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Studyof Lichen Planus Variants and An Overview of Available Management

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Abstract

Background:Lichen planus is an uncommon disorder of unknown cause that most commonly affects middle-aged adults. Lichen planus may affect the skin (cutaneous lichen planus), oral cavity (oral lichen planus), genitalia (penile or vulvar lichen planus), scalp (lichen planopilaris), nails, or esophagus.The frequency of LP varies on the basis of the population studied, with a particularly high rate of disease noted on the Indian subcontinent. LP most commonly affects middle-aged people, although childhood-onset LP has also been well described. Women are affected as frequently as men. LP is a self-limited condition that, according to one epidemiologic study, may resolve after 1 month to 7 years. A range of topical and systemic medications have been shown to improve the symptoms associated with LP and to hasten the resolution of LP.The pathogenesis of LP is not entirely understood. In general, activated T lymphocytes are recruited to the dermal–epidermal junction and induce apoptosis in basal keratinocytes. Both $CD4^+$ and $CD8^+$ T lymphocytes are found in the lichenoid infiltrate of LP, with a predominance of the latter cell type being present in established lesions.

Keywords: Lichen planus.lichen planopilaris.

Lichen Planus:

Definition:

Lichen planus is an uncommon disorder of unknown cause that most commonly affects middle-aged adults. Lichen planus may affect the skin (cutaneous lichen planus), oral cavity (oral lichen planus), genitalia (penile or vulvar lichen planus), scalp (lichen planopilaris), nails, or esophagus **(1).**

Epidemiology

Based upon data, cutaneous lichen planus is estimated to occur in less than 1 percent of the population. Cutaneous lichen planus most frequently develops between the ages of 30 and 60 years. Childhood cutaneous lichen planus occurs, but is uncommon. There is no strong sex or racial predilection for cutaneous lichen planus **(2).**

No significant differences in incidence for lichen planus are noted between male and female patients, but in women, lichen planus may present as desquamative inflammatory vaginitis **(3).**

Etiology

The etiology of lichen planus is not fully understood. An immune- mediated mechanism involving activated T cells, particularly CD8+ T cells, directed against basal keratinocytes has been proposed. Upregulation of ICAM-1 and cytokines associated with a Th1 immuneresponse, such as interferon IFN-gamma, TNF- α, IL-1 alpha, IL-6, and IL-8, may also play a role in the pathogenesis of lichen planus **(4).**

Hepatitis C virus

The association of hepatitis C virus (HCV) with lichen planus is controversial. A meta-analysis of primarily case-control studies conducted in a number of countries found a statistically significant association between HCV and lichen planus. Compared with control patients, the prevalence of HCV exposure was greater among patients with lichen planus. A systematic review also identified an increase in the proportion of lichen planus patients that were HCV positive compared with controls. However, subgroup analysis in both studies revealed that the strength of this association varied geographically, but not in all locations. Estimates of the prevalence of HCV infection among patients with oral lichen planus vary widely; studies have reported prevalence rates from 0 to 62 % **(5).**

In a study from Italy, among 178 adults with HCV antibodies, five (2.8 %) had oral lichen planus. There were also reports of the development or exacerbation of lichen planus during interferon (IFN) treatment for chronic HCV; the lesions improved when IFN was stopped **(6).**

Drugs

Clinical manifestations that resemble idiopathic lichen planus can occur as a result of drug exposure **Table (1).**

(Table 1). Drugs causing lichenoid eruptions (drug-induced lichen planus) **(2).**

Antimicrobialsubstances	Aminosalicylatesodium,ethambutol,griseofulvin,ketoconazole,streptomycin,tetracycline,trovafloxacin,isoniazid
Antihistamines(H2-blocker)	Ranitidine,roxatidine
Antihypertensives/antiarrhythmics	ACE-inhibitors(captopril,enalapril),doxazosin,betablockers(propranolol,labetalol,sotalol),methyldopa,prazosin, nifedipine,quinidine
Antimalarialdrugs	Chloroquine,hydroxychloroquine,quinine

