Lichen planus (LP) – An Overview

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Abstract

Lichen planus is an inflammatory disorder affecting the skin and mucous membranes that typically affects the mouth, nails, and hair. LP is perceived as a T cell-mediated autoimmune disease, in which cytotoxic CD8+ T cells are recruited into the skin and subsequently lead to interface dermatitis. Lichen Planus can appear in many different clinical types, including Hypertrophic lichen planus, Ulcerative lichen planus, Bullous lichen planus. Lichen Planus can take on different forms like Cutaneous Lichen Planus, Oral Lichen Planus, Nail Lichen Planus, Genital Lichen Planus. Cutaneous Lichen Planus affects the skin, leading to the purple, itchy rashes. The exact cause of Lichen Planus is unknown, but some things might trigger it or make it worse. That are Immune system Issues, Medications, Hepatitis C, Allergies, Stress. Several HLA alleles are associated with LP. In addition to the association with the HLA, single- nucleotide polymorphism (SNP) in loci encoding for NRP2 and IGFBP4 that increases or reduce risk of LP. Some report showed that CD8+ and CD45RO+ T-cells are the major cell type in the inflammatory infiltrate. Plant derived interventions like Anthocyanin, lycoene were used to treat the Lichen planus.

Keywords: Lichen planus, T cell-mediated autoimmune disease, Anthocyanin

Introduction

Lichen planus (LP) is an idiopathic sub-acute or chronic inflammatory disorder affecting the skin and mucous membranes that typically affects the mouth, nails, and hair. It is not contagious. Recently LP is perceived as a T cell-mediated autoimmune disease, in which cytotoxic CD8+ T cells are recruited into the skin and subsequently lead to interface dermatitis (Boch K et al., 2021). This condition happens when the immune system, which usually fights off infections, starts attacking the skin or mucous membranes by mistake. Although the exact cause of Lichen Planus is unknown, several factors such as autoimmune disorders, viral infections, and certain medications may contribute to its development. The condition appears as pruritic, violaceous papules and plaques, most commonly found on the wrists, lower back and ankles. The lesions are often overlaid with a lattice-like network of white lines called Wickham striae, which are most easily observed on the buccal mucosa, where erosions may also be present.

Types of Lichen Planus

Lichen Planus can appear in many different clinical types, including

Hypertrophic lichen planus is characterized by red, red-brown, or yellow-grey papules and plaques that merge with a thickened or verrucous surface on the shins and ankles. **Ulcerative lichen planus** is a erosive lesion on the soles of the feet or between the toes that make walking difficult. **Bullous lichen planus** is a blisters filled with clear or pale-yellow fluid on the legs.

Lichen planus pigmentosus is characterized by the development of macular or papular pigmented lesions often arranged in a linear or follicular pattern.

Inverse lichen planus is found in skin folds. **Lichen planopilaris** is a tiny red spiny follicular papules and extending smooth areas on the scalp or elsewhere on the hair bearing regions. Other clinical types of LP includes annular, atrophic, erosive, follicular, linear, pigmented and vesicular.

Lichen Planus can take on different forms like Cutaneous Lichen Planus, Oral Lichen Planus, Nail Lichen Planus, Genital Lichen Planus. Cutaneous Lichen Planus affects the skin, leading to the purple, itchy rashes.

The hallmark of Cutaneous LP are purple or violet, polygonal, shiny, flat-topped and plaques with white steaks (White striae). The Cutaneous LP may vary in size from several millimeters

to more than one centimeter. The lesion may be clustered or disseminated and whilst the typical locations are the wrists, lower back and ankles. The dominant symptom is pruritus. Oral Lichen Planus causes painful sores and white lines on the mouth. Nail Lichen Planus causes the nails become brittle and rough. Genital Lichen Planus causes itchiness and discomfort in genital area.

Causes of Lichen Planus

The exact cause of Lichen Planus is unknown, but some things might trigger it or make it worse. That are Immune system Issues, Medications, Hepatitis C, Allergies, Stress.

Immune system Issues- Immune system plays a major role. Sometimes it goes haywire and attacks their own skin cells, leading to Lichen Planus.

Medications- Certain medicines, like beta-blockers, can trigger Lichen Planus in some people.

Hepatitis C- People with hepatitis C are more likely to get Lichen Planus.

Allergies- Sometimes, an allergic reaction on skin or to dental fillings or other substances can lead to Lichen Planus in the mouth.

Stress: Stress might not cause Lichen Planus, but it can make the symptoms worse.

