Adalimumab in Lichen Planus: A Narrative Review of Treatment and Paradoxical Reactions

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PRACTICE **POINTS**

- Adalimumab can be beneficial when used off label for treatment of lichen planus in patients who do not respond to conventional therapies, including corticosteroids and immunosuppressants.
- Clinicians should be aware that adalimumab could potentially lead to paradoxical lichenoid eruptions and should monitor patients closely during treatment.

Lichen planus (LP) is a T-cell–mediated chronic inflammatory condition affecting the skin, mucous membranes, hair, and nails. Conventional therapies include corticosteroids and immunosuppressants, but data are lacking on therapy recommendations for patients with LP who do not respond to first-line treatments. We performed a literature review to investigate the off-label use of adalimumab for treatment of LP.

Lichen planus (LP) is a chronic inflammatory condition affecting the skin (cutaneous LP), mucous membranes (oral, ocular, or vulvar LP), hair (lichen planopilaris [LPP]), and nails that predominantly occurs in middle-aged adults. Although the true etiology remains unknown, the pathogenesis of LP is thought to involve multiple factors. Several human leukocyte antigen (HLA) alleles have been associated with LP and its variants, including HLA-B27, HLA-B51, HLA-DR1 (cutaneous and oral LP), HLA-DRB1*11, and HLA-DQB1*03 (LPP). Additionally, HLA-Bw57 has been reported to be associated with oral LP in a cohort of British patients.[1] In addition to HLA alleles, genetic polymorphisms in cytokines including IL-4, IL-6, IL-18, interferon (IFN) γ, and tumor necrosis factor (TNF) α and its receptor have been found to be associated with LP.[2] Beyond genetics, chronic viral infection has been implicated in the development of LP. Systemic infection with the hepatitis C virus has been linked to the development of oral LP by promoting the recruitment of hepatitis C virus–specific CD8+ T cells from peripheral blood to the oral lesions, where they exhibit a terminally differentiated effector status.[3] Another report found an association between human herpesvirus 7 (HHV-7) and cutaneous LP; in this study, HHV-7 RNA was detected in plasmacytoid dendritic cells but not T cells and diminished after treatment, providing evidence for dendritic cells being involved in the HHV-7–mediated pathogenesis of cutaneous LP.[4] These findings were further corroborated by another study of oral LP patients that found enhanced infiltration of plasmacytoid and myeloid dendritic cells and upregulation in toll-like receptor and IFN-γ signaling.[4]

In addition to immune cell dysregulation, LP and its variants have been linked to neurogenic inflammation. In oral LP lesions, neurokinin 1 receptor and substance P were highly expressed and demonstrated a positive correlation with the expression of apoptotic marker caspase-3 and proliferation marker Ki-67.[5] These results suggest that neuropeptides may be involved in cell proliferation and turnover in oral LP. Similarly, in patients with LPP, substance P was more abundant in affected areas, whereas another neuropeptide, calcitonin gene-related peptide, was more highly expressed in unaffected areas,[6] further supporting the pathogenic role of neurogenic inflammation in LP.

A mucosal variant that often goes undiagnosed is vulvar LP. Although no distinct pathologic mechanism for vulvar LP has been established, prior reports found an association with autoantibodies.[7,8] In patients with erosive vulvar LP, epidermal-binding basement membrane

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zone antibodies were detected in epidermal skin biopsies and in circulation with reactivity to bullous pemphigoid antigens 180 (9/11 [81.8%] patients) and 230 (2/11 [18.2%] patients).[7] A similar study in patients with vulvar lichen sclerosus found similar proportions of circulating antibodies reactive to bullous pemphigoid antigens 180 (6/7 [85.7%] patients) and 230 (1/7 [14.3%] patients).[8] Erosive vulvar LP has been shown to be associated with autoimmune disease (eg, alopecia areata, celiac disease and pernicious anemia),[9] which suggests that the previously reported autoreactive antibodies[7,8] are secondary to autoimmunity rather than primary drivers of vulvar LP pathogenesis.