Antidepressives/antianxietydrugs/antipsychotics/Anticonvulsants	Amitriptyline, carbamazepine, chlorpromazine,levomepromazine,methopromazine, imipramine,lorazepam,phenytoin
Diuretics	Thiazidediuretics,furosemide,spironolactone
Antidiabetics	Sulfonylureas(chlorpropamide,glimepiride,tolazamide,tolbutamide,glyburide)
Metals	Goldsalts,arsenic,bismuth,mercury,palladium,lithium
Nonsteroidal-antiinflammatorydrugs	Acetylsalicylic acid, benoxaprofen, diflunisal,fenclofenac,flurbiprofen,ibuprofen,indomethacin,naproxen,sulindac
Protonpumpinhibitors	Omeprazole,lansoprazole,pantoprazole
Lipidloweringdrugs	Pravastatin,simvastatin,gemfibrozil
Tumornecrosisfactor-alphaantagonists	Infliximab,adalimumab,etanercept,lenercept
Varibledrugs	Allopurinol, bleomycin,, dapsone, hydroxyurea,hepatitis B-vaccine, immunoglobulins, interferonalfa,l-thyroxin, penicillamine, procainamide.

Prognosis

The prognosis for lichen planus is good, as most cases regress within 18 months. Some cases recur. Atrophy and scarring are seen in hypertrophic lesions and in lesions on the scalp. Cutaneous lichen planus does not carry a risk of skin cancer, but ulcerative lesions in the mouth, particularly in men, do have a low rate of malignant transformation. Vulvar lesions in women may also be associated with squamous cell carcinoma **(7).**

Clinical Features

Lichen planus may affect the skin, mucous membranes (especially the oral mucosa), scalp, nails, and genitalia. The classic presentation of cutaneous lichen planus is a papulosquamous eruption characterized by the development of flat-topped, violaceous papules on the skin. Often, the clinical manifestations are described as the four "P's **(8)**:

- Pruritic
- Purple (actually a slight violaceous hue)
- Polygonal
- Papules or plaques

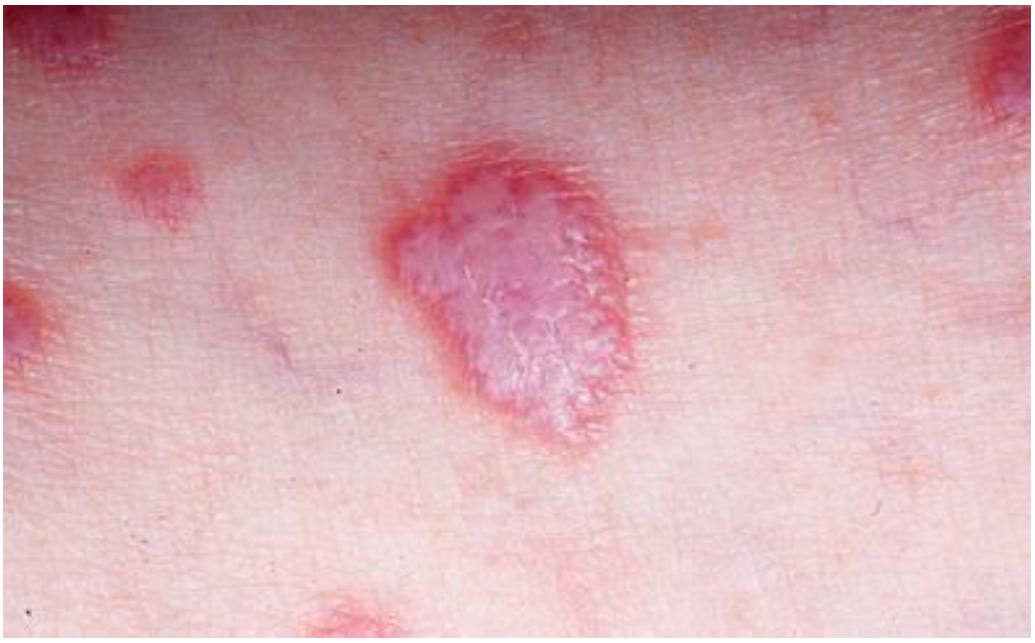

Figure (1): Macroscopicpictureoflichenplanus;thick,violaceous,hyperkeratoticplaquewithawhite,lacelikepatternonthesurface**(1)**.

