Etanercept Therapy for Severe Plaque Psoriasis in a Patient Who Underwent a Liver Transplant

William David Hoover, MD

This case report describes the successful treatment of severe plaque psoriasis with etanercept in a patient who underwent a liver transplant. It also addresses the concerns that arise in the treatment of chronic inflammatory dermatologic disease accompanied by multiple organ disorders.

Cutis. 2007;80:211-214.

Psoriasis is a common chronic inflammatory skin disease affecting approximately 2% of the US and European population combined.[1] The typical psoriatic lesion is a sharply demarcated erythematous plaque covered by silvery white scales and commonly appears on the elbows, knees, scalp, umbilicus, and lumbar area. Psoriasis is an incompletely understood immune system disorder in which activated T cells produce excess amounts of proinflammatory cytokines, particularly tumor necrosis factor (TNF).[2] Etanercept is a fully human soluble TNF receptor-Fc fusion protein that binds to TNF, thereby reducing its concentration in affected sites.[3] It is approved by the US Food and Drug Administration for the treatment of chronic moderate to severe plaque psoriasis in adults (18 years and older) who are candidates for systemic therapy or phototherapy.[4] This article describes the effectiveness of etanercept for the treatment of plaque psoriasis in a patient with diabetes mellitus who underwent a liver transplant and exhibited compromised kidney function.

Case Report

A 63-year-old white man with a history of long-standing psoriasis, type 1 diabetes mellitus, and decreased renal function presented with a severe psoriatic flare involving 50% of his body surface area (BSA). Five years earlier, he had received a liver transplant that resulted from cryptogenic cirrhosis.

The patient's psoriasis had not been treated for approximately one year prior to presentation, but various therapies were used for approximately 5 years before treatment was suspended (Figure 1). Treatments included topical steroids, oral methotrexate (MTX), UV light, and oral acitretin, as well as psoralen plus long-wavelength UVA (PUVA) radiation combined with acitretin (Re-PUVA). Because of its potential hepatotoxic effects, MTX was administered at a low dosage of 5 mg weekly. However, despite the low dosage, MTX was not tolerated, as manifested by worsening liver function test results. PUVA therapy was discontinued after the patient developed an outbreak of bullous pemphigoid, a potentially life-threatening, blistering, autoimmune disease reported to occasionally occur in patients with psoriasis treated with PUVA therapy.[5-8] Light microscopy and positive direct immunofluorescence biopsy results confirmed the presence of bullous pemphigoid. With the cessation of PUVA therapy, the bullous pemphigoid resolved, except for a single blister occurring approximately once every 2 months thereafter. After the discontinuation of PUVA therapy, acitretin was continued until blood test results detected elevated triglyceride levels and a liver biopsy result revealed steatosis, though it could not be confirmed that this medication was the sole cause of the hepatic pathology.

At the time of presentation, the patient had been on long-term therapy with oral tacrolimus 1 mg twice daily and oral sirolimus tablets 5 mg once daily to prevent transplant rejection. Despite immunosuppression induced by the combination of tacrolimus and sirolimus, the patient's psoriasis worsened. Psoriatic plaques were confluent on the anterior legs below the knees (Figure 2). Nail pits

Accepted for publication June 29, 2007.
From private practice, Concord, North Carolina.
Dr. Hoover received an honorarium from Amgen Inc.
Reprints: William David Hoover, MD, 335 Penny Ln, Concord, NC 28025-1221 (e-mail: chiph@vnet.net).

