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Lichen planus: A Systematic Review

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Abstract

Lichen planus (LP) is a chronic skin, mucous membrane, and nail disease. Lichen planus is a rare skin condition occurring in less than 1% of the general population, affecting both children and adults. Oral lichen planus (OLP) involvement is much more common. It is an autoimmune disease caused by T lymphocytes, with epigenetic factors playing a significant role in the development of autoimmune skin diseases. MicroRNAs (miRNAs), a group of non-coding RNAs, play a substantial role in regulating the immune response.[1] The etiology of lichen planus in not fully understood. It can be triggered by antihypertensive drugs, beta-blockers, infections, viral hepatitis, psychological stress, and others. Cases of lichen planus appearing after recovering from COVID-19 have been reported, as well as a significant increase in cases after COVID-19 vaccination.[2–5] Diagnosis is based on clinical presenstation and characteristic histopathological findings. The disease is often self-limiting, accompanied by persistent itching and painful erosions of the mucous membrane, affecting the patient's quality of life and mental well-being. First-line treatments inculde topical corticosteroids and/or oral corticosteroids. There are reports of new potential treatments, such as biologic drugs (anti-IL12/13, anti-IL17) and Janus kinase inhibitors. Consequently, a dramatic change in lichen planus treatment can be expected in the near future. The majority of patients suffering from lichen planus develop metabolic syndrome which is the cause of other diseases. This article provides a comprehensive overview of current knowledge about lichen planus and its variants.

Keywords: Lichen planus (LP); Oral lichen planus (OLP); autoimmune; CD8+cytotoxic T-cell (CTL); COVID-19; skin disease

Introduction

Lichen planus is a chronic inflammatory skin disease with an immunological basis that induces a persistent inflammatory state. It is characterized by the presence of flat, shiny, polygonal skin lesions in the form of purple, itchy papules. On close inspection, a Wickham's striae network is visible [6] , and the lesions may follow a linear arrangement (Koebner phenomenon). [7] The eruptions are typically located on the lower back, wrists, forearms, and ankles of the lower limbs. Lichen planus can also affect mucous membranes (oral cavity, esophagus, genital organs), the hairy skin of the scalp, and nail plates. Branching lesions on mucous membranes may appear white and painful, located on the cheek mucosa along the tooth occlusal line, less frequently on the tongue, and rarely on the vermilion border of the lips. Oral mucous membranes are affected in 50% of patients, and this may be the only site of involvement. The appearance of lesions varies depending on the duration and location. They do not leave scars, only atrophy (atropic form). The disease can occur at any age, most commonly between the ages of 30 and 60. The frequency increases around the perimenopausal period women. Oral musous membranes are more frequently affected in women, while mucous membranes of the genital organs are more often affected in men. [8] Despite extensive research, the exact etiology remains unknow. Histopathological features include degeneration of basal layer cells and infiltrating cells in the lamina propria of the oral mcous membrane. Lichen planus is a chronic disease often resistant to treatment, characterized by relapses despite ongoing therapy. Multiple forms of lichen planus may coexist in the same patient.[8] Lichen planus induceds is a chronic inflamatory state, altering the microenvironment and releasing factors conductive to the development of future noeplastic processes. The highest likelihood of malignant transformation is in the erosive subtype. The probability of developing cancer in the oral cavity is around 1% in the presence of lichen planus. [9] Recently, many studies have shown the presence of immunological markers in the course of lichen planus, offering prospects for improved diagnostics and modern treatment. This provide hope for non-invasive diagnostic. The course of lichen planus can be chronic and recurrent. It is considered a self-limiting disease, with an average duration of 1-2 years.[10]

Histopathology

Changes occur in the skin and mucous membranes of the oral cavity and genital organs. Thease alterations may result form a cytotoxic immune response by CD8+ T cells, reacting to antigens in the basal layer of the epidermis and at the dermo-epidermal junction. Excessive pigmentation may result from the release of melanin into the skin from damaged keratinocytes.

