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Oral Lichen Planus: Theory and Management

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ABSTRACT

Oral Lichen Planus (OLP) is a chronic inflammatory disease that affects the mucous and cutaneous tissue inside our mouth. It is a T cell mediated autoimmune disease. The two major types of OLP are Reticular OLP and Erosive OLP. They appear as white, lacy, patches, red coloured, swollen tissues or open sores. Its cause is unknown. The oral lichen planus do not pass from one person to another. This disease may be sometimes responsible for developing mouth cancer. Proper monitoring is needed for the patients who are having oral lichen planus. Personal oral hygiene is believed to reduce the symptoms of OLP. The topical or systemic corticosteroids modulate the patient's immune response. The natural treatments by using aloe vera, yogurt, turmeric, almonds, baking soda and lemon are very much effective in treating OLP. The commonly used homeopathic medicines used for the treatment of OLP are plantaga, mercsol and borax. The non pharmacological approaches used for treating OLP include PUVA therapy, laser therapy, cryotherapy and CO2 laser. Nowadays modalities like retinoids, dapsone, hydroxychloroquine, calcineurin inhibitors and mycophenolatemofetil are used for treatment.

Keywords: oral lichen planus, corticosteroids, basal keratinocytes, immunosuppressant.

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INTRODUCTION

Oral Lichen Planus (OLP) is a chronic inflammatory disease that affects the mucous and cutaneous tissue inside our mouth (1). It is a T cell mediated autoimmune disease (2). The most common mucosal condition affecting the oral cavity is OLP. They appear as white, lacy, patches, red coloured, swollen tissues or open sores (3). These lesions are commonly seen in gum, tongue, inside the cheek and in the inner tissues of lips. These may cause pain, burning sensation and other discomforts such as inflammation of the gums (gingivitis), bleeding and irritation with tooth brushing, sensitivity to acidic, hot and spicy food materials (4). The oral lichen planus do not pass from one person to another. This disease may be sometimes responsible for developing mouth cancer. So proper monitoring is needed for the patients who are having oral lichen planus. It affects 0.5%-2.0% of total population. This disease occurs in adults older than 40 years. This disease can be seen commonly in women than men and it is rare in case of children (5). The lesions that appear as a result of OLP will last for 20 years or longer. Its cause is unknown (6).

Reticular Oral Lichen Planus

The most common OLP is reticular OLP. It is characterized by a net like appearance of lacy white line, oral variants of Wickham's striae. Wickham striae are the white lines that can be seen in the buccal cavity, mucosa, mucobuccal fold, gingiva and also in tongue, lips and palate. The plaque like form and papular like form are the variants of reticular OLP. The plaque type lichen planus appears as lesion on the tongue and papular type lichen planus are seen on the lateral border of tongue (fig: 1). The reticular form and plaque like variant are asymptomatic (7).



Figure: 1: Lesion On the Tongue

Erosive oral lichen planus

It is also termed as ulcerative OLP. It is the second most common OLP. It appears as a mix of erythematous and ulcerated areas surrounded by finely radiating keratolytic striae. This disease has a chance of occurring in one or more areas of the mouth. In some people suffering with erosive OLP, the gums are involved termed as desquamative gingivitis. The major symptom that is shown

by the people is severe pain (8). The other two additional presentation involve are a atrophic and bullous form which are the variants of erosive OLP. Atrophic OLP which appears as erythematous patches that are surrounded by white striae and in a diffuse form (9). Bullous OLP which appears as fluid filled vesicles that project from its surface (10)

Etiology:

The cause is unknown. This may be sometimes due to genetic background. The T cell mediated immune response in which basal epithelial cells are considered as foreign particle due to the changes in the antigenicity of their cell surface is believed as the major cause for OLP. Sometimes it can be caused due to certain medications such as using painkillers, drugs used for high BP, diabetes, heart disease, beta blockers or penicillamine etc (11). The other etiological factor includes reactions to metal fillings in your teeth. It may be sometimes due to allergy causing agents such as dental materials-silver amalgam, gold, cobalt, palladium, chromium and even non-metals such as epoxy resins and prolonged use of denture wear (12, 13, 14). The OLP may be accompanied with autoimmune disorders such as primary biliary cirrhosis, chronic active hepatitis, ulcerative colitis, myasthenia gravis and thymoma (15). It may sometimes occur due to bowel diseases such as coeliac disease, ulcerative colitis and Crohn's disease (16). OLP is also associated with food. One of the major factors responsible for the OLP is anxiety and stress (17). Cigarette smoking and alcohol consumption is the other reason (18). OLP has been related to bacteria such as Gram negative bacillus and spirochetes. But this not confirmed too.