Common symptoms of Lichen Planus

Lichen Planus symptoms may vary from person to person, but some common sings will occur for all thr persons who have Lichen Planus that are Skin Rashes, Mouth sores, Hair loss, Itching, Nail changes.

Skin Rashes is one of the most noticeable sings in the skin. These rashes are often shiny, flat-topped, and purple or reddish in color. They can appear on wrists, ankles, legs, and even genitals.

Mouth Sores is a painful sores occur in mouth. These might make it hard to eat or drink. Hair Loss occurs in the affected areas. Itching occurs in the affected areas. Nail Changes- The nails will become grooved, ridged, or pitted

Epidemiology

The incidence of LP is less well- characterized and displays considerable geographical heterogeneity as it ranges between 14 and 250 cases/100,000 person-years. The prevalence of cutaneous lichen planus is approximately 0.2% to 1% among adults worldwide. This variability more likely mirrors methodological differences in the sampled populations rather than the existence of an ethnic pre-disposition. Oral lichen planus is more common and reported in 1% to 4% of the population. Overall, women are more frequently affected compared to men at a ratio of 1.5:1, and most cases develop between the ages of 30 and 60. The condition is rare in children, representing less than 5% of all affected patients. Oral LP tends to develop 10 years later than cutaneous LP. The recent studies suggest a higher incidence of the disease in African Americans and individuals of Indian and Arabian descent.[14][15] There appears to be a familial component, as up to 10% of first-degree relatives of patients may also develop the disease.[16]

Pathogenesis

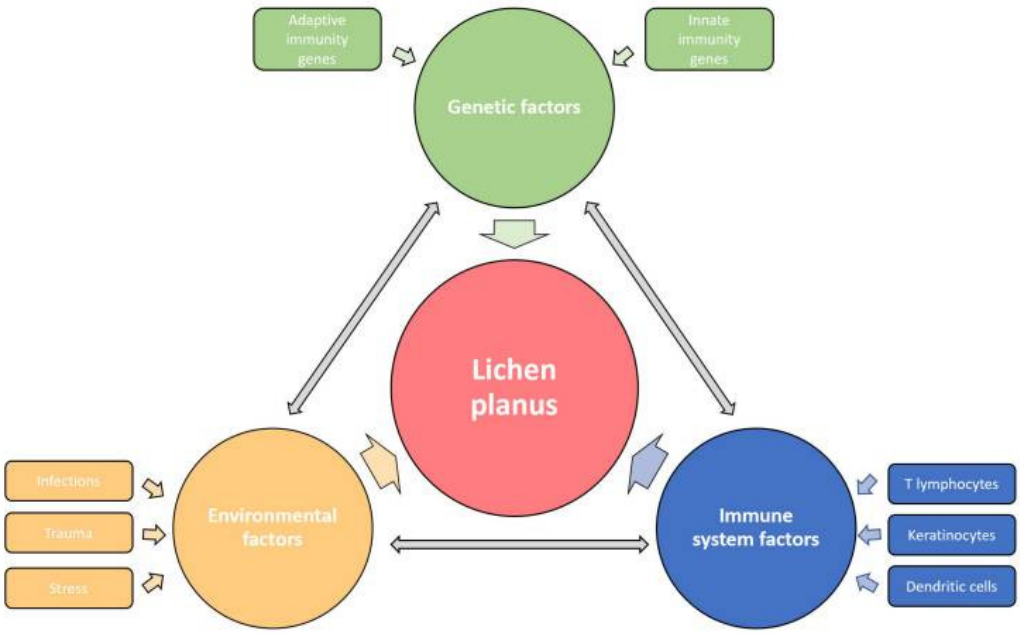

Figure 1: Factors involved in the Pathogenesis of LP. The influences of genetic, environmental and immune factors in LP development are dependent and mutually interconnected.

Genetics

Several HLA alleles are associated with LP, for example between HLA-B27, HLA-B51, HLA-Bw57 (Oral LP), HLA- DR1 (Cutaneous / oral LP), HLA-DR9, HLA DR6 (HCV-associated oral LP). In addition to the association with the HLA, single- nucleotide polymorphism (SNP) in loci encoding for NRP2 and IGFBP4 that increases or reduce risk of LP association respectively.a phenome, wide association study confirmed the HLA association in LP and additionally found two more SNPs to be associated with LP. These SNP encode for three genes: TSBP1, HCG23 and BTNL2. Further gene associations had been described for several cytokines (IFN-γ, TNFαR, IL-4, IL-6, IL-18) and others (NFκB, PGE2, Prothrombin).