Individual papules are usually a few millimeters in diameter, but may coalesce to form larger plaques. With close inspection, fine white lines may be visible on the surface of papules or plaques of cutaneous lichen planus. These lines are described by the term "Wickham's striae" **(1).**
The extremities, particularly the ankles and the volar surface of the wrists, are common sites for cutaneous involvement. Involvement of the trunk or generalized involvement also can occur. Rare Blaschkoid, zosteriform, and inverse (intertriginous) distributions of cutaneous lichen planus have been observed **(9).**

Cutaneous variants

In addition to the classic presentation of cutaneous lichen planus, multiple other clinical presentations of cutaneous disease have been described. Shared histologic findings support the classification of these disorders as variants of cutaneous lichen planus **(1)**. Examples of variants of cutaneous lichen planus include:

Hypertrophic lichen planus is characterized by the development of intensely pruritic, flat-topped plaques. The typical site of involvement is the anterior lower legs. Of note, the occasional development of cutaneous squamous cell carcinoma has been reported in patients with longstanding hypertrophic lesions **(10).**

Annular lichen planus is characterized by the development of violaceous plaques with central clearing. Although the penis, scrotum, and intertriginous areas are common sites of involvement, annular lesions may occur in other areas. Central atrophy may be present **(11).**

Bullous lichen planus: Patients with bullous lichen planus develop vesicles or bullae within the sites of existing lichen planus lesions. The legs are a common site of lesion development **(1).**

Actinic lichen planus (also known as lichen planus tropicus) presents with a photodistributed eruption of hyperpigmented macules, annular papules, or plaques. This variant is most commonly seen in the Middle East, India, and East Africa **(12).**

Lichen planus pigmentosuspresents with gray-brown or dark brown macules or patches that are most commonly found in sun-exposed or flexural areas. Pruritus is minimal or absent. The term "lichen planus pigmentosus-inversus" is used to describe patients with primarily flexural involvement **(13).**

Inverse lichen planus is characterized by erythematous to violaceous papules and plaques in intertriginous sites, such as the axillae, inguinal creases, inframammary area, or limb flexures. Associated hyperpigmentation is common. Scale and erosions may be present **(1).**

Atrophic lichen planus presents with violaceous, round or oval, atrophic plaques. The legs are a common site of involvement, and lesions often clinically resemble extragenital lichen sclerosus. A rare annular atrophic variant of lichen planus characterized by violaceous papules that enlarge peripherally leaving an atrophic center that demonstrates complete loss of elastic fibers on pathology has also been reported **(14).**

Lichen planopilaris (follicular lichen planus) in which the scalp is the classic site for lichen planopilaris where patients present with areas of hair loss that if left untreated can progress to scarring alopecia and hair regrowth does not occur once follicles are destroyed. However, follicular involvement manifesting as follicular papules may be observedin other body sites, particularly in patients with the Graham-Little- Piccardi-Lasseursyndrome.This syndrome is a type of lichen planopilaris (follicular lichen planus consists of atriad of patchy cicatricial alopecia of the scalp, noncicatricial alopecia of the axilla and groin, and a follicular spinous papule on the body, scalp, or both **(15).**

Overlap syndromes: lichen planus pemphigoides and lichen planus-lupus erythematous overlap syndrome are disorders that are characterized by the presence of features of cutaneous lichen planus and a second disease **(16).**

Lichen planus pemphigoidespresents with overlapping features of lichen planus and bullous pemphigoid. The onset of lichen planus usually precedes the onset of bullous lesions. Patients develop bullae in sites of previously normal appearing skin and on top of lesions of lichen planus. This contrasts with bullous lichen planus, which presents with bullae that are limited to longstanding lichen planus lesions. Similar to bullous pemphigoid, direct immunofluorescence studies of lichen planus pemphigoides demonstrate linear deposition of IgG and C3 at the dermal-epidermal junction **(17).**

Lichen planus-lupus erythematous overlap syndrome refers to a rare condition in which patients develop skin lesions with clinical, histologic, and/or immunopathologic features of both diseases. Clinically, patients often present with blue-red atrophic plaques or upper extremity verrucous papules or nodules **(18).**

Management

Reticular lesions that are asymptomatic generally require no therapy but only observation for change. In general, management should be aimed at treating atrophic and erosive/ulcerative lesions, alleviating accompanying symptoms and reducing the potential risk of malignant transformation**(19).**

Mechanical trauma or irritants such as sharp filling margins, rough surfaces or badly fitting dentures should receive attention. A drug history should be obtained to identify reversible causes of lichenoid eruptions as discontinuation of the offending agent, when possible, can be curative **(19).**

