Alefacept in the Treatment of Recalcitrant Palmoplantar and Erythrodermic Psoriasis

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Alefacept is the first biologic agent approved by the US Food and Drug Administration for moderate to severe chronic plaque psoriasis. Prior clinical studies excluded patients with palmoplantar psoriasis or erythroderma. We report 2 patients with recalcitrant psoriasis who responded completely to a full course of alefacept. One patient presented with severe palmoplantar psoriasis recalcitrant to acitretin and methotrexate; another patient presented with erythroderma and was transitioned successfully from cyclosporine A. Alefacept provides another treatment option for palmoplantar and erythrodermic psoriasis and should be considered in the management of patients with these conditions.

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Alefacept, the first biologic agent approved by the US Food and Drug Administration for moderate to severe chronic plaque psoriasis, is a fusion protein that binds to CD2 on T cells, thus blocking the co-stimulatory interaction with leukocyte function–associated antigen-3 (LFA-3) on antigen-presenting cells. Alefacept also interacts with FcγRIII immunoglobulin G receptors on natural killer cells and macrophages, resulting in apoptosis of activated memory T cells. The resultant reduction in the number of activated memory T cells in the skin correlates with the efficacy of alefacept in the treatment of psoriasis.[1] Prior clinical studies demonstrated efficacy in chronic plaque psoriasis but excluded patients with palmoplantar psoriasis or erythroderma.[2-4] We report 2 patients with recalcitrant psoriasis who responded completely to a full course of alefacept: one patient with severe palmoplantar psoriasis recalcitrant to acitretin and methotrexate, and another patient with erythroderma who was transitioned successfully from cyclosporine A.

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Case Reports

Patient 1—A 35-year-old healthy Guatemalan man presented with a 6-month history of pruritic hand and foot dermatitis. His medical and family histories were unremarkable, and a review of systems revealed negative findings, except for the skin. Results of a physical examination demonstrated erythematous scaly plaques on his palms and soles with extension onto the dorsal hands and feet. Results of a potassium hydroxide examination and fungal culture were negative. The patient initially was given diflorasone diacetate ointment 0.05% and urea cream 40%, with minimal improvement. Because of his lack of response, 2 biopsies of the skin were performed, the results of which confirmed the diagnosis of psoriasis vulgaris.

Because of the patient's poor response to various potent topical steroids and keratolytics, he was given systemic treatment. Initially, he was treated with sulfasalazine 1500 mg/d in divided doses, but this therapy was discontinued after 4 months because of lack of improvement. Acitretin 50 mg/d then was started, which provided some relief but was discontinued after 5 months because of moderate hair loss. The patient subsequently failed a 6-month course of methotrexate 15 mg/wk. Alefacept 15 mg was initiated and administered intramuscularly once weekly along with the use of potent topical steroids. Within 8 weeks, the patient demonstrated a response, with complete clearance by the end of the course. Weekly monitoring of his CD4 cell count

demonstrated a decline to less than 250 cells/μL (reference range, 500–1500 cells/μL) on 2 separate occasions, which subsequently necessitated holding off the medication twice and thus extended the total course duration to 14 weeks. Otherwise, the medication was well-tolerated and the patient had no subjective complaints. On cessation of treatment, the patient flared back to baseline within 2 weeks despite the use of topical steroids. Because he was within the recommended 12-week treatment-free follow-up period, alefacept could not be reinitiated. He was started on dexamethasone 6 mg and tapered over 18 days, and subsequently went into a prolonged (>4 months) remission.

Patient 2—A 32-year-old white man presented with a 3-year history of diffuse erythematous patches and scaly plaques treated intermittently by his primary care medical doctor with prednisone. He had a history of adult-onset asthma, and his medications included fluticasone proprionate/salmeterol (250 μg/50 μg) inhalation powder and fexofenadine hydrochloride. A review of systems was positive only for asthma symptoms. Prior evaluation by an allergist demonstrated immunoglobulin E radioallergosorbent test results that were positive for cat dander, dust mites, and tree pollens. Despite these results, the patient continued to reside with 7 cats. On physical examination, the patient was erythrodermic, with generalized scale. There was no lymphadenopathy or hepatosplenomegaly present. At his initial visit, the differential diagnoses for his erythroderma included psoriasis vulgaris, atopic dermatitis, allergic contact dermatitis, seborrheic dermatitis, drug eruption, and pityriasis rubra pilaris. Routine laboratory tests demonstrated results within reference range for complete blood count, chemistry panel, and liver function tests. Screening results for human immunodeficiency virus were negative. Histopathologic evaluation of results from 2 separate biopsies of the skin was consistent with psoriasis vulgaris.