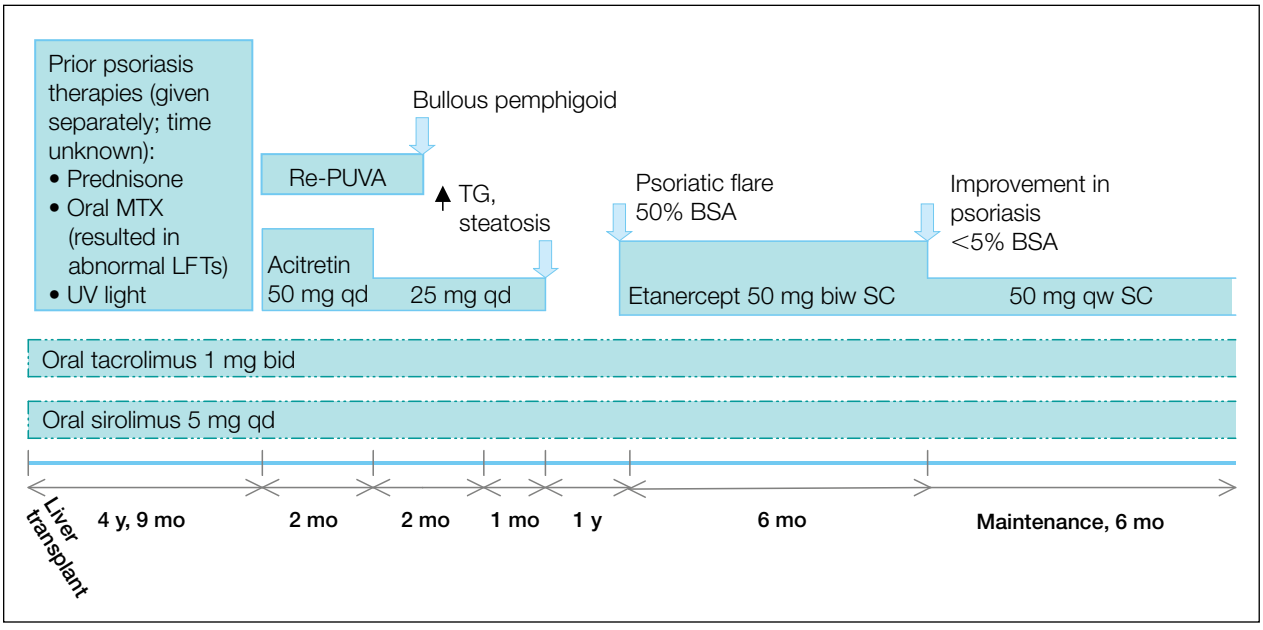

Figure 1. Treatment timeline for a patient with a severe psoriatic flare. MTX indicates methotrexate; LFTs, liver function tests; bid, twice daily; qd, once daily; Re-PUVA, psoralen plus long-wavelength UVA combined with acitretin; TG, triglycerides; BSA, body surface area; biw, twice weekly; SC, subcutaneously; qw, once weekly. Boxes indicate therapies for psoriasis and antirejection medications. Reduction in height of boxes notes reduced dose. Broken lines indicate dose adjustments over time. Open boxes indicate continuing treatments.

were present. Although the patient reported vague joint pain and tenderness, no red swollen joints were observed, and the diagnosis of psoriatic arthritis was not established. Results of laboratory tests revealed a 2+ proteinuria level, which was considered to be secondary to the patient's diabetes. In addition, long-standing leukopenia (white blood cell count, 2200/μL [reference range, 4500−11,000/μL]) and thrombocytopenia (platelet count, 51×10^3/μL [reference range, $150-450\times10^3$/μL]) were present and thought to be caused by long-term immunosuppression from the antirejection medications tacrolimus and sirolimus.

Severe psoriasis therapy that would not aggravate the patient's preexisting multiple organ system pathology and not interfere with the tacrolimus and sirolimus therapy was sought. In addition, the agent had to be safe for this patient who was at heightened risk for infection because of his iatrogenic immunocompromised condition. Treatment with etanercept was initiated based on its safety profile and the lack of reported concomitant organ toxicity.[9] The most common adverse events associated with etanercept are injection site reactions, which abate with time in most patients.[4] However, isolated serious infections have been reported (ie, cellulitis, gastroenteritis, pneumonia, abscess, osteomyelitis),[4] and the use of etanercept in patients with poorly controlled diabetes could predispose them to infection. Nevertheless, because this patient's diabetes was controlled, the benefit-to-risk ratio appeared favorable. After receiving approval from the transplant surgeon, the patient was given etanercept 50 mg twice weekly subcutaneously. The topical corticosteroid cream halobetasol propionate was applied once daily as needed.