Darker skin tones are predisposed to more significat discoloration. Microscopically, lichen planus (LP) is characterized by interface dermatitis, an inflamation of the splitting surface. Changes occur at the interface between the epidermis and dermal papillae, with lymphocytic infiltration at the dermo-epideraml junction. In the early stages, macrophages and CD4+ lymphocytes predominate, while in later stages, there is an abundance of CD8+ lymphocytes.[11] Within the dermal papillae, altered necrotic cells are visible (colloid bodeis – Civatte bodies) [10] . Additionally, excessive keratynization is observed. The histopathological appearance is similar to that of erythema multiforme. It's important to emphasize that histopathological analysis is a curcial tool in diagnosing lichen planus, and the described features help in identifying and confirming this condition, The final diagnosis should be accurately determinated by an experienced pathologist based on all available clinical and laboratory information. Direct immunofluorescence (DIF) shows spherical deposits of various immunoglobylins, especially IgM, as well as complement components and fibrynogen, mixed with apoptotic keratinocytes (Civatte bodies)[6,11–13].

Epidemiology

The exact frequency of lichen planus in not known. It is estiamted to affect approximately 1% of the population. Oral lichen planus (OLP) is more common in women, while in its cutaneous from the frequency is similar in both genders. Lichen planus can occur at any age. It is more common in women around perimenopausal age, typically between 50-60 years, whereas in men, it trends to occur earlier. [10] The disease is rarely found ich children, constituting 1-3% of all cases. In children, mucous membrane involvement is very rare. [14] Subungual (under the nail) location is extremely rare. Studies suggest that lichen planus is more prevalent among individuals of Asian origin, although confirming data is lacking.

Genetics

Research confirms the occurrence of a familial from of lichen planus. The familial from constitutes 10% of all lichen planus cases and is characterized by an erlier onest, more frequent relapses, resistance to treatment, and involvement of mucous membranes. Several genotypes associated with the development of lichen planus have been identified. In the familial from of lichen planus, genotypes such as HLA-A3, HLA-Aw19, HLA-B7, HLA-B18,

HLA-Cw8 have been distinguished. In cases involving mucous membranes, genotypes such as HLA-B8, HLA-Bw57, HLA-Bw61 have been identified. In addition to the association with HLA, a significant link with single nucleotide polymorphism (SNP) has been demonstrated – rs794275 has been identified as the most significant in the development of lichen planus. It has been shown that SNPs have a significant impact on genes with immunological functions, and associations of these genes have been described for several cytokines, including IL-4, IL6, IL-18, TNF and IFN. [8]

Etiology

The etiology of disease, despite numerous studies, is not fully undrestood, and the target antigen remains unknown. There are many potential factors. The coexistence of lichen planus with other autoimmune diseases, such as psoriasis, ulcerative colitis, autoimmune hepatitis, and thyroid diseases (Hashimoto's thyroiditis) [15,16] , has been described. A significant association has been demonstrated between lichen planus and infections such as hepatitis C virus (HCV), hepatitis B virus (HBV), human papillomavirus (HPV), and herpes simplex virus. Results from two meta-analyses indicate that HCV infection is five times more common in patients with lichen planus than in the control group. The risk of developing lichen planus in individuals with viral hepatitis C is 2,5-4,5 times higher. [3,17–19]

A correlation has been observed between the onset or exacerbation of lichen planus and a history of COVID-19 or vaccination against COVID-19. According to hypotheses, the spike protein of the SARS-CoV-2 virus may lead to an increase in cytocine levels and the activation of CD8+ T lymphocytes. Antigens of the SARS-CoV-2 virus may mimic antigens of basal layer keratinocytes, potentially influencing the onset of lichen planus after recovering from the infection or vaccination. [4]

Numerous medications taken in the last two years before the appearance of skin lesions may contritube to the development of lichen planus. Medications that may be implicated include antihypertensive drugs (ACE inhibitors, beta-blockers, nifedipine, methyldopa, diuretics) [20] , non-sterodial anti-inflammatory drugs (NSAIDs), phenothiazine derivaties, anticonvulsants (carbamazepine, phenytoin), tuberculosis therapy drugs, antifungal drugs (e.g., ketoconazole) chemotherapeutics (hydroxycarbamide, 5-fluorouracil, imatinib), antimalarials (hydroxychloroquine), sulfonylureas (e.g., dapson, sulfasalazine), metals (gold salts), TNF-alpha antagonists (infliximab, etanercept, adalimumab), tyrosine kinase inhibitors,

mizoprostol (prostaglandin E1 agonist), vaccines against hepatitis B, vaccines against COVID-19, and other drugs such as allopurinol, contrast agents, interferon-alpha, omeprazole, penicillamine, tetracycline, antidepressants, and mood stabilizers. Stress may also be a contributing factor. After excluding possible causes, the etiology often remains idiopathic.