Initially, the patient underwent UVB treatment 3 times weekly and was restarted on a prednisone taper. Toward the end of this taper, sulfasalazine 1500 mg/d in divided doses was added to his therapeutic regimen but was unsuccessful in preventing a flare. Acitretin 50 mg/d then was given, but once the patient discontinued the prednisone, the erythroderma recurred. Biopsies of the skin were performed again, with histopathologic findings now demonstrating a spongiotic dermatitis with prominent eosinophils. Cyclosporine A 2.3 mg/kg daily was started in addition to another prednisone taper. Again, the patient continued to flare whenever the prednisone was decreased. Good control finally was achieved after a gradual increase to high-dose cyclosporine A 4 mg/kg daily in divided doses. While the patient was being given cyclosporine A, amlodipine 5 mg/d was added to his therapeutic regimen for renal protection, which stabilized the small increase in his blood urea nitrogen and creatinine levels. In addition, the patient developed hypertrichosis, a known side effect of cyclosporine, and pedal edema that likely was secondary to the calcium channel blocker.[5] As the cyclosporine gradually was decreased, the patient flared once again. UVB treatment 3 times weekly was restarted but was ineffective in controlling the exacerbation during the attempt to taper the cyclosporine. The patient then was given alefacept 15 mg intramuscularly every week, which allowed the cyclosporine to be tapered every 2 weeks with only minor flaring that was controlled with topical tacrolimus ointment 0.1%. By the 13th week of treatment, the patient was completely clear and the cyclosporine was discontinued. Other than a one-time decrease in his CD4 cell count to less than 250 cells/μL, the patient tolerated the medication without complaints. The patient continued to do well during the observation period but began flaring approximately 5 months following his last injection. A second course of alefacept was instituted, which controlled his flare.

Because of the patient's repeat skin biopsy that demonstrated features of an allergic component, patch testing to the North American Contact Dermatitis Group standard allergen tray, as well as the Kansas University Medical Center supplemental and textile allergen trays, were evaluated after the patient was clear and no longer receiving cyclosporine. The only positive test reaction was to sodium gold thiosulfate; however, the patient did not possess any gold dental amalgams, wear gold jewelry, or drink any gold-containing liquor. We believe his erythroderma was caused by underlying psoriasis vulgaris treated intermittently with oral prednisone and possibly exacerbated by an allergic reaction to cat dander.

Comment

Psoriasis is recognized as a T-cell–mediated immune disease, and the new biologic agents have shown promising efficacy. In a double-blinded, randomized, placebo-controlled phase 3 trial of 507 patients with chronic plaque psoriasis, 33% of patients in the intramuscular alefacept group achieved a 75% or more reduction in the Psoriasis Area and Severity Index (PASI) at any time during the study period compared with 13% of patients in the placebo group.[2] In a follow-up extension study to the phase 3 trial, the median duration of a 50% or more

reduction in PASI was 209 days in those patients who achieved a score of 75, and longer in patients who received 2 courses of alefacept.[3] Alefacept was well-tolerated in the clinical trials, with the most common adverse events being chills, accidental injury, pharyngitis, headache, and injection site inflammation/pain. The only marked laboratory abnormalities observed during the phase 3 trials were reductions in weekly lymphocyte counts; however, no opportunistic infections were noted.[4] In these phase 3 clinical trials, the following groups of patients were excluded: patients with lymphocyte counts below reference range, human immunodeficiency virus, hepatitis B or C infection, erythrodermic or pustular psoriasis, and palmoplantar psoriasis.

In this report, we described 2 patients with recalcitrant psoriasis. One patient had primarily palmoplantar psoriasis and demonstrated a complete response by the end of the 14-week course yet flared back to baseline approximately 2 weeks after discontinuation of alefacept. Because this occurred during the treatment-free follow-up period when patients normally continue to show improvement and he had failed other oral therapy previously, a short course of dexamethasone was instituted to provide symptomatic relief. Because of the destabilization of psoriasis seen after dexamethasone is tapered, oral steroids are not preferred in the treatment; however, our patient did not demonstrate a flare afterwards and likely was controlled by the alefacept. Our other patient presented with erythroderma, which was confirmed by the results of the original skin biopsies and was exacerbated by the intermittent use of prednisone. Although results of repeat skin biopsies demonstrated a possible allergic component, patch testing did not reveal an allergic etiology. It is possible, however, that this patient's chronic exposure to cat dander may have been an exacerbating factor. Because he was previously treated with oral steroids, attaining clearance after the tapers was difficult and required repeat treatments. Good control was attained with high-dose cyclosporine, but because of the adverse effects of hypertension and renal toxicity, the use of cyclosporine generally is limited to no more than once a year.[5] Alefacept provided a safe and tolerable way to taper the cyclosporine and maintain good control after the patient was no longer receiving any treatment, including oral steroids.

In both patients, the only adverse event noted from alefacept was a decreased CD4 cell count. Otherwise, the medication was well-tolerated. Despite a reduction in CD4 cell counts to less than 250 cells/μL in both patients, no opportunistic infections were noted, and the CD4 cell count returned to reference range level when the medication was withheld for one week and remained within reference range after discontinuation of the medication.

Although the clinical trials with alefacept did not evaluate patients with palmoplantar psoriasis or erythrodermic psoriasis, our case reports demonstrate the efficacy and tolerability of alefacept in providing clearance in these cases. Alefacept provides another treatment option and should be considered in the management of patients with these conditions.

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