Environmental Factors

Several environmental factors have been implemented to trigger LP. Systemic viral infection, such as hepatitis C may modify self-antigens on the surface of basal keratinocytes, or alter the immune balance, promoting a lichenoid inflammation. Other viruses (HHV) family especially HHV-6, HHV-7, herpes simplex viruse, varizella zoster or human papilloma virus 16 may cause LP. There are also reports that vaccine administration including influenza and hepatitis B also associated with LP development. Oral microbiome (e.g., *Candida sp*., various other bacterial infections) and mercury, copper and gold like dental metals also contribute the the development of Oral LP. Skin bacterial communities are associated with an increased expression of proinflammatory cytokines (TNFα and CXCL1) and CD11c, pointing toward an increased infiltration with Macrophages. Drugs like angiotensin-converting enzyme inhibitors, thiazide diuretics, antimalarials, anti-inflammatory drugs, antimicrobials, antihypertensives, psychiatric drugs, antidiabetics, PD-1-inhibitors, quinidine, penicillamine and metals may also elicit the lichenoid like reactions. UV-filters in sunscreens and hair care products also be associated with frontal fibrosing alopecia and lichen planopilaris.

Molecular pathogenesis

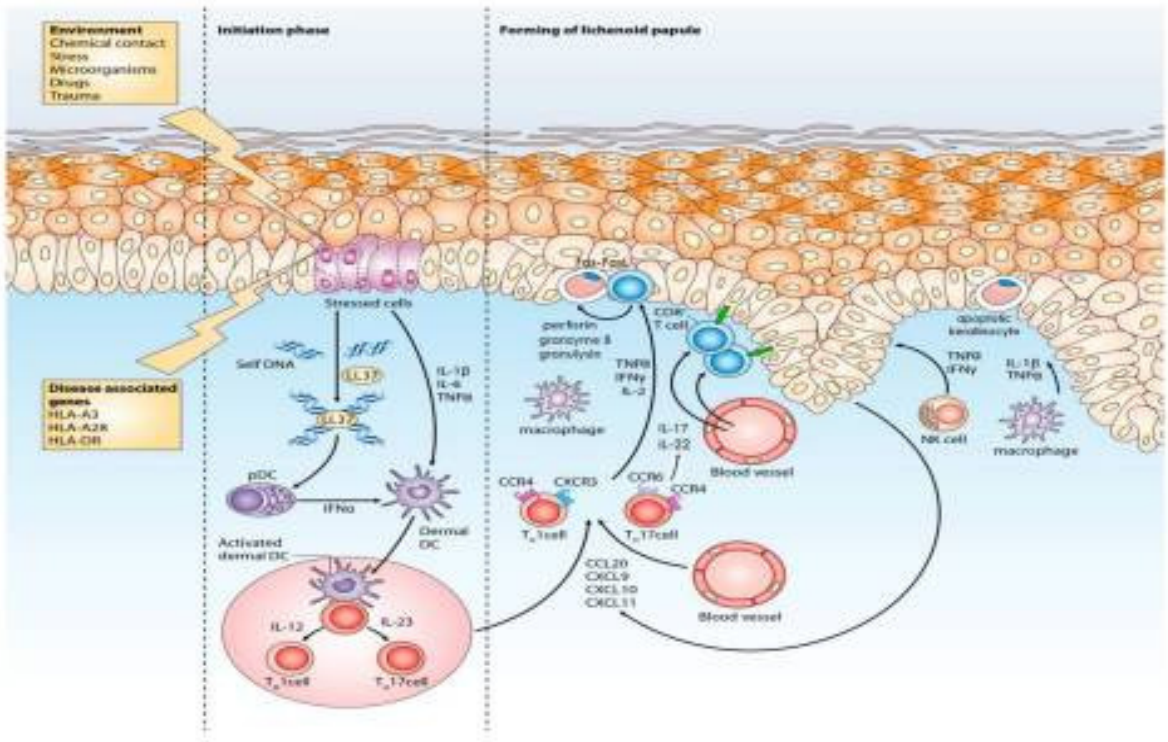

Figure 2: Major cells and Signaling pathways including in the LP complex inflammatory network. LP inflammation begins as an antigen-directed reaction, resulting the activation and differentiation of effector T lymphocytes. Th1 and Th17 lymphocytes form part of the Th1 and IL-23/Th-17 axis and influence this pathway by secreting key inflammatory cytokines such as IFN-γ and IL-17. At the same time, the key effector CD8+ lymphocytes (tc1 and Tc17) mediate epidermal injury by the Fas- FasL and TNFα- TNFα receptors interaction, but primarily by engaging cytotoxic mechanisms through granule exocytosis. The release of cytotoxic molecules such as perforin, granzyme B and granulysin causes keratinocyte apoptosis with consequent epidermal and dermal changes and the development of specific LP lesions. Other inflammatory cells such as Dcs, macrophages, and NK cells also initiate and maintain the inflammatory process.