Certain medications also have been reported to cause cutaneous lichenoid drug eruptions. Although they can clinically and histologically mimic classic LP, lichenoid drug eruptions are a distinct entity. Common inciting medications include thiazide diuretics, angiotensin-converting enzyme inhibitors, anti-inflammatory drugs, antimalarials, checkpoint inhibitors, antimicrobials, antihypertensives, antidiabetics, and psychiatric drugs. The exact pathologic mechanism of lichenoid drug eruptions currently is unclear but is thought to involve the binding of drug molecules to the cell-surface proteins of the epidermis, creating an antigenic hapten stimulus for CD8+ T cells and triggering apoptosis of keratinocytes.[1]

The clinical severity of LP can range from mild localized disease to widespread and debilitating involvement. Multiple treatment modalities have been developed for management of LP, including topical and intralesional corticosteroids, phototherapy, Janus kinase inhibitors, phosphodiesterase-4 inhibitors, and anti–TNF-α inhibitors. Herein, we provide a narrative review and summary of the use of the TNF-α inhibitor adalimumab as a potential effective treatment for patients with LP.

Methods

We conducted a PubMed search of articles indexed for MEDLINE from 2005 to 2025 using the terms *adalimumab AND lichen planus* or *adalimumab AND lichen*. Articles that reported cases of oral LP, cutaneous LP, LPP, or lichenoid eruptions and adalimumab therapy were included in our review. Articles that used non-adalimumab TNF-α inhibitors were excluded. Using the search terms, 2 independent reviewers (M.G. and N.E.) conducted the literature review then screened the articles based on the inclusion and exclusion criteria. Our literature search yielded 40 articles, of which 20 met the criteria for inclusion in our narrative review.

Results

Our literature search yielded 11 patients with LP who were treated with adalimumab across studies (Table 1).[10-16] Prior LP treatments included topical corticosteroids (11/11 [100%]), disease-modifying antirheumatic drugs (6/11 [54.5%]), retinoids (4/11 [36.4%]), and psoralen plus UVA (1/11 [36.4%]). Adalimumab was administered subcutaneously following 4 treatment regimens: (1) 160 mg in week 1, then 80 mg in week 2, then 40 mg weekly for a median duration of 36 weeks (6/11 [54.5%]); (2) 80 mg in week 1, then 40 mg in week 2, 40 mg every 2 weeks for 20 weeks (1/11 [9.1%]); (3) 80 mg in week 1, then 40 mg every 2 weeks for a median duration of 12 weeks (2/11 [18.2%]); and (4) 40 mg every 2 weeks (2/11 [18.2%]). Adalimumab generally was well tolerated, with only 1 (9.1%) patient experiencing minor stress-related mucocutaneous flares on the tongue and extremities that resolved spontaneously.[12] Remission was achieved in 5 (45.5%) patients, with time to remission ranging from 2 to 4 months after adalimumab therapy, with a median of 2.5 months. In 1 (9.1%) patient with bullous LP, adalimumab therapy led to remission after 10 weeks. In both cases of oral and cutaneous LP (2/11 [18.2%]), remission was achieved after 2 months of treatment. Of the 2 LPP patients reported, 1 had hair regrowth after 9 months, and the other experienced remission after 3 months of adalimumab therapy. In the 1 (9.1%) case of annular LP, adalimumab treatment led to remission after 4 months. Five (45.5%) patients with vulvar LP treated with adalimumab for at least 9 months demonstrated improved Vulvar Quality of Life Index scores without improvement in their mucosal LP lesions. In 4 of the 5 (80.0%) patients who experienced remission after adalimumab treatment, remission lasted at least 6 to 10 months, with a median of 6 months; remission duration was not reported in 1 (20.0%) patient.

Paradoxically, our review of the literature yielded 12 patients in whom adalimumab was associated with lichenoid-type eruptions across 9 studies (Table 2).[17-29] The conditions for which these patients were undergoing treatment with adalimumab included ulcerative colitis,[17] psoriasis,[18,19] Crohn disease,[20,26] rheumatoid arthritis,[21-23,26] oligoarthritis,[24] and ankylosing spondylitis.[25] Lichenoid drug eruptions occurred on the legs (5/12 [41.7%]), arms (3/12 [25%]), oral mucosa (2/12 [16.7%]), and forehead or scalp (2/12 [16.7%]). Onset of time to these lichenoid eruptions ranged from 2 weeks to 17 months, with a median of 4 months. Adalimumab was discontinued in 9 (75.0%) patients and was continued in 3 (25.0%). One patient who had an onset of their lichenoid eruption after 17 months of treatment with adalimumab continued to receive adalimumab therapy with the addition of topical corticosteroids, which led to resolution of their oral lesions and partial remission of their cutaneous lesions. In 1 (8.3%) patient with localized buccal lichenoid eruptions, discontinuation of adalimumab on its own was sufficient to completely clear the lesions. Seven patients (7/12 [58.3%]) received topical corticosteroids with minimal (2/12 [16.7%]) or moderate (4/12 [33.3%]) improvement, and 1 (8.3%) patient did not have reported outcomes data. Eosinophils were detected within the adalimumab-associated lichenoid eruptions in 3 (25.0%) patients.[17,20,22]