Clinical apperience

Lichen planus has many clinical variants and can vary in terms of location and morphology. Typical lesions of lichen planus may appear as: plaques, hyperkeratosis, ulcers, or blisters. It can manifest in various morphological forms, including erythroderma, inverted form, and linear form. The histopathological form remains consistent, facilitating the diagnosis.

Cutaneous lichen planus

The primary lesion is a polygonal, bluish-purple papule with a diameter ranging from a few millimeters to over one centimeter. The lesions are covered with Wickham's striae, visible under dermatoscopy. The papules may be grouped or appear as a papular rash. The isomorphic Koebner phenomenon is present, where new skin lesions emerge approximately 2 weeks after mechanical skin injury, such as scratching in that area. The lesions are accompanied by presistent itching that is challenging to treat. Predilection areas include the wrists, dorsal aspects of the hands, forearms, sacral/lumbar region, and the ankles of the lower limbs.[21]

Mucosal lichen planus (MLP)

The most common location of mucosal lichen planus is the oral cavity (oral lichen planus OLP), specifically the buccal mucosa (mcous membrane of the cheeks). The morphology varies, and accordnig to Andersen, oral lichen planus six different forms: reticular, plaque-like, atrophic, papular, erosive, and bullous. The plaque-like type most commonly affects the upper and lateral surface of the tongue. [10] There is no observed correlation between the other morphological forms and specific locations. Erosive or atrophic forms may be accompanied by a burning pain, exacerbated by hot and acidic foods.[22] Research indicates that oral lichen planus may serve as a precancerous condition and can be a cause for future cancer development, with malignant transformation occurring in 0,4-5,3% of cases. [23] Authors emphasize the involvement of the esophageal mucosa. Esophageal changes are more commonly diagnosed in women reporting odynophagia and dysphagia. Mucosal changes in

the esophagus can lead to fibrosis and narrowing of the esophageal lumen. Approximately 50% of patients with esophageal involvement are asymptomatic. Isolated esophageal involvement has also been reported.[24] Another location affected is the mucous membranes of the genital organs, with the glans penis in men and the vulva in women. The risk of malignant transformation into squamous cell carcinoma of the vulva is estimated to be 2,4%. Simultaneous presence of mucosal changes in the oral cavity and genital organs is referred to as vulvovaginal-gingival syndrome. In 80% of women, the HLA DQb1*0201 gene is detected, suggesting a genetic predisposition. Changes in genital mucous membranes are often observed in the vicinity of previously implanted dental materials. [25,26]

Nail lichen planus

Involvement of the nail plates in lichen planus does not exhibit any pathognomic symptoms. The morphological changes can vary. Clinical features of lichen planus affecting the nail plates icnclude nail plate thinning, longitudinal grooving, pterygium (adhesion of the nail fold to the nail plate), roughness of the nail plates (trachyonychia), separation of the nail plates (onycholysis), longitudial ridges on the nail plates (onychorrhexis), depression of the nail plate (kolionychia), subungual hyperkeratosis, changes in nail plate color (chromonychia), and shedding of the nail plate (onychomadesis). The nail plates become thin with longitudinal grooving and roughness. Pterygium occurs due to the connection between the nail fold and the matrix, leading to nail plate splitting and complete detachment. The nail plate loses transparency and turns gray. Changes can occur stimultaneously in several nail plates, and up to 20 nails can be affected at the same time. Nail changes can be isolated or may precede or follow skin changes.[10]

There are many other clinical variants of lichen planus, and the classification has been created based on various morphological features and the distribution of skin lesions. Lichen planus can be classified into several types, including: annular (ring-like), hypertrophic (thickened), atrophic (wasting), ulcerative, vesicular (blistering), pemphigoid-type, pigmentary, erythrodermic, inverse, linear, follicular, causing alopecia, and actinic. [27]

