tissue that histologically displays intraepithelial or subepithelial split. Erythema multiforme (EM), although more severe and frequently affecting the labial mucosa, can occasionally resemble bullous lichen planus. The immune-mediated illness known as Chronic Ulcerative Stomatitis (CUS), which affects the oral mucosa, is comparable to lichen planus both clinically and histopathologically. Autoantibodies against p63 found in the basal and parabasal layers of the epithelium can be used to diagnose CUS via direct immunofluorescence tests. CUS requires antimalarial medication since it does not respond to corticosteroid therapy, and these lesions must be separated from lichen planus. [12]

RECENT CONCEPTS IN TREATMENT
Although corticosteroids have been the cornerstone of OLP therapy, additional strategies such calcineurin inhibitors, retinoids, dapsone, hydroxychloroquine, mycophenolate mofetil, and enoxaparin have also made important contributions to the management of the condition. Increasing TGF-1 activity in OLP or suppressing IL-12, IFN, TNF, RANTES, or MMP-9 activity may someday

be useful therapies, according to recent research on the disease's origin. [1,13]

CORTICOSTEROIDS

This class of drugs is the one that is most frequently used to treat OLP. [14] They are used because of their capacity to manage immune response and inflammation. By reducing lymphocytic exudate and re-establishing the integrity of the lysosomal membrane, they function. [15] The use of topical high-potency fluorinated corticosteroids, such as clobetasol, disodium betamethasone phosphate, fluocinonide acetonide, and more recently, super-potent halogenated corticosteroids, depends on the severity of the lesion. Topical corticosteroids can't adhere to the mucosa for a long time, which is their main drawback. Despite research using topical steroids with an adhesive base having been done, none of them have demonstrated that they are superior than steroids alone (carboxymethyl cellulose). [16] Nevertheless, the same study suggests using denture adhesive paste, which only has inactive components, as a delivery route for the topical drug. Due to its high molecular weight (above 100,000) and flexible polymeric chain, it possesses excellent bio-adhesive charact- eristics. Small, easily accessible erosive lesions on the gingiva and palate can be treated with an adhesive paste in a custom tray. This approach guarantees that the therapy covers the whole lesional area and gives precise control over the contact time. [17] It has an outstanding bio-adhesive properties because of its large molecular weight (above 100,000) and the flexibility of the polymeric chain. Treatment of small, readily treatable erosive lesions on the gingiva and palate with an adhering paste in a custom tray allows for better control of the contact time and ensures that the therapies are applied to the whole lesional surface. [14]

OTHER IMMUNOSUPPRESSENT AND IMMUNOMODULATORY AGENTS CALCINEURIN INHIBITORS

The transcription of IL-2 is encouraged by a protein phosphatase known as calcineurin, which in turn encourages T-cell proliferation and differentiation. [18] The immune suppressive drugs pimecrolimus, tacrolimus, and cyclosporine all inhibit calcineurin. These medicines are calcineurin inhibitors.

CYCLOSPORINE

To reduce the patient's immune system activity after receiving an allogenic organ transplant, immunosuppressants such the calcineurin inhibitor cyclosporine are routinely given. As a result of lowering T-cell activity—the primary cause of transplant rejection—foreign organ absorption is improved. The cytosolic protein cyclophilin is present in immunocompetent cells, particularly T lymphocytes, and cyclosporine binds to it. Normal calcineurin stimulation of IL-2 production is blocked by the interaction of cyclosporine and cyclophilin. They also impair the capacity of effector T-cells by inhibiting the synthesis of lymphokines and interleukin (IL). In OLP, cyclosporine is either orally or topically applied with adhesive bases. Due to the high cost of treatment, it should only be used in the most severe instances of OLP. Nutrient absorption by the body happens extremely slowly. [14] It has been connected to a specific dose-related gingival hyperplasia that disappears when the medicine is discontinued.

TACROLIMUS

Tacrolimus is a topical immunosuppressive drug without steroids that is specifically used for atopic dermatitis. Moreover, it inhibits calcineurin. Compared to cyclosporine, it is 10-100 times more powerful and absorbs more readily via the skin. It has been demonstrated to work well in situations with resistant OLP. The macrolide family includes a macrolide made by Streptomyces tsukubaensis. Tacrolimus has an immunosuppressive effect equivalent to that of cyclosporine, however it penetrates the mucosa more quickly. It stops the first stage of T-cell activation by reducing calcineurin's phosphatase activity. While relapses of OLP after cessation have also been observed, burning is the most typical adverse effect. According to a new US Food and Drug Administration warning, using tacrolimus should be avoided owing to the possibility of cancer and should only be done for brief periods of time. [14,18]

PIMECROLIMUS

Pimecrolimus reduces T-cell activation by preventing T cells from producing and releasing cytokines. Moreover, pimecrolimus stops mast cells from releasing inflammatory mediators and cytokines. OLP has been effectively treated with 1% topical pimecrolimus cream. Pimecrolimus has substantial anti-inflammatory and immunomodulatory benefits and a minimal risk of systemic immunosuppression. [19,20]

