

Plantar Ulcerative Lichen Planus: Rapid Improvement With a Novel Triple-Therapy Approach

Prasanthi Kandula, MD; Raven Elosiebo, MD; Nico Mousdicas, MD

PRACTICE POINTS

- Consider ulcerative lichen planus (ULP) for chronic wounds on the soles.
- Topical therapeutic options may present a rapidly effective and relatively safe alternative to conventional immunosuppressive agents for long-term management of plantar ULP.

Ulcerative lichen planus (ULP) is a rare variant of lichen planus that is characterized by chronic, painful, and disabling ulcerations. Ulcerative lichen planus has been known to be resistant to many treatments, and therapeutic interventions often involve use of aggressive immunosuppressive medications without satisfactory remission of symptoms. We present the case of a 56-year-old man with an 8-year history of painful ulcerations on the right plantar foot as well as a large ulceration of the left lateral tongue. Biopsy confirmed a suspected diagnosis of plantar ULP. The patient developed marked clinical improvement of the cutaneous and oral mucosal lesions with oral and topical steroids, topical tacrolimus, and oral doxycycline after only 4 weeks of treatment. It is important for dermatologists to be aware of the potential diagnosis of plantar ULP, especially in the evaluation of chronic treatment-resistant ulcers that often have been previously misdiagnosed. We introduce this novel therapeutic regimen as a rapidly effective and relatively safe alternative to conventional immunosuppressive agents for long-term management of plantar ULP.

Cutis. 2018;102:131-135.

Ulcerative lichen planus (ULP) (also called erosive) is a rare variant of lichen planus. Similar to classic lichen planus, the cause of ULP is largely unknown. Ulcerative lichen planus typically involves the oral mucosa or genitalia but rarely may present as ulcerations on the palms and soles. Clinical presentation

usually involves a history of chronic ulcers that often have been previously misdiagnosed and resistant to treatment. Ulcerations on the plantar surfaces frequently cause severe pain and disability. Few cases have been reported and successful treatment is rare.

Case Report

A 56-year-old man was referred by podiatry to the dermatology clinic for evaluation of painful ulcerations involving the dorsal and plantar surfaces of the right great toe as well as the second to third digits. The ulcers had been ongoing for 8 years, treated mostly with local wound care without clinical improvement. His medical and family history was considered noncontributory as a possible etiology of the ulcers; however, he had been taking ibuprofen intermittently for years for general aches and pains, which raised the suspicion of a drug-induced etiology. Laboratory evaluation revealed positive hepatitis B serology but was otherwise unremarkable, including normal liver function tests and negative wound cultures.

Physical examination revealed a beefy red, glazed ulceration involving the entire right great toe with extension onto the second and third toes. There was considerable scarring with syndactyly of the second and third toes and complete toenail loss of the right foot (Figure 1). On the insteps of the bilateral soles were a few scattered, pale, atrophic, violaceous papules with overlying thin lacy white streaks that were reflective of Wickham striae. Early dorsal pterygium formation also was noted on the bilateral third fingernails. Oral mucosal examination revealed lacy white plaques on the bilateral buccal mucosa with a large ulcer of the left lateral tongue (Figure 2). No genital or scalp lesions were present.

Histologic examination of a papule on the instep of the right sole demonstrated a dense lichenoid lymphocytic infiltrate in the papillary dermis with basal vacuolar

Dr. Kandula is from the Division of Pediatrics, Children's Mercy Hospital, Kansas City, Missouri. Drs. Elosiebo and Mousdicas are from the Department of Dermatology, Indiana University School of Medicine, Indianapolis.

The authors report no conflict of interest.

Correspondence: Raven Elosiebo, MD, 545 Barnhill Dr, EH 139, Indianapolis, IN 46202 (relosieb@iupui.edu).



FIGURE 1. Plantar ulcerative lichen planus revealing a beefy red, glazed, irregularly shaped ulceration involving the right great, second, and third toes with associated syndactyly and anonychia of right foot.



FIGURE 2. Ulcerative lichen planus with a large ulceration of the left lateral tongue and surrounding lacy white patches.