The Graham-Little-Piccardi-Lasseur syndrom

The Graham-Little-Piccardi-Lasseur syndrome is a skin disorder characterized by three components: lichen planopilaris, non-scarring loss of pubic and axillary hair, and scarring

alopecia on the hairy scalp. Not all components of the syndrome need to be present simultaneously. Additionally, patients may have brown patches on the face, trunk, and limbs, as well as classic lichen planus. The etiopathogenesis of the syndrom is not fully understood, with some scientists considering it a variant of lichen planopiliaris. Itching is not a constant symptom. In the differentail diagnosis, conditions such as psoriasis, pityriasis rubra pilaris, and lichenoid eruptions should be considered. The syndrom is more commonly described in women around the menopausal age. Some patients have been associated with HLA-DR1. A connection with HBV infection and HBV vaccination has been observed. Immunopathological examination shows deposits od IgG, IgM and IgA at the dermoepidermal junction. The presence of autoantibodies against the INCENP protein complex, which regulates mitosis, has been noted. The immune response against ACA is similar to that in systemic sclerosis. The syndrome is very challenging to treat, and therapeutic approaches include topical corticosteroids, retinoids, and PUVA phototherapy. [28]

Immunopathology and diagnosis, biomarkers

The diagnosis of the classic form of lichen planus is usually not a problem. However, the recognition of other forms of lichen planus can be decidedly more challenging. Therefone, histopathological examination of the skin lesions plasys a curcial role. The morphological appearance and clinical characteristics of the skin changes are described in the paragrahps above. In recent times, numerous studies point to the presence of immunologic markers in lichen planus, offering the potential for future development of non-invasive diagnostic.

Cellular markers: Increased expression of CD3+, CD4+, CD8+, CD19+, CD3+ markers specific for T and B lymphocytes. Dominance of CD27+ cells – present deep in the dermis, not directly influencing the disease process but having a correlation with the autoimmune process. Elevated levels of Th9 lymphocytes, which increase Th17 lymphocytes, acting synergistically to intensify the disease process. Macrophages are present in chronic inflammatory infiltrates, and the breakdown products of macrophages may induce malignant transforamtion. Increased infiltration of CD11c+/CD123+ dendritic cells. High concentrations of Toll-like receptors 7 (TLR7), TLR8, and TLR9. Deactivation of TLR2. Low concentrations of Toll-like receptor 4 (TLR4) are observed in the epidermis, while they are high in the dermis of patients. This receptor induces the expression of programmed death ligand 1 (PDL-1) on keratinocytes. PDL-1, in turn, inhibits the proliferation of CD8+ T lymphocytes and CD4+ T lymphocytes, while simultaneously inducing apoptosis. Interferon-alpha stimulates the

development of the disease and exacerbations. Antigen receptors on T lymphocytes recognize specific foregin antigens through MCH I/II. CD4+ lymphocytes release IL-2 and INF – gamma to activate CD8+ T lymphocytes, initiating apoptosis. Studies identify heat shock protein 27 (Hsp27) in keratinocytes as an antigenic stimulus. Interlekins play a crucial role in non-invasive diagnostics, with particular importance in differentiating between the erosive from and the reticular od lichen planus. In the erosive form, key interleukins include Il-4, Il-17, Th17, TNF, IL-22 and IL-6. In the reticular form IL-25 and Il-10 are significant. Il-6 is considered the most useful interleukin in lichen planus diagnostics, associated with proinflammatory processes, angiogenesis, invasion, and metastasis. The most useful interleukin in the diagnosis of lichen planus is IL-6.[11] It is a proinflammtory cytokine involved in angiogenesis, invasion, and metastasis processes. Differentiating between forms of lichen planus can be achived through IL-6 levels, with significantly higher concentrations in the saliva of patients with the erosive form.[29] IL-4 plays a role in the Th-2 – dependent humoral response, and its concentration in the saliva of patients is also higher. IL-4 serves as a biomarker for the severity of the disease. Based on IL-22 levels, disease recurrence can be predicted. In recurrent erosive forms, a ninefold increase in IL-22 concentration was observated compared to the control group. [11,16,30]

The new molecular studies indicate that after an increase in INF-gamma activit, the expression of MHC I by keratinocytes is mainly enhanced through the JAK2/STAT1 pathway. These studies suggest that inhibiting the JAK2/STAT1 pathway may protect keratinocytes from cytotoxic responses. These findings provide hope for more effective and modern treatments that those available thus far. [31]