RETINOIDS

Due to their immunomodulating properties, topical retinoids including tretinoin, isotretinoin, and fenretinide have been demonstrated to be helpful in OLP. Although the results may only be temporary, topical retinoids can aid in the reversal of white striae. Systemic retinoids have been used with

various degrees of success in cases with severe lichen planus. The advantages of retinoids must be weighed against their harmful side effects, which include teratogenicity, cheilitis, elevated blood levels of liver enzymes, and triglycerides. [8,21]

DAPSONE

An antibacterial drug called dapsone is used to treat leprosy because it prevents bacteria from producing dihydrofolic acid. It most likely functions as an anti-inflammatory drug when given for the treatment of skin conditions by lowering the synthesis of chemotactic factors for mast cells. [22] The most typical side effect of dapsone is hematolysis, which can occur to varied degrees. It depends on the dosage and almost invariably occurs in those who take 200–300 mg of oral dapsone daily. Those using dapsone may be more susceptible to hemolytic anaemia or methemoglobinemia due to the lack of glucose-6-phosphate dehydrogenase (G6PD). Before giving dapsone, a G6PD deficiency test is required. The dapsone response, which is an allergic reaction to dapsone, is a frequent side effect of many medicinal therapies. Rashes, fever, and jaundice are typical skin ailments. Corticosteroids can be used to treat it throughout the first six weeks of therapy.[23]

MYCOPHENOLATES

After being used to treat psoriasis, mycophenolic acid—now available under the name mycophenolate mofetil—has been returned to dermatological treatment. Since it is an immunosuppressive drug that is well-tolerated and used in organ transplant, it has been used to treat severe instances of OLP with success. When used for a long time, mycophenolates are both costly and productive. [24]

LOW-DOSE, LOW MOLECULAR WEIGHT HEPARIN (ENOXAPARIN)

The function of T-lymphocyte heparinase, which is essential for T-cell migration to target tissues, is inhibited by low-dose, non-anticoagulant heparin. This has no adverse effects when administered subcutaneously, and it promises to be an easy, reliable, and secure therapy for OLP.[25]

EFALIZUMAB

It is an immunosuppressive recombinant humanized monoclonal antibody that is used to treat psoriasis. A CD11a monoclonal antibody, efalizumab, enhances OLP by attaching to this adhesion molecule and lowering T cell activation and trafficking. Mononuclear cells in OLP were examined in vitro, and the results showed that pretreatment with anti-CD11a antibodies inhibited peripheral blood mononuclear cell migration by 60%. Once a week, a subcutaneous injection is administered. Currently, it has FDA approval for treating plaque psoriasis. [26]

NON - PHARMACOLOGICAL MODALITIES

PUVA therapy

This non-pharmaceutical method that uses long-wave ultraviolet light and photo chemotherapy using 8-methoxypsoralen (PUVA). Psoralens are plant-based compounds that momentarily increase the skin's sensitivity to UV light. Two hours after taking oral methoxypsoralen, the affected regions get intraoral UV radiation. It has been demonstrated to be successful in treating patients with severe OLP. [27] The uncomfortable side effects of psoralen-induced nausea and dizziness as well as 24-hour photosensitivity when this treatment is given orally are two key drawbacks of PUVA therapy. Due to the complicated geometry of the mouth and the frequent application of PUVA to skin across expansive, open areas, dosimetry in this area can be challenging [28]

PHOTODYNAMIC THERAPY

In photodynamic treatment (PDT), a photosensitizing agent, such as methylene blue, is activated at a certain laser light wavelength in order to kill the targeted cell by inflicting cellular damage, membrane rupture, and protein inactivation by potent oxidizers. PDT has shown some success in the battle against cancer, particularly when it comes to treating head and neck tumours. PDT has been reported to have immunomodulatory properties and may induce apoptosis in the hyperproliferating inflammatory cells observed in psoriasis and lichen planus. The lichen planus may experience less inflammation and hyperproliferation as a result. [29]

LASER THERAPY

Individuals with severe erosive OLP who have failed to respond to cryosurgery and other laser treatments, including topically applied super-potent corticosteroids, have attempted these methods. Investigations into pulsed diode lasers employing 904-nm pulsed infrared rays and low-dose excimer lasers at 308 nm with UV-B rays for bio-stimulation have been conducted. [30]. Despite the fact that a number of the published trials are highly encouraging, their effectiveness has not yet been established. .[31].

OLP cannot be completely cured; the aim of treatment for symptomatic individuals is palliation. Corticosteroids can be used topically to relieve symptoms in the vast majority of instances, either

by themselves or in conjunction with other immunomodulators. Just a very small percentage of people need systemic therapy. The use of laser therapy and other cutting-edge methods is a last resort.[32]

CONCLUSION

One of the most frequent mucosal disorders observed by dentists is OLP, a widespread oral dermatosis. Accurate diagnosis of the lesion and prompt administration of necessary treatment are essential. To deliver the optimal care, it is essential to have a firm understanding of the pathophysiology of the disease.

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