TABLE 1. Reported Cases of LP and its Variants Treated Off-Label With Adalimumab

Reference (year)	No. of patients	Diagnosis	Prior LP treatment	ADA regimen	ADA side effects	Time to remission after ADA, duration of remission
Alam and LaBelle[10] (2020)	1	LPP	DMARDs, corticosteroids	160 mg wk 1; 80 mg wk 2; 40 mg/wk beginning wk 4 for 3 mo	NR	Remission not achieved; hair regrowth after 9 mo
Alhubayshi et al[11] (2025)	1	Bullous LP	Corticosteroids	80 mg wk 1; 40 mg wk 2; 40 mg every 2 wk beginning wk 3 for 5 mo	NR	10 wk, remission lasted >40 wk
Chao[12] (2009)	1	Cutaneous and oral LP	DMARDs, corticosteroids, retinoids	40 mg every 2 wk for 50 wk	Minor mucocutaneous flares wk 14, 18, and 22	2 mo, remission lasted >28 wk
Courtney et al[13] (2025)	5	Vulvar LP	DMARDs, corticosteroids, retinoids	160 mg day 1; 80 mg wk 2; 40 mg/wk beginning wk 3 for 9 mo	NR	Remission not achieved, improvement in VQLI after 9 mo; treatment discontinuation in 1 patient
Holló et al[14] (2012)	1	Cutaneous LP	Corticosteroids, retinoids, PUVA	80 mg wk 1; 40 mg every 2 wk for 2 mo	NR	2 mo, remission lasted >6 mo
Khodeir et al[15] (2025)	1	Annular LP	Corticosteroids, retinoids, DMARDs	80 mg wk 1; 40 mg every 2 wk for 4 mo	NR	4 mo, remission lasted >6 mo
Kreutzer and Effendy[16] (2014)	1	LPP	DMARDs, corticosteroids	40 mg every 2 wk for 3 mo	NR	3 mo

Abbreviations: ADA; adalimumab; DMARDs, disease-modifying antirheumatic drugs; LP, lichen planus; LPP, lichen planopilaris; NR, not reported; PUVA, psoralen plus UVA; VQLI, Vulvar Quality of Life Index.

In addition to its association with lichenoid drug eruptions, adalimumab also was reported to induce LPP in a patient who was being treated for Behçet disease,[29] oral LP in a patient being treated for Crohn disease,[27] and cutaneous LP in a patient being treated for Crohn disease (Table 2).[28] Time to onset ranged from 4 to 10 months, with a median of 6 months. Adalimumab was discontinued in 2 of 3 (66.7%) patients and was continued in the other patient (33.3%). After cessation of adalimumab therapy, administration of topical steroids led to complete resolution in the case of associated oral LP. In contrast, in adalimumab-induced cutaneous LP, initial topical corticosteroid treatment led to progression of lesions, which mostly resolved after adalimumab cessation. In 1 patient with LPP in whom adalimumab therapy could not be discontinued, topical corticosteroid and methotrexate therapy reduced the perifollicular erythema and stabilized the alopecia without full remission.

Comment

Conventional treatment modalities for LP often include topical corticosteroids as first-line therapy, with systemic corticosteroids, phototherapy, retinoids, or immunosuppressants (eg, cyclosporine or methotrexate) reserved for more severe or widespread disease. Historically, these approaches primarily have aimed to control symptoms rather than achieve long-term resolution; however, novel therapies including biologics and targeted immunomodulators show potential to induce sustained remission and improve quality of life for patients with refractory or mucosal LP.

In all reports where adalimumab was used to treat LP, patients initially received topical corticosteroids. While corticosteroids and other immunosuppressive agents are standard therapies, they often provide only temporary relief and may have an unfavorable side effect profile.