Metabolic syndrom in patients with lichen planus

The conducted research indicates a significant association between metabolic syndrome and lichen planus. Studies show that metabolic syndrome is significantly linked to the severity, duration, and morphology of lichen planus. It is suspected that autoimmune theory underlies the metabolic syndrom in lichen planus. Interleukins IL-1, IL-6,IL-9,IL-23, TNF-alpha and INF-gamma are overexpressed on lichen planus. TNF-alpha reduces insulin sensitivity by inactivating the peroxisome proliferator – activated receptor. IL-6 increases the synthesis of C-reactive protein in the liver, leading to reduction in prostacyclin synthesis. Prostacyclin is a potent cytokine that dilates blood vessels. Reduced prostacyclin synthesis may contritube to the development of arterial hypertension in LP patients. Reduced insulin sensitivity becomes

that cause of hyperglycemia. Metabolic syndrome is significantly associated with duration of LP, possibly due to prolonged inflammation. Chronic inflammation in LP causes a significant increase in cytokine levels and the development of metabolic syndrome. Additionally, it has been shown that oral lichen planus (OLP) occurs more frequently in patients with poor dietary habits, such as a diet rich in animal fats (red meat, highly processed food, fried food). [32] Dislipidemia observed in up to 81,4% of cases in patients with lichen planus. Dyslipidemia in lichen planus may be caused by cytokine-mediated lipolysis. Different patterns of dyslipidemia occur in lichen planus patients, with elevated trigliceride levels, elevated low-density lipoprotein levels and low high – density lipoprotein levels being the most common.[33] [32,34]

Treatment and Managment

In the first-line treatment of cutaneous LP, topical corticosteroids with very high or high potency are recommended, such as triamcinolone acetonide, fluocinolone acetonide, clobetasol propionate, and betamethasone dipropionate. In hypertrophic lesions, triamcinolone can be administered by intralesional injections over 2-4 weeks. If local therapy is ineffective, systemic corticosteroids are recommended orally or by injection. Prednisone at a dose of 30-80 mg/day orally for 4-6 weeks or tramcinolone 40-80 mg by intramuscular injection every 6-8 weeks can be considered. Acitretin or isotretinoin may also be used. For presistent itching, antihistamines can be used. [35]

In second-line treatment, narrowband or broadband UVB, combination of UVB with acitretin, locally acting calcineurin inhibitors (tacrolimus, pimecrolimus) for 1-2 months, or mycophenolate mofetil can be employed. [35] Nd:YAG laser, low-dose excimer laser (308nm), apremilast (used for psoriasis, psoriatic arthritis, Behcet's disease), and ustekinumab (human monoclonal antibody) are other therapeutic options. [36,37]

Treatment of oral lichen planus (OLP) is challenging and mainly symptomatic, aiming to reduce the risk of malignant transformation. In OLP, the first-line treatment involves the application of potent steroids, available in the form of ointments, adhesive pastes, mouthwash solutions, or aerosols. In conventional therapy, the medication is typically administred once or twice daily for 1-2 months. Systemic treatment with retinoids or corticosteroids may also be used for OLP. [27,38]

Recently published scientific studies provide evidence that the activation of the JAK2-STAT1 kinase is one of the causes of the development of lichen planus. Cytokines activated through the JAK2-STAT1 pathway contritube to the pathogenesis of lichen planus. Inhibition of the JAK2-STAT1 pathway potentially may yield positive results in the treatment of persistent lichen planus. This is particularly relevat as the use of topical coricosteroids often only limits the disease during their application. Systemic administration of corticosteroids may lead to various complications such as weight gain, hypertension, stretch marks, osteoporosis, patechiae, acne and iatrogenic Cushing's syndrome. The safety profile of JAK2-STAT1 pathway inhibitors appears to be very good. Adverse effects were reported in only 2 out of 56 patients, which is 3,3%. The drugs belonging to this gropu that were studied include tofacitinib, baricitinib, ruxolitinib, and upatacitinib. These promising results underscore the need for further research on JAK inhibitors in the treatment of lichen planus. Currently, the FDA has not approved this gruop of drugs for treatment of lichen planus. [31,39,40]

