Treatment of Generalized Lichen Planus With Alefacept

David P. Fivenson, MD; Barbara Mathes, MD; Fivenson Dermatology, Ann Arbor, Mich (Dr Fivenson), and Biogen Idec, Inc, Cambridge, Mass (Dr Mathes)

The Cutting Edge: Challenges in Medical and Surgical Therapeutics

REPORT OF CASES

CASE 1

A 25-year-old white woman with a 2-year history of lichen planus (LP) presented with widespread violaceous, hyperpigmented, pruritic papules involving the upper part of the arms, forearms, abdomen, thighs, lower part of the legs, and lower back area (Figure, A). There were several lacy white patches without ulceration on the buccal mucosa of the mouth, but there was no vulvovaginal or scalp involvement. Previous treatments had included antihistamines, hydroxychloroquine sulfate, topical tacrolimus, systemic and topical corticosteroids, cyclosporine, griseofulvin, and narrow-band UV-B. Each systemic therapy was used for at least 3 months. The results of hepatitis screening were negative. The patient had no known medical allergies, and her medical history was unremarkable.

CASE 2

A 57-year-old woman presented with a 1-year history of generalized hypertrophic LP and a more than 3-year history of oral LP involving the buccal mucosa, tongue, upper back area, presacral area, buttocks, feet, thighs, lower part of the legs, abdomen, scalp, and arms. The results of hepatitis screening were negative. The patient had no known medical allergies, and her medical history was significant only for hypertension. Biopsy of the tongue lesions confirmed mucosal LP and excluded squamous cell carcinoma. Previous treatments had included topical and systemic corticosteroids, antihistamines, hydroxychloroquine, azathioprine, cyclosporine, and mycophenolate mofetil. Each systemic therapy was used for at least 3 months.

THERAPEUTIC CHALLENGE

The 2 patients described herein had recalcitrant generalized LP, which is a heterogeneous autoimmune disease, and LP affects approximately 1% of the population. The variant known as generalized LP can involve any or all of these sites. Lichen planus is characterized by pruritic, scaling, violaceous papules that preferentially affect the flexural creases of the body. Severe LP can cause scarring alopecia, intractable pruritus, oral and vaginal ulcers, and oral squamous cell carcinoma. No medications have been recommended by the Food and Drug Administration for the treatment of LP, and there are few therapeutic trials on which to base treatment decisions. Treatments currently used for LP are aimed at suppressing inflammation, relieving pruritus, and preventing ulceration. They include high-potency topical corticosteroids, cyclo-

Figure. Patient 1 before (A) and after (B) treatment with alefacept. A, Raised erythematous and violaceous papules on the posterior aspect of the calf. B, After 12 weeks of alefacept therapy (15 mg/wk), the remaining lesions on the calf are flat and hyperpigmented.
sporine rinses, and topical and systemic retinoids as well as systemic therapies such as corticosteroids, phototherapy, gold, dapsone, azathioprine, methotrexate, mycophenolate mofetil, and cyclophosphamide.10-13

SOLUTION

Alefacept is a fully human dimeric fusion protein that affects T-cell disorders in 2 ways. It interferes with lymphocyte activation by binding to the lymphocyte antigen CD2, thereby disrupting the lymphocyte function-associated antigen 3/CD2 interaction, and it induces T-cell apoptosis via natural killer cell–induced granzyme release.8 Alefacept has been approved by the Food and Drug Administration for the treatment of moderate to severe plaque psoriasis. Lichen planus is also known to be a CD4+ T-cell-mediated disorder,1,9 making alefacept a potentially effective agent in treating extensive disease. To our knowledge, there have been no reported cases involving the treatment of generalized LP lesions with alefacept.

Because all other therapies had failed, a 12-week intramuscular course of alefacept (15 mg/wk) was initiated in each patient. Both patients reported considerable diminution of itching and noticeable lesion improvement within 4 weeks. CD4 T-cell counts were obtained weekly, and no abnormalities were noted in either patient. After 12 weeks, patient 1 was 99% free of new lesions (Figure B), patient 2 was 100% free of new lesions, and both patients had no residual itching. Twelve to 20 weeks after alefacept therapy was completed, both patients were completely free of new lesions, had no pruritus, and showed considerable lightening of old lesions.

COMMENT

The cases reported herein illustrate a dramatic response to alefacept therapy in 2 patients with recalcitrant generalized LP. Lichen planus is classically described as a benign disease with spontaneous remissions and exacerbations. Lichen planopilaris and erosive mucocutaneous LP typically persist longer and are more recalcitrant to therapy than cutaneous LP.1 Generalized LP is a chronic inflammatory disease of the skin and mucosa. Patients with generalized LP lesions are typically resistant to or impractical candidates for topical treatment, and the lesions tend to pursue a chronic course, with rare spontaneous resolution. Two thirds of patients with generalized LP have oral mucosal involvement, often requiring systemic immunosuppressive therapy to control their disease.1 Immunosuppressive therapies can be effective in generalized LP, but significant adverse effects, including adrenal suppression, cushingoid facies, candidiasis, hypertension, and lethargy, frequently limit their continued use. Discontinuation of systemic treatment often leads to a recurrence of both mucosal and cutaneous lesions.

It has been suggested that activated CD4+ T lymphocytes play a central role in the pathogenesis of LP.8 Cytokines such as tumor necrosis factor α, interleukin 2, and interferon gamma have been shown to be involved in the activation and persistence of inflammation in LP, making this a prototypical Th1 inflammatory pattern. This cytokine profile has also been shown to drive disease processes similar to LP, most notably psoriasis and graft-vs-host disease.10-13

The results observed in the 2 patients described herein suggest a role for alefacept in the treatment of generalized and oral LP. Both of our patients had long-standing, recalcitrant disease with no evidence of spontaneous resolution. Neither of our patients reported any adverse events associated with alefacept therapy. Also, the clearance of their resistant lesions with alefacept therapy obviated the need for other, more toxic systemic treatments. The rapid onset of action that we noted in these patients also suggests that there may be a more direct role for the CD4+ CD2 antigen in the pathogenesis of LP as opposed to psoriasis, in which the onset of action may be delayed for up to 8 to 12 weeks after therapy is initiated. Further studies should be conducted to confirm these observations and to establish the efficacy and safety of alefacept therapy for severe, generalized cutaneous and mucosal LP.

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Correspondence: David P. Fivenson, MD, 25 Research Dr, Ann Arbor, MI 48103 (fivensondermatology@comcast.net).
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REFERENCES