After 6 weeks of etanercept therapy, the patient's psoriasis had 20% BSA involvement, which was a 60% improvement in his disease burden. Further improvement was seen after 6 months, with less than 5% BSA involvement (Figure 2). The patient then was prescribed a maintenance dosage of etanercept 50 mg once weekly. After the reduction in dosage, he was closely followed for 6 months and did not have any worsening of his psoriasis. His mood was greatly improved. At no time during treatment did the patient experience infections, injection site reactions, liver toxicity, or other adverse events. Importantly, there were no signs of liver rejection.

Comment

It is noteworthy that despite substantial immunosuppression with both oral tacrolimus and oral sirolimus to prevent liver transplant rejection, the patient continued to have psoriasis, with 50% BSA involvement. However, the addition of etanercept at the recommended dosage resulted in near-total

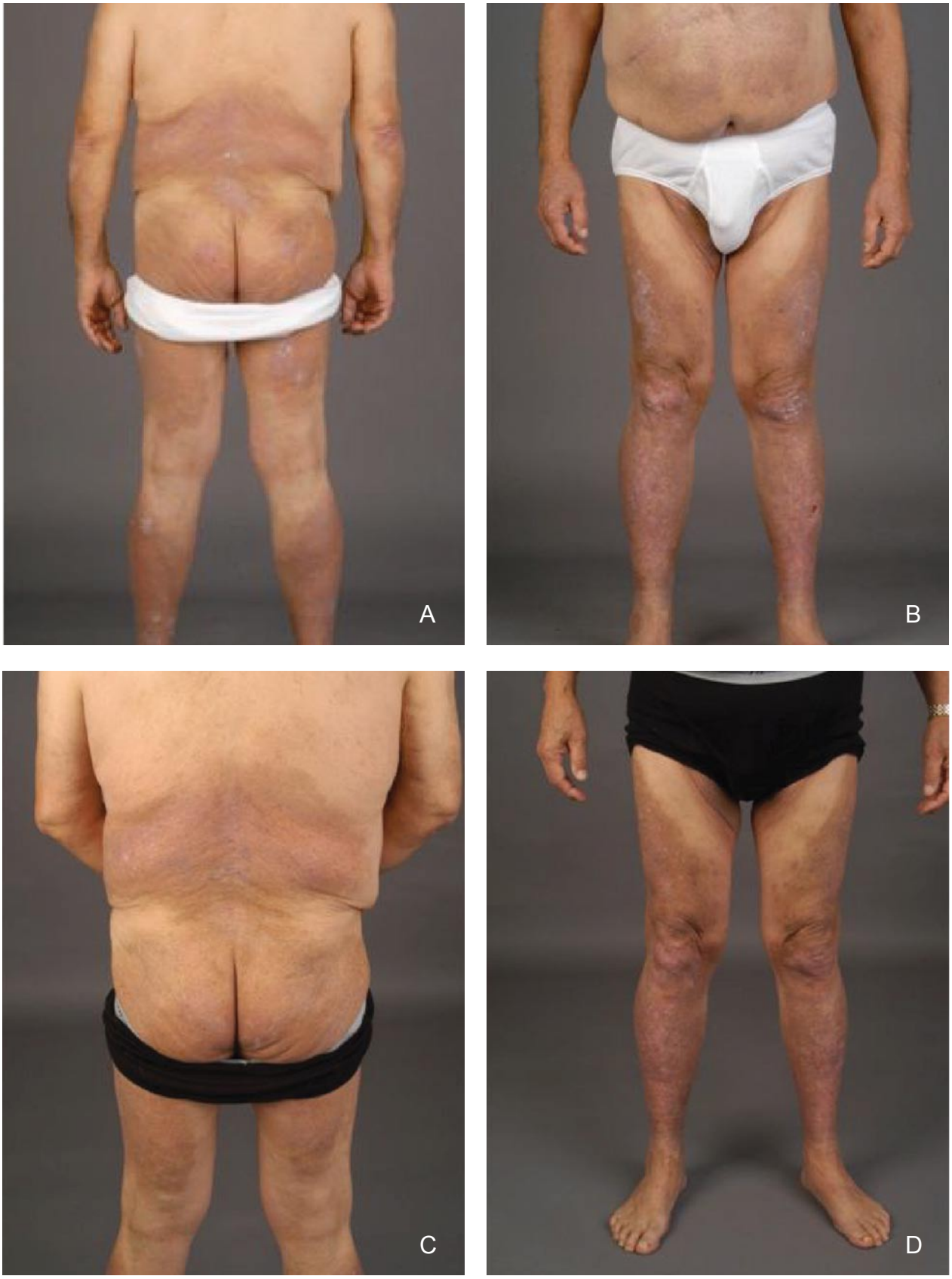

Figure 2. Psoriatic plaques were confluent on the anterior legs below the knees (A and B). Less than 5% body surface area involvement of psoriasis after 6 months' treatment with etanercept 50 mg twice weekly subcutaneously (C and D).

clearing of psoriasis without any signs of increased immunosuppression, such as infection. Furthermore, use of etanercept did not result in new or exacerbated laboratory abnormalities in this patient, who already had multiple medical problems and had not tolerated other systemic psoriatic therapies in the past. Most important, etanercept did not interfere with the antirejection medications, which could have increased the risk for liver transplant rejection.