An optimal oral hygiene program should be instituted in patients with gingival disease. Drug treatment with topical agents is preferred as it has fewer adverse effects. The most commonly employed and useful agents for the treatment of OLP are topical corticosteroids. A response to treatment with midpotency corticosteroids such as triamcinolone, potent fluorinated corticosteroids such as fluocinolone acetonide and fluocinonide and superpotent halogenated corticosteroids such as clobetasol has been reported in 30–100 % of treated patients **(20).**

Topical corticosteroids are available in adhesive vehicles or can be used as mouth rinses. Empirical evidence seems to suggest that mouth rinses are of value in patients with widespread symptomatic OLP where the lesions are not easily accessible to the placement of ointments or gels. The evidence also suggests that higher potency corticosteroids, such as clobetasol are probably more effective **(21).**

Few serious side effects arise with topical corticosteroids as they are generally well tolerated. Side effects reported include; secondary candidosis; nausea; oral use not tolerated; refractory response; mucosal atrophy; oral dryness; sore throat; bad taste; and delayed healing**(22).**
Systemic absorption has been reported and it is thought that absorption of small amounts through the oral mucosa can take place but clinical experience and laboratory studies have shown this not to be of clinical significance in almost all cases **(22).**

Other topical agents that can be alternatively used to manage recalcitrant OLP include calcineurin inhibitors (e.g., tacrolimus, cyclosporine) and less commonly retinoids **(21).**
A recent systematic review and meta-analysis has shown comparable effects of topical tacrolimus (0.01 %) and clobetasol in the treatment of OLP. Although not widely accepted as a complication of the use of topical calcineurin inhibitors on the oral mucosa, the potential carcinogenicity of these agents remains a concern**(21).**

Several studies have reported that systemic corticosteroids are the most effective treatment for OLP; however, a comparative study that involved a total of 49 OLP patients did not find differences in response between systemic prednisone (1 mg/kg/day) with topical clobetasol in an adhesive base and topical clobetasol after a mean follow-up period of 36 months. Systemic corticosteroids are, therefore, usually reserved for cases where topical approaches have failed, where there is recalcitrant, erosive, or erythematous OLP, or for widespread OLP when skin, genitals, oesophagus or scalp are also involved. Systemic mycophenolate mofetil was also shown

to be effective in managing recalcitrant erosive OLP in some studies. Other reported helpful systemic agents include azathioprine and methotrexate **(23).**

However, it is noteworthy that the literature on the use of systemic agents in OLP management is generally limited to non-randomized clinical trials and is generally inconclusive**(24).**
Newly emerging treatment modalities to manage OLP are under investigation and these include; topical aloe vera, biologics, low intensity laser and oral curcuminoids **(24).**

Several studies showed resolution of OLR following replacement of causative restorations**(25).**Gingival OLR lesions, in particular, were reported to be nonresponsive to amalgam replacement for unknown reasons**(26).** The most reliable method to diagnose and manage lichenoid drug reactions is to note if the reaction resolves after the offending drug is withdrawn, and if it returns when the patient is challenged again. However, as this is both impractical and potentially unsafe, empiric withdrawal of a potentially offending drug and substitution with another agent may not be warranted**(19).**

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References

1. **Wagner G, Rose c and Sachse M M (2013):**Clinical variants of lichen planus. J Dtsch Dermatol Ges; 11 (4) : 309-319.
2. **Pandhi D, Singal A, and Bhattacharya SN.** (**2014**) : Lichen planus in childhood: a series of 316 patients. *PediatrDermatol; 31 (1) :59-67*.
3. **MurphyR,andEdwardsL**(**2008**):Desquamativeinflammatory vaginitis: what is it?. *J Reprod Med; 53(2):124-128*
4. **Pittelkow MR and Daoud MS. (2008):** Lichen planus. In Fitzpatrick's Dermatology in General Medicine: Wolff KGL, Katz SI, Gilchrest BA, et al., Vol. 1. 7th ed. New York: McGraw-Hill: 244-55.
5. **Shengyuan L, Songpo Y, Wen W, Wenjing T, Haitao Z, and Binyou W** (**2009**)**:** Hepatitis C virus and lichen planus: a reciprocal association determined by a meta-analysis. *Arch Dermatol.;145(9):1040-1047*.
6. **Campisi G, Di Fede O, Crax A, Di Stefano R and Margiotta V (2004)** Oral lichen planus, hepatitis C virus, and HIV: no association in a cohort study from an area of high hepatitis C virus endemicity. J.Am.Acad.Dermatol; 51(3):364-370.
7. **IngafouM ,Leao JC, Porter SR and Scully C** (**2006**) Oral lichen planus: a retrospective study of 690 British patients.*Oral Diseases; 12: 463–468*.
8. **Le Cleach L and Chosidow O** (**2012**): Clinical practice. Lichen planus. *N Engl J Med.;366(8):723–732*.
9. **Akarsu S, Ilknur T, Özer E, and Fetil E (2013):** Lichen planus pigmentosus distributed along the lines of Blaschko. *Int J Dermatol ; 52(2):253-254*.
10. **Manz B, Paasch U, and Sticherling M (2005).** Squamous cell carcinoma as a complication of long-standing hypertrophic lichen planus. *Int J Dermatol; 44(9):773–774*.
11. **Reich HL, Nguyen JT, and James WD** (**2004**). Annular lichen planus: a case series of 20 patients. *J Am Acad Dermatol; 50(4):595–599*.
12. **Lehman JS, Tollefson MM and Gibson LE** (**2009**). Lichen planus.*Int J*