Pathophysiology:

OLP is a T cell mediated autoimmune disorder in which apoptosis of the basal cells of the oral epithelium is triggered by the auto-cytotoxic CD8⁺ T cell. The T cell (CD8⁺ and some CD4⁺ cells) present in the epithelium by the migration due to the rapid encounter of the antigen during a routine surveillance or a chemokine mediated migration towards the basal keratinocytes (19). The CD8⁺ cells are activated by the antigen binding to histocompatibility complex (MHC)-1 on the keratinocyte. It is also possible through the activated CD4⁺ lymphocytes. After the activation of CD8⁺ apoptosis of the basal cells of the oral epithelium is triggered. The activated CD8⁺ T cells release cytokines (broad and loose category of small proteins that helps in cell signalling. The released cytokines attract the additional lymphocytes into the developing lesions. In the lesions of OLP increased amount of the cytokine tumor necrosis factor (TNF)-alpha, Fas –Fas L mediated or granzyme B activated apoptosis. The OLP can be treated by using thalidomide which is known to suppress the production of TNF (20).

Clinical Significance Of OLP:

The OLP is the most common disease affecting the oral cavity (21). The dentist will check the patients regularly. It is because that the atrophic and erosive forms of OLP cause severe discomfort. So knowledge about the treatment is very much important. There are various similar diseases like OLP. For example OLP and GVHD (Graft-Versus-host disease) have same clinical and histological presentations. The GVHD is a condition that may occur in bone marrow transplant patients. It occurs when the transplanted marrow cells react against host tissues. It is possible to distinguish the histological and clinical properties of erosive OLP and lichenoid drug reactions. It is very much necessary to distinguish the reticular or erosive lesions from the lichenoid reactions to dental amalgam. Some new studies found an increased risk of squamous cell carcinoma in patients suffering with OLP. Here the chance of developing squamous cell carcinoma in patients with OLP is 10 times higher than in the unaffected common population. Newly published reports have noted a possible similarity between the OLP and hepatitis C, sclerosing cholangitis and primary biliary cirrhosis (22).

Histopathology:

The great histopathologic highlights of OLP incorporate liquefactive degeneration of the basal cell joined by apoptosis of the keratinocytes, a thick band-like lymphocytic penetrate at the interface between the epithelium and the connective tissue, (fig:5) central regions of hyper keratinized epithelium (which offer ascent to the clinically evident Wickham's striae) and periodic zones of atrophic epithelium where the rete pegs might be abbreviated and pointed (a trademark known as observed tooth rete pegs). Eosinophilic colloid bodies (Civatte bodies), which speak to worsening keratinocytes, are regularly obvious in the lower half of the surface epithelium (23). Degeneration of the basal keratinocytes and interruption of the securing components of the epithelial BM and basal keratinocytes (e.g. hemi desmosomes, fibers, fibrils) debilitate the epithelial connective tissue interface. Therefore, histologic clefts (Max-Joseph spaces) may shape and rankles on the oral mucosa (bullous LP) might be seen at clinical examination. B cells and plasma cells are extraordinary findings (24).

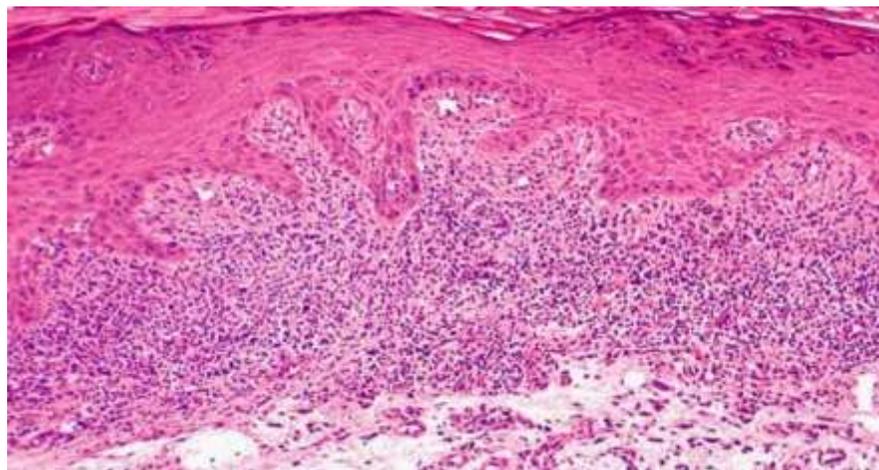


Figure:2

Symptoms:

- Sensitive to hot, acid or spicy foods.
- Inflammations of gum (gingivitis).
- Burning sensation.
- Sever pain.
- Difficulty in swallowing and speaking.
- Dryness in mouth.
- Metallic taste in the mouth.
- Appearance of white patches on your tongue cheeks and gums (25).

Complications:

- Oral cancer
- Depression
- Weight loss, scarring from erosive lesions
- Stress and anxiety
- Severe pain
- Fungal infections or secondary oral yeast (26) .

Diagnosis:

Initially the patient has to consult the doctor to make the diagnosis of oral lichen planus. The doctor will make a diagnosis for your disease after examining your mouth and its surrounding areas, then will make a discussion on your dental medication history and the medications that are taken by you (patient), also review of symptoms including white lesions on the mouth and other areas of the body (27). The diagnosis of reticular OLP is based on the appearance of white striae

bilaterally on the posterior buccal mucosa. Oral leukoplakia has a similarity with plaque form of reticular OLP. The diagnosis of erosive OLP includes discoid lupus erythematosus, cell carcinoma, pemphigoid, candidiasis, pemphigus vulgaris, lichenoid reactions to dental amalgam or drugs, chronic cheek chewing, hypersensitivity mucositis, etc. (28). After observing the patient doctor advice many lab tests such as:

1. Biopsy: Take a small tissue sample from one or more lesions in your mouth and observed under a microscope in order to evaluate the indication of OLP (29).

2. Cultures: Collect a sample of cell from your mouth by using a clean cotton swab. The collected sample has to be observed under microscope to determine whether you have any fungal, viral or bacterial infections.

3. Blood tests: This may be carried out to identify various conditions such as hepatic C that is very rarely associated with OLP and lupus which show similarity with OLP (30).

Treatment:

Currently there is no cure for OLP (31). Personal oral hygiene is believed to reduce the symptoms of OLP. The primary aim of the treatment is to reduce the length and severity of symptomatic outbreaks. The diagnosis must be confirmed before starting the treatment (32).

- **Corticosteroids**

These are the most regularly utilized gathering of medications for the treatment of OLP. The method of reasoning behind their use is their capacity to adjust aggravation and resistant reaction. They act by decreasing the lymphocytic exudate and balancing out the lysosomal membrane. Topical mid potency corticosteroids, for example, triamcinolone Acetonide, high-strong fluorinated corticosteroids, for example, fluocinonide acetone, disodium betamethasone phosphate, and all the more as of late, super potent halogenated corticosteroids, for example, clobetasol are utilized in view of the seriousness of the sore. The best detriment in utilizing topical corticosteroids is their absence of adherence to the mucosa for an adequate time allotment. Despite the fact that trials were finished utilizing topical steroids alongside glue base, no examination demonstrates their prevalence when analyzed over steroids without the base (carboxymethyl cellulose) (33). However, a similar report likewise suggests the utilization of cement glue utilized for dentures, which contains just idle fixings as a vehicle to convey the topical application. This has demonstrated fantastic bio adhesive properties, because of its high atomic weight (over 100,000) and the adaptability of the polymeric chain. Little and open erosive injuries situated on the gingiva and sense of taste can be dealt with by the utilization of a follower glue in a made-to-gauge plate (custom plate), which takes into account precise control over the contact time and guarantees that

the whole lesional surface is presented to the drugs⁽³⁴⁾. Patients with across the board types of OLP are recommended high-powerful and super potent corticosteroids mouthwashes and intra lesional infusions. Long haul utilization of topical steroid can prompt the improvement of auxiliary candidiasis which requires antifungal therapy. The potential tachyphylaxis and adrenal deficiency is high when utilizing super potent steroids like clobetasol, particularly when utilized for a more drawn out timeframe. Fundamental corticosteroids are held for refractory erosive or erythematous LP where topical methodologies have fizzled. Fundamental prednisolone is the medication of decision, however ought to be utilized at the most reduced conceivable dose for the briefest length (40– 80 mg for 5– 7 days) ⁽³⁵⁾.