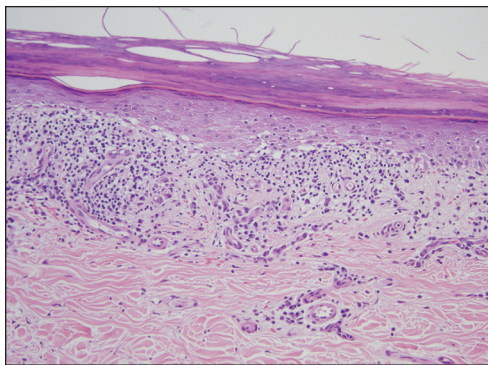


FIGURE 3. Dense lichenoid lymphocytic infiltrate with epidermal atrophy, basal vacuolar degeneration, and necrotic keratinocytes (H&E, original magnification $\times 200$).

degeneration and early focal Max-Joseph space formation. Additionally, there was epidermal atrophy with mild hypergranulosis and scattered necrotic keratinocytes (Figure 3). A similar histologic picture was noted on a biopsy of the buccal mucosa overlying the right molar, albeit with epithelial acanthosis rather than atrophy.

Based on initial clinical suspicion for ULP, we suggested that our patient discontinue ibuprofen and



FIGURE 4. Reepithelialization (70%) of the right foot (A) and near-complete resolution of the left lateral tongue (B) was noted after 4 weeks of treatment with oral and topical steroids, topical tacrolimus, and oral doxycycline.



FIGURE 5. Complete reepithelialization of the right foot ulceration was noted at 4-month follow-up.

started him on a regimen of oral prednisone 40 mg once daily and clobetasol ointment 0.05% applied twice daily to the plantar ulceration, both for 2 weeks. Dramatic improvement was noted after only 2 weeks of treatment. This regimen was then switched to oral doxycycline 100 mg twice daily combined with tacrolimus ointment 0.1% applied twice daily to the plantar ulceration to avoid side

Clinical Manifestations and Successful Treatments of Ulcerative Lichen Planus (January 1985 to Present)

Reference (Year)	Patient Age, y/ Sex	Areas of Involvement/ Conditions	Comorbidities	Treatment Administered	Successful Treatment (Time to Treatment Success ^a)
Falk et al ³ (1985)	57/M	Ventral and dorsal surfaces of the bilateral feet and hands, bilateral dorsal forearms, oral involvement	Not reported	Topical corticosteroids, oral prednisone, oral azathioprine, oral hydroxychloroquine, oral dapsone	Oral dapsone (9 mo)
Sonnex et al ⁴ (1986)	73/F	Bilateral soles, onychia, toe webbing, cicatricial alopecia, pterygium nail formation, oral involvement	Not reported	Excision and split-skin grafting	Excision and split-skin grafting (immediate)
Dereure et al ⁵ (1996)	60/F	Bilateral feet, arms, and legs; oral involvement	None	Topical/oral corticosteroids, photochemotherapy, oral etretinate, oral dapsone, oral cyclosporine A, oral thalidomide	Oral thalidomide (3 mo [near-complete resolution])
Patrone et al ⁶ (1998)	68/M	Bilateral soles, onychia	Not reported	Oral cyclosporine A, skin grafting	Temporary treatment in acute phase: oral cyclosporine A; permanent treatment: skin grafting (immediate)
Wollina et al ¹ (2001)	42/F	Bilateral palms and soles, onychia, oral involvement	Positive serology for autoantibodies	Topical corticosteroids, bath PUVA, oral chloroquine, oral mycophenolate mofetil, UVA1 phototherapy, recombinant human platelet-derived growth factor gel	Oral mycophenolate mofetil, UVA1 phototherapy, and platelet-derived growth factor gel (21 mo)
Eisman and Orteu ⁷ (2004)	79/F	Flexural involvement (below the bilateral breasts, inguinal region, perianal area, below large abdominal fold)	Not reported	Tacrolimus ointment 0.1%, oral thalidomide (discontinued after 3 mo due to side effect of constipation)	Tacrolimus ointment 0.1% (5 mo)
Henderson et al ⁸ (2004)	50/F	Unilateral pretibial area	Hypertension	Oral acitretin, intralesional triamcinolone injection, clobetasol propionate ointment	Oral acitretin, intralesional triamcinolone injection, clobetasol propionate ointment (4 wk)
Meyer et al ⁹ (2005)	79/M	Bilateral soles, bilateral palms, onychia, pterygium nail formation, oral involvement	Hypertension treated with metoprolol (may exacerbate ULP manifestations)	Systemic retinoid, PUVA phototherapy, oral methotrexate, topical corticosteroids, tacrolimus ointment 0.1%	Tacrolimus ointment 0.1% (1 mo)

CONTINUED ON NEXT PAGE

(continued)