Differential diagnosis

In the differential diagnosis of lichen planus (LP), various dermatological conditions should be considered, inculding: lichen nitidus, lichen sclerosus (lichen sclerosus et atrophicus) lichen spinulosus, Graft-versus-host disease (GVHD), lichen striatus, linear epidermal nevus, nevus unius lateralis, eczema, lichen simplex chronicus, prurgio nodularis, pityriasis rosea, guttate psoriasis, psoriasis vulgaris, drug eruptions, syphilis, fungal infections of the smooth skin, papular acrodermatitis of childhood, granuloma annulare, lichen amyloidosus, pityriasis lichenoides, Kaposi's sarcoma. These conditions exhibit various clinical and histological features that help differentiate them from lichen planus. A thorough examination, including history, clinical presentation, and, if necessary, biopsy, is essential for accurate diagnosis and appropriate management. [10]

Conclusion

With the advancements in scientific research in recent years, numerous sciencific papers have been published on LP and its clinical variants. Studies are conducted from various perspectives, with researches particulary exploring the pathophysiology and pathomechanism underlying the development of lichen planus. Progress in this field and the discovery of the involvement of the JAK2-STAT1 kinase in the molecular development of lichen planus offer hope for new pharmacological treatment methods. The search for new treatment methods

provides an opportunity to find effective therapy that can halt the recurrence of the disease. It is reassuring that effective OLP therapy reduces the risk of malignant transformation in the future. I want to emphasize that scientist continue to extensively and diligently search for the triggering causes of lichen planus. Identifying and eliminating a specific cause holds the potential for more effective therapy. According to the current state of knowledge, cytotoxic mechanisms of cellular immunity play a major role in pathogenesis. In addition to lymphocytes, macrophages, NK cells, keratinocytes, mast cells, and Treg cells paticipe in the development of lichen planus. Studing disease biomarkers, such as IL-6, may contribue to the development of non-invasive diagnostics that would be more accessible to patients. In the post-COVID-19 pandemic era, where millions of people have recovered from COVID-19 and been vaccinated against COVID-19, researches are investigating the impact of the SARS-CoV-2 virus on skin diseases and exploring its association with lichen planus. Detailed immunopathogenetic studies could contribute to the developmentof targeted therapies. Meta-analyses show that patients with lichen planus are significantly more like to develop metabolic syndrom. This information suggests that it is worthwhile to conduct dignostic assessments for metabolic syndrome in patients with lichen planus. Treating metabolic syndrom is essential to prevent conditions such as colorectal cancer, cardiovascular diseases like stroke or heart attac, and many other diseases where metabolic syndrome serves as an underlying factor. [32,34] Finding effective targeted therapy would improve the physical and mental health of patients. It is essential to remember that dermatological diseases significantly reduce the quality of life, often causing embarrassment and distress. A holistic approach to the patient and their condition will help achieve the goal of complete healing.

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References:

1. Dopytalska K, Czaplicka A, Szymańska E, Walecka I. The Essential Role of microRNAs in Inflammatory and Autoimmune Skin Diseases—A Review. *Int J Mol Sci*. 2023;24(11). doi:10.3390/ijms24119130

2. Picone V, Fabbrocini G, Martora L, Martora F. A Case of New-Onset Lichen Planus after COVID-19 Vaccination. *Dermatol Ther (Heidelb)*. 2022;12(3):801-805. doi:10.1007/s13555-022-00689-y

3. Quattrini L, Verardi L, Caldarola G, Peluso G, De Simone C, D'Agostino M. New onset of remitting seronegative symmetrical synovitis with pitting oedema and palmoplantar psoriasis flare-up after Sars-Cov-2 vaccination. *Journal of the European Academy of Dermatology and Venereology*. 2021;35(11):e727-e729. doi:10.1111/jdv.17502

4. Zou H, Daveluy S. Lichen planus after COVID-19 infection and vaccination. *Arch Dermatol Res*. 2023;315(2):139-146. doi:10.1007/s00403-022-02497-y

5. Tamer F, Polat M. the onset or exacerbation of lichen planus following coVid-19 and vaccination against coVid-19. *Przegl Dermatol*. 2023;110(4):529-546. doi:10.5114/dr.2023.131386