- **Natural Treatment**

1. Aloe vera: The application of Aloe vera to cure the OLP is in form of gel. It has to be applied on the affected area of mouth. It will give relief from pain and inflammation ⁽³⁶⁾.

2. Yogurt: It is produced by the bacterial fermentation of milk. The pain experienced due to OLP will be cleared by using yogurt.

3. Turmeric: It is responsible for clearing out the lesions and white patches that occurred in gums and tongue due to OLP. It can be used in our diet or can be apply in to our mouth ⁽³⁷⁾.

4. Almonds: The almonds have to be taken in our diet daily. It helps to get rid of OLP because it is a rich source of vitamin E.

5. Baking soda: It has to be applied on the affected area of the mouth (gums and tongue). Reduce the formation of lesions in mouth and helps in the healing process ⁽³⁸⁾.

6. Lemon: It has to be taken in form of lemon juice. It is a rich source of vitamin C provides freshness to mouth and protect the mouth from microbial infections.

7. Bee propolis: It is also termed as bee glue is a resinous mixture that is produced by the honey bee by mixing the saliva and beeswax together. It protects the mouth from microbial infections ⁽³⁹⁾.

- **Homeopathic Medicines**

The commonly used homeopathic medicines used for the treatment of OLP are plantaga, mercsol and borax. The borax is beneficial for the patients having moth ulcer inside the tongue or in cheeks. This medicine is used when the mouth remains dry for a long period, experience bitter taste and heat in mouth. Mercsol is the most effective medicine used for treating OLP. This medicine is used when the patients show the following symptoms.

- Irregular ulcers inside the cheek.
- Unhealthy and dirty appearance of cheek.

- Increased salivation in mouth.
- Odour in mouth.
- Thirst for the water.
- Metallic taste in mouth ⁽⁴⁰⁾.

Role Of Immunosuppressant And Immunomodulatory Agent:

Calcineurin Inhibitors: They are medicines which inhibit the action of calcineurin. It is the enzyme that activates the T cell of the immune system. The calcineurin inhibitors come under the category of immunosuppressant. The calcineurin is inhibited by cyclosporine, Tacrolimus and pimecrolimus ⁽⁴¹⁾.

1. Cyclosporine: It is a calcineurin inhibitor –immunosuppressant. It suppress the T cell activity. The cyclosporine binds with the cytosolic protein cyclophilin. The complex of cyclosporine and the cyclophilin is responsible for the inhibition of calcineurin, which also induces the transcription of IL-2. They are also responsible for the inhibition of IL release and lymphokine production. These all result in the reduced function of T cells. Cyclosporine is used as mouth rinse commonly and also used in treating recalcitrant OLP. Systemic absorption is less.

2. Tacrolimus: It is a calcineurin inhibitor-immunosuppressive agent. It is 10-100 times more potent than cyclosporine and also has greater absorption capacity than cyclosporine. It is used in recalcitrant OLP. The mechanism of action is same as that of cyclosporine. It is responsible for the inhibition of first phase of T cell activation and also inhibits the phosphatase activity of calcineurin. The US Food and Drug Administration recently issued to reduce the continuous use of this drug because the continuous use may develop a chance for cancer.

3. Pimecrolimus: It inhibits the T cell activation by blocking the production and release of cytokines. 1% topical cream is commonly used for treating OLP ⁽⁴²⁾ ⁽⁴³⁾.

4. Sirolimus: Also known as rapamycin, an immunosuppressant. It prevents the activation of T cell by reducing the production of Interleukin-2 (IL-2). Initially it was developed as an antifungal agent later considered as immunosuppressive and as an Antiproliferative.

Retinoid: Tretinoin, isotretinoin and fenretinide etc are the topical retinoid that have immunomodulating properties are very much effective in treating OLP. In case of severe lichen planus systemic retinoid are used. The side effects include disease of serum liver enzymes and triglycerides levels ⁽⁴⁴⁾.

Mycophenolates: Initially used to treat psoriasis, mycophenolic corrosive (now reformulated as mycophenolatemofetil) has been reintroduced in dermatological solution. Being an exceptionally

very much endured immunosuppressive medication utilized as a part of organ transplant, it has been effectively used to treat serious instances of OLP (45).