Reference (Year)	Patient Age, y/ Sex	Areas of Involvement/ Conditions	Comorbidities	Treatment Administered	Successful Treatment (Time to Treatment Success ^a)
Mansura et al ¹⁰ (2006)	65/F	Right sole, abdomen, back, genital mucosa, anonychia, cicatricial alopecia	Not reported	Topical/systemic steroids, Unna boot, antibiotics, oral acitretin, tacrolimus ointment 0.1%, topical PUVA photochemotherapy, UVA1 phototherapy	UVA1 phototherapy (6–7 wk [5 treatments per wk])
Tsuboi and Katsuoka ¹¹ (2007)	79/F	Bilateral palms and soles	Sjögren syndrome	Zinc oxide ointment, steroid ointment, oral etretinate	Oral etretinate (2 mo)
Al-Khenaizan and Al-Mubarak ¹² (2008)	65/F	Left sole	Hepatitis B carrier	Tacrolimus ointment 0.1%, clobetasol propionate ointment 0.05%	Tacrolimus ointment 0.1%, clobetasol propionate ointment 0.05% (4 wk)
Schepis et al ² (2010)	56/M	Upper back, both nostrils, nail dystrophy, bilateral legs	Chronic smoker	Topical steroid ointment, oral cyclosporine A	Topical steroid ointment, oral cyclosporine A (1 mo [near-complete resolution])
Goucha et al ¹³ (2011)	38/F	Bilateral palms and soles, melanonychia	Not reported	Oral prednisone	Oral prednisone (3 wk)
Current report	56/M	Dorsal and plantar right great toe, 2nd and 3rd toes of right foot, soles of feet, buccal mucosa and tongue, syndactyly, anonychia	Hepatitis B	Prednisone, clobetasol ointment 0.05%	Doxycycline, tacrolimus ointment 0.1% (4 wk)

Abbreviations: M, male; F, female; PUVA, psoralen plus UVA; ULP, ulcerative lichen planus.

^aTreatment success is defined as complete resolution of the lesion.

effects of prolonged steroid use. Topical therapies were not used for the mucosal lesions. At 4-week follow-up, the patient continued to demonstrate notable clinical response with a greater than 70% physician-assessed improvement in ulcer severity (Figure 4) and near-complete resolution of the oral mucosal lesions. Our patient also reported almost complete resolution of pain. By 4-month follow-up, complete reepithelialization and resolution of the ulcers was noted (Figure 5). This improvement was sustained at additional follow-up 1 year after the initial presentation.

Comment

Ulcerative (or erosive) lichen planus is a rare form of lichen planus. Ulcerative lichen planus most commonly presents as erosive lesions of the oral and genital

mucosae but rarely can involve other sites. The palms and soles are the most common sites of cutaneous involvement, with lesions frequently characterized by severe pain and limited mobility.²

We conducted a review of the Ovid MEDLINE database using the search terms *ulcerative lichen planus* and *erosive lichen planus* for articles from the last 30 years, focusing specifically on articles that reported cases of cutaneous involvement of ULP and successful therapeutic modalities. The Table provides a detailed summary of the cases from 1985 to present, representing a spectrum of clinical manifestations and successful treatments of ULP.¹⁻¹³

Hepatitis C is a comorbidity commonly associated with classic lichen planus, while hepatitis B immunization has a well-described association with classic and oral

ULP.^{12,14} Although hepatitis C was negative in our patient, we did find a chronic inactive carrier state for hepatitis B infection. Al-Khenaizan and Al-Mubarak¹² reported the only other known case of ULP of the sole associated with positive serology for hepatitis B surface antigen.

Ulcerative lichen planus of the soles can be difficult to diagnose, especially when it is an isolated finding. It should be differentiated from localized bullous pemphigoid, epidermolysis bullosa acquisita, ulcerative lupus erythematosus, and dermatitis artefacta.¹³ The characteristic associated clinical features of plantar ULP in our patient and lack of diagnostic immunofluorescence helped us to rule out these alternative diagnoses.⁴ Long-standing ulcerations of ULP also pose an increased risk for neoplastic transformation. Eisen¹⁵ noted a 0.4% to 5% frequency of malignant transformation into squamous cell carcinoma in those with oral ULP. Therefore, it is important to monitor previously ulcerated lesions long-term for such development.

Plantar ULP is difficult to treat and often is unresponsive to systemic and local treatment. Historically, surgical grafting of the affected areas was the treatment of choice, as reported by Patrone et al.⁶ Goucha et al¹³ reported complete healing of ulcerations within 3 weeks of starting oral prednisone 1 mg/kg once daily followed by a maintenance dosage of 5 mg once daily. Tacrolimus is a macrolide immunosuppressant that inhibits T-cell activation by forming a complex with FK506 binding protein in the cytoplasm of T cells that binds and inhibits calcineurin dephosphorylation of nuclear factor of activated T cells.¹² Al-Khenaizan and Al-Mubarak¹² reported resolution of plantar ULP ulcerations after 4 weeks of treatment with topical tacrolimus. Eisman and Orteu⁷ also achieved complete healing of ulcerations of plantar ULP using tacrolimus ointment 0.1%.