6. Ianoși S, Forsea A, Lupu M, et al. Role of modern imaging techniques for the in vivo diagnosis of lichen planus (Review). *Exp Ther Med*. Published online November 16, 2018. doi:10.3892/etm.2018.6974

7. Fagotto L, Gnesotto L, Vincenzi C, Piraccini BM, Naldi L, Sechi A. Wickham striae on skin appendages: a helpful dermoscopic feature. *Dermatol Reports*. Published online June 6, 2023. doi:10.4081/dr.2023.9698

8. Boch K, Langan EA, Kridin K, Zillikens D, Ludwig RJ, Bieber K. Lichen Planus. *Front Med (Lausanne)*. 2021;8. doi:10.3389/fmed.2021.737813

9. González-Moles MÁ, Keim-del Pino C, Ramos-García P. Hallmarks of Cancer Expression in Oral Lichen Planus: A Scoping Review of Systematic Reviews and Meta-Analyses. *Int J Mol Sci*. 2022;23(21). doi:10.3390/ijms232113099

10. Solimani F, Forchhammer S, Schloegl A, Ghoreschi K, Meier K. Lichen planus – a clinical guide. *JDDG - Journal of the German Society of Dermatology*. 2021;19(6):864-882. doi:10.1111/ddg.14565

11. Ostrowska A, Susło A. Immunological abnormalities in lichen planus. *Przegl Dermatol*. 2022;109(3):217-228. doi:10.5114/dr.2022.120179

12. Rotaru DI, Sofineti D, Bolboacă SD, Bulboacă AE. Diagnostic Criteria of oral lichen planus: A narrative review. *Acta Clin Croat*. 2020;59(3):513-522. doi:10.20471/acc.2020.59.03.16

13. Gupta S, Ghosh S. 4 Biopsy is reserved for noncharacteristic lesions Oral lichen planus Interventions for the manage-ment of oral lichen planus: a review of the conventional and novel therapies. *J Oral Pathol Med*. 2020;192:1029-1071. doi:10.1503/cmaj.200309/-/DC1

14. Joshi A, Rathi S, Manchanda Y. Childhood lichen planus. *Indian Journal of Paediatric Dermatology*. 2021;22(4):306. doi:10.4103/ijpd.ijpd_132_20

15. Wu P, Luo S, Zhou T, et al. Possible Mechanisms Involved in the Cooccurrence of Oral Lichen Planus and Hashimoto's Thyroiditis. *Mediators Inflamm*. 2020;2020. doi:10.1155/2020/6309238

16. De Porras-Carrique T, Ramos-García P, Aguilar-Diosdado M, Warnakulasuriya S, González-Moles MÁ. Autoimmune disorders in oral lichen planus: A systematic review and meta-analysis. *Oral Dis*. 2023;29(4):1382-1394. doi:10.1111/odi.14127

17. Cozzani E, Herzum A, Burlando M, Parodi A. Cutaneous manifestations of HAV, HBV, HCV. *Italian Journal of Dermatology and Venereology*. 2021;156(1):5-12. doi:10.23736/S2784-8671.19.06488-5

18. Alaizari NA, Al-Maweri SA, Al-Shamiri HM, Tarakji B, Shugaa-Addin B. Hepatitis C virus infections in oral lichen planus: a systematic review and meta-analysis. *Aust Dent J*. 2016;61(3):282-287. doi:10.1111/adj.12382

19. García-Pola M, Rodríguez-Fonseca L, Suárez-Fernández C, Sanjuán-Pardavila R, Seoane-Romero J, Rodríguez-López S. Bidirectional Association between Lichen Planus and Hepatitis C—An Update Systematic Review and Meta-Analysis. *J Clin Med*. 2023;12(18). doi:10.3390/jcm12185777

20. Tatu A, Elisei A, Chioncel V, Miulescu M, Nwabudike L. Immunologic adverse reactions of β-blockers and the skin (Review). *Exp Ther Med*. Published online April 18, 2019. doi:10.3892/etm.2019.7504

21. Watanabe T, Yamaguchi Y. Cutaneous manifestations associated with immune checkpoint inhibitors. *Front Immunol*. 2023;14. doi:10.3389/fimmu.2023.1071983