Biologic agents such as etanercept are designed to target specific cytokines that mediate the inflammatory response; therefore, they may deliver their immune modulating benefit with fewer side effects than traditional systemic therapies and phototherapies.[10] Both the favorable safety profile and effectiveness of etanercept in the treatment of severe psoriasis in this severely compromised patient underscores the benefits of etanercept therapy.

Acknowledgments—Dr. Hoover initiated this report, and Amgen Inc provided editorial assistance. I wish to thank Frank Dann, MD, of Amgen Inc, for valuable discussion, and Edward Mancini, DPM, on behalf of Amgen Inc, for editorial assistance.

REFERENCES

1. Weinberg JM, Bottino CJ, Lindholm J, et al. Biologic therapy for psoriasis: an update on the tumor necrosis factor inhibitors infliximab, etanercept, and adalimumab, and the T-cell-targeted therapies efalizumab and alefacept. *J Drugs Dermatol*. 2005;4:544-555.
2. Schon MP, Boehncke WH. Psoriasis. *N Engl J Med*. 2005;352:1899-1912.
3. Papp KA. Etanercept in psoriasis. *Expert Opin Pharmacother*. 2004;5:2139-2146.
4. Enbrel [package insert]. Thousand Oaks, Calif: Immunex Corporation; 2006.
5. Abel EA, Bennett A. Bullous pemphigoid. occurrence in psoriasis treated with psoralens plus long-wave ultraviolet radiation. *Arch Dermatol*. 1979;115:988-989.
6. Albergo RP, Gilgor RS. Delayed onset of bullous pemphigoid after PUVA and sunlight treatment of psoriasis. *Cutis*. 1982;30:621-624.
7. George PM. Bullous pemphigoid possibly induced by psoralen plus ultraviolet A therapy. *Photodermatol Photoimmunol Photomed*. 1996;11:185-187.
8. Perl S, Rappersberger K, Fodinger D, et al. Bullous pemphigoid induced by PUVA therapy. *Dermatology*. 1996;193:245-247.
9. Papp KA, Tyring S, Lahfa M, et al. A global phase III randomized controlled trial of etanercept in psoriasis: safety, efficacy, and effect of dose reduction. *Br J Dermatol*. 2005;152:1304-1312.
10. Galadari I, Sharif MO, Galadari H. Psoriasis: a fresh look. *Clin Dermatol*. 2005;23:491-502.