In our patient, doxycycline also was started at the time of initiating the topical tacrolimus. We chose this treatment to take advantage of its systemic anti-inflammatory, antiangiogenic, and antibacterial properties. Our case represents rapid and successful treatment of plantar ULP utilizing this specific combination of oral doxycycline and topical tacrolimus.

Conclusion

Ulcerative lichen planus is an uncommon variant of lichen planus, with cutaneous involvement only rarely reported in the literature. Physicians should be aware of this entity and should consider it in the differential diagnosis in patients presenting with chronic ulcers on the soles, especially when lesions have been unresponsive to appropriate wound care and antibiotic treatment or when cultures have been persistently negative for microbial growth. The

possibility of drug-induced lichen planus also should not be overlooked, and one should consider discontinuation of all nonessential medications that could be potential culprits. In our patient ibuprofen was discontinued, but we can only speculate that it was contributory to his healing and only time will tell if resumption of this nonsteroidal anti-inflammatory drug causes a relapse in symptoms.

In our patient, a combination of systemic and topical steroids, topical tacrolimus, and oral doxycycline successfully treated his plantar ULP. Our findings provide further support for the use of topical tacrolimus as a steroid-sparing anti-inflammatory agent for the treatment of plantar ULP. We also introduce the combination of topical tacrolimus and oral doxycycline as a novel therapeutic combination and relatively safer alternative to conventional immunosuppressive agents for long-term systemic anti-inflammatory effects.

REFERENCES

1. Wollina U, Konrad H, Graefe T. Ulcerative lichen planus: a case responding to recombinant platelet-derived growth factor BB and immunosuppression. *Acta Derm Venereol.* 2001;81:364-383.
2. Schepis C, Lentini M, Siragusa M. Erosive lichen planus on an atypical site mimicking a factitial dermatitis. *Acta Derm Venereol.* 2010;90:185-186.
3. Falk DK, Latour DL, King EL. Dapsone in the treatment of erosive lichen planus. *J Am Acad Dermatol.* 1985;12:567-570.
4. Sonnex TS, Eady RA, Sparrow GP, et al. Ulcerative lichen planus associated with webbing of the toes. *J R Soc Med.* 1986;79:363-365.
5. Dereure O, Basset-Sequin N, Guilhou JJ. Erosive lichen planus: dramatic response to thalidomide. *Arch Dermatol.* 1996;132:1392-1393.
6. Patrone P, Stinco G, La Pia E, et al. Surgery and cyclosporine A in the treatment of erosive lichen planus of the feet. *Eur J Dermatol.* 1998;8:243-244.
7. Eisman S, Orteu C. Recalcitrant erosive flexural lichen planus: successful treatment with a combination of thalidomide and 0.1% tacrolimus ointment. *Clin Exp Dermatol.* 2004;29:268-270.
8. Henderson RL Jr, Williford PM, Molnar JA. Cutaneous ulcerative lichen planus exhibiting pathergy, response to acitretin. *J Drugs Dermatol.* 2004;3:191-192.
9. Meyer S, Burgdorf T, Szeimies R, et al. Management of erosive lichen planus with topical tacrolimus and recurrence secondary to metoprolol. *J Eur Acad Dermatol Venereol.* 2005;19:236-239.
10. Mansura A, Alkalay R, Slodownik D, et al. Ultraviolet A-1 as a treatment for ulcerative lichen planus of the feet. *Photodermatol Photoimmunol Pathomed.* 2006;22:164-165.
11. Tsuboi H, Katsuoka K. Ulcerative lichen planus associated with Sjögren's syndrome. *J Dermatol.* 2007;34:131-134.
12. Al-Khenaizan S, Al-Mubarak L. Ulcerative lichen planus of the sole: excellent response to topical tacrolimus. *Int J Dermatol.* 2008; 47:626-628.
13. Goucha S, Khaled A, Rammeh S, et al. Erosive lichen planus of the soles: effective response to prednisone. *Dermatol Ther.* 2011;1:20-24.
14. Binesh F, Parichehr K. Erosive lichen planus of the scalp and hepatitis C infection. *J Coll Physicians Surg Pak.* 2013;23:169.
15. Eisen D. The clinical features, malignant potential, and systemic associations of oral lichen planus: a study of 723 patients. *J Am Acad Dermatol.* 2002;46:207-214.