Mostly LP pathogenesis are based on morphology. Multiple mechanisms explain the pathophysiology of lichen planus. Current understanding suggests that the immunopathogenesis of LP is caused by cell- mediated cytotoxicity, particularly cytotoxic T lymphocytes. A cell

mediated immune response with cytotoxic, CD+ T-cells accumulate in the dermis and oral mucosa, at the same time a CD8+ T-cell dominant infiltrate is visible within the epidermis.

Some report showed that CD8+ and CD45RO+ T-cells are the major cell type in the inflammatory infiltrate and that the T cell receptor (TCR) αβ, and to a lesser extent TCR γδ, are expressed. The functional contribution of T-cells to LP pathogenesis is further supported by a recent study that showed granule exocytosis with the release of perforin and granzyme B. In addition to T-cells, mast cells may contribute to LP pathogenesis given that they are often found in the inflammatory infiltrate and show signs of activation. Immunohistochemistry of oral LP also demonstrated the presence of dendritic cells. The CD8+ T-cells and mast cells are detected in lesions of LP patients led to the non-specific mechanisms like mast cell degranulation and protease activation, that are involved in the pathogenesis of LP. These mechanisms may combine to cause T-cell accumulation in lesions and induce keratinocyte apoptosis. An increased protease expression in LP lesions contributes to the disruption of the basement membrane gelatinases (e.g., MMP-2, MMP-7, and–9), chymase, tryptase, capthepsins and caspase-3. In LP patient's serum interleukin (IL)- 5, 6,8,10,12,17,22, tumor necrosis factor (TNF)-α, transforming growth factor-β, interferon (IFN)- γ, CXCR-3, 4,10,12, CCR-1,3,4,5&17 have been elevated. In some cases the off-label treatment of LP patients with Janus kinase (JAK) inhibitors (JAKi), such as tofacitinib, led to marked improvement of the disease. As IFN-γ-induced signaling centers on the activation of JAK, IFN-γ and JAK are likely to be central to the pathogenesis of LP.

Diagnosis

Histopathology

A skin/mucosal biopsy is recommended for the diagnosis of LP. The typical histological findings are acanthosis and hyperkeratosis, wedge-shaped hypergranulosis, vacuolic degeneration of the basal layer, alteration or loss of rete ridges resulting in a sawtooth appearance and a dense, band-like lymphocytic infiltrate in the upper dermis along the dermal-epidermal junction. Apoptotic keratinocytes are often seen near the basal layer and are termed colloid bodies. For LP affecting the scalp, for example LPP, shows beside the penitent LP features often the destruction of hair follicle root sheaths and follicular plugging as well as the loss of sebaceous glands as well.

Immunofluorescence

Additionally, a lesional biopsy for direct IF microscopy can be a useful, especially when trying to differentiate between LP and other autoimmune diseases, such as pemphigus vulgaris, mucous membrane pemphigoid, or lupus erythematosus (LE). In LP, direct IF microscopy may reveal globular deposits of IgA, IgM, IgG, C3, or fibrinogen mixed with apoptotic keratinocytes.

Treatment

Plant- based interventions

Aloe vera gel was significantly more effective than a placebo in improving OLP ($p< 0.001$). **Lycopene** is a red, fat soluble carotenoid that gives tomatoes and other vegetables its color. It has antioxidant activity by reducing free radicles (Elenbaas A et al., 2022). Many patients have adverse conditions for conventional steroid treatment because of systemic diseases. Antioxidants, Anthocyanins, and flavonoids found in the diet could be advantageous (Kristo A S et al., 2016). Anthocyanins are natural antioxidants that can be found in grapes skin, plums, Pomegranate, cherries, cauliflower, cabbage, black Rice, Black bean etc. which showed significant result in treating OLP.

Phototherapy

Photochemotherapy with 8-methoxypsoralen and long-wave ultraviolet light (PUVA) has become a usefulalternative in dermatologic therapy. PUVA, therapy has been successfully used in the treatment of severe psoriasis and cutaneous lichen planus. Photodynamic therapy was very effective as the dexamethasone mouth rinse in the treatment of OLP (Bakhtiari S et al., 2017).

Surgical excision

Surgical excision is recommended for non-healing lesions as it might cure the disease but is not recommended for atrophic or erosive forms. Cryosurgery has also been used in erosive OLP, but recurrences are common (Gangshetty et al., 2015)

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