Enoxaparin: Low-molecular weight heparin without anticoagulant properties represses T lymphocyte heparinase action which is pivotal in T-cell movement to target tissues. This guarantees to be a straight forward, successful and safe treatment for OLP when infused subcutaneously as it has no symptoms (46).

Efalizumab: It is used to treat autoimmune diseases, especially to treat psoriasis. Efalizumab is a recombinant humanized monoclonal antibody administered subcutaneously once in a week. It is responsible for the improvement in OLP by the reduced activation of T lymphocytes (47).

Dapsone: As an antibacterial agent, dapsone inhibits bacterial synthesis of dihydrofolic acid and hence is used in the treatment of leprosy. When used for the treatment of skin diseases, it probably acts as an anti-inflammatory agent by inhibiting the release of chemo tactic factors for mast cells (48). The most common untoward effect of dapsone is hemolysis of varying degree, which is dose related and develops in almost every individual administered 200–300 mg of oral dapsone daily. Glucose-6-phosphate dehydrogenase (G6PD) deficiency can increase the risk of hemolytic anemia or met-hemoglobinemia in patients receiving dapsone. Screening for G6PD deficiency is required before prescribing dapsone. Hypersensitivity reaction to dapsone called Dapsone reaction is frequent in patients receiving multiple drug therapy. The symptoms of rash, fever and jaundice generally occur within the first 6 weeks of therapy and can be ameliorated by corticosteroid therapy (49).

Levamisole: It is an anti-helminthic drug. Its mechanism include the following action

- It restores the phagocytic activity of macrophage and neutrophils.
- It immune potentiate the T-cell mediated immunity.
- It improves the human interferon and interleukin-2.
- Responsible for the alteration of the natural course of chronic recurrent
- Inflammatory disease.
- It is taken at a dose 50mg. Its side effects include nausea , vomiting , headache and
- Agranulocytosis (50).

Non Pharmacologic Approach For Treating OLP.

- **Puva Therapy:** It is an ultraviolet light therapy (Psoralen and ultraviolet A) (51). The psoralens are the compounds seen in the plants that make the skin sensitive to uv radiation temporarily. The Egyptians were the first to utilize the Psoralen for the treatment of skin diseases.

The methoxy psoralen is administered orally later followed by administration of uv radiation intra orally in the affected area. It is successfully used in treating OLP. The PUVA therapy has some side effects too. It includes nausea and dizziness. The patients suffering from the side effects should follow PUVA bath therapy (52).

- **Laser Therapy:** For the treatment of OLP 308nm excimer laser has been used. The patients subjected to this treatment achieved greater clinical improvement. Mainly the excimer 308nm laser is used in treating symptomatic OLP. The main advantage of this treatment is painless and well tolerated (53). Management of OLP can also be done by 980nm Diode Laser and ND: YAG Laser (54).

- **CO₂ Laser:** It is by heat generation that the tissue effect of CO₂ laser is produced. This laser produces a beam of infra red light with wavelength bands focusing on 9.4 and 10.6 micrometers. The CO₂ laser is the best surgical laser for the smooth tissue. When we compared the wounds made with a scalpel with that of laser wounds we can see a small contraction of tissue repair. This contraction mainly seen in the excisions with a loss of tissue. This may result in scarring. The sterilization of surgical wounds is one of the major benefits of CO₂ laser. This is used in treating OLP. The advantages of the laser treatment include less bleeding, less infection, less swelling and shorter surgical time. The other applications include gynecology, oral and maxillofacial surgery and many others too.

- **Cryotherapy:** The therapy includes usage of low temperatures in medical therapy. It is used to treat the lesions. It also helps in decreasing inflammation, pain and spasm (55). Nowadays many studies have done by comparing the effects of cryotherapy with nitrous oxide gas and topical corticosteroids in the treatment of OLP. The conclusion of the studies says that cryotherapy with nitrous oxide gas is most effective than topical corticosteroids (triamcinolone, acetamide) in the treatment of OLP. The main advantages include no systemic side effect and it also needs less patient compliance (56).

CONCLUSION

The OLP is a common oral dermatitis and is the most common mucosal pathoses that are encountered by the dental practitioners. The OLP can be easily identified and proper treatment can be administered at the early stage itself. A proper understanding about the pathogenesis, clinical presentation, diagnosis of the disease becomes very much important for providing the proper treatment.

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