22. Massimo P, Petruzzi M, Della Vella F, et al. DIAGNOSTIC DELAY IN AUTOIMMUNE ORAL DISEASES. doi:10.48350/176517

23. Migliari D. Will there be a critical review on the malignant transformation of oral lichen planus? *Clinics*. 2023;78. doi:10.1016/j.clinsp.2022.100146

24. Decker A, Schauer F, Lazaro A, et al. Esophageal lichen planus: Current knowledge, challenges and future perspectives. *World J Gastroenterol*. 2022;28(41):5893-5909. doi:10.3748/wjg.v28.i41.5893

25. Khurana A, Tandon S, Marfatia Y, Madnani N. Genital lichen planus: An underrecognized entity. *Indian J Sex Transm Dis AIDS*. 2019;40(2):105. doi:10.4103/ijstd.ijstd_45_19

26. Villa TG, Sánchez-Pérez Á, Sieiro C. Oral lichen planus: a microbiologist point of view. doi:10.1007/s10123-021-00168-y/Published

27. Grover C, Bansal S. A compendium of intralesional therapies in nail disorders. *Indian Dermatol Online J*. 2018;9(6):373. doi:10.4103/idoj.idoj_280_18

28. Owcza W, Ziaj E, Pa E, Chow Ska L. *Postępy Dermatologii i Alergologii XXVII; 2010/1 66*.

29. Melguizo-Rodríguez L, Costela-Ruiz VJ, Manzano-Moreno FJ, Ruiz C, Illescas-Montes R. Salivary biomarkers and their application in the diagnosis and monitoring of the most common oral pathologies. *Int J Mol Sci*. 2020;21(14):1-17. doi:10.3390/ijms21145173

30. Vičić M, Hlača N, Kaštelan M, Brajac I, Sotošek V, Prpić Massari L. Comprehensive Insight into Lichen Planus Immunopathogenesis. *Int J Mol Sci*. 2023;24(3). doi:10.3390/ijms24033038

31. Yeung J, Abduelmula A, Bagit A, Mufti A, Yeung KC. *The Use of Janus Kinase Inhibitors for Lichen Planus: An Evidence-Based Review*. Vol 27.; 2023.

32. Mathur M, Thakur N, Jaiswal S, et al. Metabolic syndrome in patients with lichen planus: A case-control study. *Skin Health and Disease*. Published online 2023. doi:10.1002/ski2.315

33. Nowowiejska J, Baran A, Flisiak I. Lipid Aberrations in Lichen Planus. *Metabolites*. 2022;12(11). doi:10.3390/metabo12111008

34. Ying J, Xiang W, Qiu Y, Zeng X. Risk of metabolic syndrome in patients with lichen planus: A systematic review and meta-analysis. *PLoS One*. 2020;15(8 August). doi:10.1371/journal.pone.0238005

35. Usatine RP, Tinitigan M. *Diagnosis and Treatment of Lichen Planus*. Vol 84.; 2011. www.aafp.org/afpAmericanFamilyPhysician53

36. Branisteanu D, Dirzu D, Toader M, et al. Phototherapy in dermatological maladies (Review). *Exp Ther Med*. 2022;23(4). doi:10.3892/etm.2022.11184

37. Nagi R, Muthukrishnan A, Rakesh N. Effectiveness of photodynamic therapy (PDT) in the management of symptomatic oral lichen planus -A systematic review. *J Oral Biol Craniofac Res*. 2023;13(2):353-359. doi:10.1016/j.jobcr.2023.03.003

38. Rotaru D, Chisnoiu R, Picos A, Picos A, Chisnoiu A. Treatment trends in oral lichen planus and oral lichenoid lesions (Review). *Exp Ther Med*. 2020;20(6):1-1. doi:10.3892/etm.2020.9328

39. Hammers CM, Parlatescu I, Takashi Hashimoto R, et al. *OPEN ACCESS EDITED BY Therapeutic Strategies for Oral Lichen Planus: State of the Art and New Insights*.

40. Huang MY, Armstrong AW. Janus-kinase inhibitors in dermatology: A review of their use in psoriasis, vitiligo, systemic lupus erythematosus, hidradenitis suppurativa, dermatomyositis, lichen planus, lichen planopilaris, sarcoidosis and graft-versus-host disease. *Indian J Dermatol Venereol Leprol*. 2023;90:30-40. doi:10.25259/ijdvl_15_2023