Dermatol;48(7):682- 694.

13. **Al-Mutairi N, and El-Khalawany M (2010):** Clinicopathological characteristics of lichen planus pigmentosus and its response to tacrolimus ointment: an open label, non-randomized, prospective study. *J Eur Acad Dermatol Venereol.;24(5):535-540*.
14. **Li B, Li JH, Xiao T, He CD, Gao XH, and Chen HD** (**2010**). Annular atrophic lichen planus. *Eur J Dermatol;20:842-843*.
15. **Odom RB, James WD and Berger TG** (**2000):** Lichen planus and related Conditions chpter (12) in Andrews' Diseases of the skin. James WD, Berger TG, and ElstonDM.(editors) *Philadelphia: WB Saunders Company;9th ed: 274–275*.
16. **Gutte R, and Khopkar U (2011).** Perforating lichen planus. *Indian J Dermatol VenereolLeprol; 77(4):515-517*.
17. **Zaraa I, Mahfoudh A, Sellami MK, Chelly I, El Euch D, Zitouna M, Mokni M, Makni S, and Ben Osman A** (**2013**). Lichen planus pemphigoides: four new cases and a review of the literature. *Int J Dermatol. 2013;52(4):406-412*.
18. **Kim H, and Pomeranz MK** (2004). Lupus erythematosus and lichen planus overlap syndrome. *J Drugs Dermatol; 3(2):311-312*.
19. **Eisen D, Carrozzo M, Bagan Sebastian JV, Thongprasom K (2005)** Number V oral lichen planus: clinical features and management. Oral Dis 11:338–349.
20. **Thongprasom K, Luengvisut P, Wongwatanakij A, Boonjatturus C (2003)** Clinical evaluation in treatment of oral lichen planus with topical fluocinolone acetonide: a 2-year follow-up. J Oral Pathol Med 32:315–322.
21. **Al-Hashimi I, Schifter M, Lockhart PB, Wray D, Brennan M, Migliorati CA, Axell T, Bruce AJ, Carpenter W, Eisenberg E et al (2007**) Oral lichen planus and oral lichenoid lesions: diagnostic and therapeutic considerations. Oral Surg Oral Med Oral Pathol Oral RadiolEndod 103(Suppl: S25) e21–12.
22. **Savage NW, McCullough MJ (2005)** Topical corticosteroids in dental practice. Aust Dent J 50:S40–S44.
23. **Wee JS, Shirlaw PJ, Challacombe SJ, Setterfield JF (2012)** Efficacy of mycophenolate mofetil in severe mucocutaneous lichen planus: a retrospective review of 10 patients. Br J Dermatol 167:36–43.
24. **O'Neill ID, Scully C (2013)** Biologics in oral medicine: ulcerative disorders. Oral Dis 19:37–45.
25. **Thornhill MH, Pemberton MN, Simmons RK, Theaker ED (2003)** Amalgam-contact hypersensitivity lesions and oral lichen planus. Oral Surg Oral Med Oral Pathol Oral RadiolEndod 95:291–299.
26. **Henriksson E, Mattsson U, Hakansson J (1995)** Healing of lichenoid reactions following removal of amalgam. A clinical follow-up. J Clin Periodontol 22:287–294.