TABLE 2. Reported Cases of Adalimumab-Associated Lichenoid Eruptions and Variants Side Effects

Reference (year)	No. of patients	Reaction site	Time to onset	Treatment course and outcome
Lichenoid eruptions				
Alkheraiji et al[17] (2024)	1	Cutaneous: right leg, thigh, forearm	2 wk	ADA discontinued, treated with topical corticosteroids
Asarch et al[18] (2009)	1	Buccal; cutaneous: palms and soles	17 mo	ADA continued, treated with topical corticosteroids, remission of oral and partial improvement of cutaneous lesions
De Simone et al[19] (2008)	1	Buccal	1 mo	ADA discontinued, no additional intervention, spontaneous resolution
El Habr et al[20] (2014)	1	Cutaneous: forehead, forearms, dorsal hands	6 mo	ADA discontinued, treated with oral and topical corticosteroids and oral antihistamines, mild improvement
Exarchou et al[21] (2009)	1	NR	NR	NR
Flendrie et al[22] (2005)	1	Cutaneous: neck, axillae, legs, generalized	3 wk	ADA discontinued; treated with topical corticosteroids, NSAIDs, analgesics; complete recovery (time to recovery NR)
Inoue et al[23] (2017)	1	Cutaneous: legs, trunk	4 mo	ADA discontinued, treated with topical corticosteroids, gradual improvement
Jayasekera et al[24] (2016)	1	Cutaneous: legs and scalp	3 mo	ADA discontinued, treated with topical corticosteroids, most lesions resolved
Oliveira et al[25] (2020)	1	Cutaneous: extremities	6 mo	ADA discontinued, treated with topical corticosteroids, improvement with residual hyperchromic spots
Seneschal et al[26] (2009)	3	Cutaneous: scalp, palms, trunk, arms, limbs	1.5, 6, and 7 mo	ADA continued in 1 patient and discontinued in 2 patients
LP and variants				
Andrade et al[27] (2015)	1	Oral LP	6 mo	ADA discontinued, treated with topical corticosteroids, complete resolution
Au and Hernandez[28] (2015)	1	Cutaneous LP	4 mo	ADA discontinued; treated with topical corticosteroids, then eruptions spread; after ADA discontinued, most lesions resolved
McCarty et al[29] (2015)	1	LPP (site NR)	10 mo	ADA continued; treated with topical corticosteroids, MTX; decrease in perifollicular erythema and stabilization of alopecia

Abbreviations: ADA, adalimumab; LP, lichen planus; LPP, lichen planopilaris; MTX, methotrexate; NR, not reported; NSAIDs, nonsteroidal anti-inflammatory drugs

Our review highlights the emerging role of adalimumab, a TNF-α inhibitor, in off-label management of LP subtypes, including cutaneous, mucosal, and vulvar LP and LPP. In several small case series and reports, patients treated with adalimumab experienced clinical improvement, including symptom resolution and quality-of-life enhancement, as well as complete remission, indicating a durable response.

The potential benefit of adalimumab in treating LP must be balanced with its paradoxical risk for inducing lichenoid eruptions as well as LP and its variants, as identified in our narrative review that included reports of patients receiving this biologic for other indications.[17-29] Since adalimumab is a fully humanized antibody, the development of neutralizing antibodies may not account for drug-induced LP and lichenoid eruptions. Given that it blocks TNF-α, adalimumab may induce these lesions through a cytokine imbalance. This is supported by data demonstrating enhanced type I IFN-related proteins in plaques of patients with psoriasiform lesions treated with TNF-α inhibitors.[26] These drug-induced eruptions often resolved or improved with topical corticosteroids after discontinuation, but their occurrence underscores the complexity of therapeutically targeting TNF-α in the management of LP. Our literature review suggests that adalimumab may offer therapeutic benefit in select cases of LP refractory to conventional therapy, especially when systemic control is required. Nonetheless, the risk for LP and lichenoid reactions necessitates cautious use and further investigation.

Conclusion

While the current evidence is limited to case reports and series, adalimumab shows promise as an effective and tolerable off-label treatment for LP, particularly in patients who are unresponsive to conventional immunosuppressive therapies. Remission or clinically significant improvement was achieved in several cases; however, the potential for adalimumab to induce LP and lichenoid eruptions underscores the need for careful patient selection and monitoring. Further prospective studies and larger cohorts are warranted to better define the safety and efficacy of adalimumab in treating LP lesions.

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