Use of etanercept for psoriasis in a liver transplant recipient

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INTRODUCTION

Psoriasis, a chronic cutaneous inflammatory disease, is an immune-mediated disorder caused by complex interactions between dendritic cells, T cells, and keratinocytes. Tumor necrosis factor alfa (TNF- α) is a cytokine that plays a major role in the inflammatory cascade. Biologic agents that target TNF- α such as etanercept, infliximab, and adalimumab are effective in the treatment of psoriasis.

Psoriasis has been described as a systemic inflammatory disease, given its association with comorbid conditions such as cardiovascular disease, metabolic syndrome, and psoriatic arthritis. Of note, other autoimmune diseases such as inflammatory bowel disease (IBD), primary sclerosing cholangitis, celiac disease, systemic sclerosis, and alopecia areata are reported to occur with a higher prevalence in patients with psoriasis. The relationship between psoriasis and IBD may be related to the overlapping role of T-helper—17 cells, interleukin-12, interleukin-23, and TNF- α in the pathogenesis of these inflammatory disorders.

There is a dearth of literature regarding the treatment of psoriasis with biologic agents in patients with organ transplants. Given the immunosuppressive regimens of the posttransplant population, psoriasis flares are uncommon and are thus a challenge to treat. Treating psoriasis with additional immunosuppression poses significant risks, including the increased risk of infection. This article describes the efficacy of using etanercept in a patient with psoriasis and ulcerative colitis/primary sclerosing cholangitis after liver transplantation.

Abbreviations used:

IBD: inflammatory bowel disease TNF- α : tumor necrosis factor alfa

CASE REPORT

A 52-year-old white woman with a 10-year history of plaque psoriasis presented with a moderate-tosevere flare of plaque psoriasis in the setting of immunosuppressive therapy for a liver transplant performed 5 years prior. The patient had a history of primary sclerosing cholangitis, ulcerative colitis after colectomy and J-pouch, and gallbladder carcinoma in remission. Her psoriasis began to flare after her transplant, and she was subsequently treated with topical triamcinolone acetonide, clobetasol propionate, and calcipotriol as well as narrow-band ultraviolet B phototherapy, but these treatments were not helpful. The posttransplantation immunosuppressive regimen included tacrolimus, 3 mg daily, prednisone, 5 mg daily, and everolimus, 0.25 mg daily. Previous use of mycophenolate mofetil resulted in worsening of psoriasis. Despite this immunosuppression, her flare involved 30% to 35% of her body surface area. On physical examination, she had erythematous nonscaly plaques on the bilateral aspect of her legs and arms and guttate plaques, some with scale, on her trunk. Her scalp was clear, she had pitting of her nails, and there was no reported joint involvement or features of psoriatic arthritis.

Topical treatment with triamcinolone acetonide and calcipotriol was initiated, but the patient

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experienced burning with topical treatments and continued worsening of the psoriasis. Subsequent discussion with the transplant team led to the decision to initiate treatment with the anti-TNF biological agent, etanercept. Weekly injections of subcutaneous etanercept, 50 mg, were started with no modifications to the patient's posttransplantation immunosuppressive regimen. Within a month of initiating etanercept therapy, the patient's lesions improved dramatically. A month later, body surface area involvement was less than 5% with only limited involvement on her extremities. In addition, the patient reported a decrease in the frequency of episodes of pouchitis (inflammation of her J-pouch created after her colectomy) after beginning etanercept.

With regard to infection, the patient had a previous history of postprocedure cholangitis after an endoscopic retrograde cholangiopancreatography before to starting etanercept. One year after starting etanercept therapy, the patient experienced multiple infections including several episodes of asymptomatic urinary tract infections and multiple hospitalizations for recurrent cholangitis, requiring systemic antibiotics. The etanercept was withheld during hospital admissions and restarted at her standard dosing after resolution of her infections. Her psoriasis recurred when the etanercept was held but has cleared each time it was restarted. At the time of the writing of this report, the patient's etanercept was being held because of an infection.

DISCUSSION

This case shows the efficacy of etanercept in treating psoriasis in an organ transplant patient. The decision to initiate etanercept was made on the basis that it targeted TNF- α , an arm of the immune system not already targeted by our patient's other transplant medications. The patient was already receiving tacrolimus, a calcineurin inhibitor, and everolimus, a mechanistic target of rapamycin inhibitor. We considered cyclosporine as a potential treatment, but because the patient was already taking a calcineurin inhibitor, etanercept presented a better choice in this case. If the patient is unable to continue on etanercept in the future, altering her immunosuppression regimen from tacrolimus to cyclosporine might be beneficial based on the observation of Foroncewicz et al⁶ that cyclosporine may have better efficacy for recurrent psoriasis than tacrolimus.

The use of etanercept for psoriasis in posttransplant patients has not been studied in clinical trials but there are several reports of its efficacy in the

literature. To our knowledge, there have been 3 cases of patients with organ transplants, 2 liver and 1 pancreas-kidney, that have had marked improvement of their severe psoriasis after treatment with etanercept.7-10 There are also multiple reports of patients with organ transplants who have had a clinical response in their IBD after treatment with other anti-TNF- α agents, including infliximab and adalimumab.9

Interestingly, our patient received an organ transplant and had 2 diseases that typically respond to TNF- α inhibitors, psoriasis, and ulcerative colitis. The initiation of etanercept resolved her psoriasis, and she reports a decrease in her pouchitis. The patient's infections are a reminder that blocking multiple pathways of the immune system confers a markedly higher risk of infection, and this must be discussed carefully with patients and their transplant team. The use of TNF- α inhibitors in organ transplant patients should be used with caution, and further study in a larger population is necessary to evaluate the overall benefits and risks.

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REFERENCES

- 1. Nestle FO, Kaplan DH, Barker J. Psoriasis. N Engl J Med. 2009; 361:496-509.
- 2. Reich K, Burden AD, Eaton JN, Hawkins NS. Efficacy of biologics in the treatment of moderate to severe psoriasis: a network meta-analysis of randomized controlled trials. Br J Dermatol. 2012;166:179-188.
- 3. Makredes M, Robinson D, Jr, Bala M, Kimball AB. The burden of autoimmune disease: a comparison of prevalence ratios in patients with psoriatic arthritis and psoriasis. J Am Acad Dermatol. 2009;61:405-410.
- 4. Wu JJ, Nguyen TU, Poon KY, Herrinton LJ. The association of psoriasis with autoimmune diseases. J Am Acad Dermatol. 2012:67:924-930.
- 5. Rupp C, Mummelthei A, Sauer P, et al. Non-IBD immunological diseases are a risk factor for reduced survival in PSC. Liver Int.
- 6. Foroncewicz B, Mucha K, Lerut J, Majewski S, Krawczyk M, Paczek L. Cyclosporine is superior to tacrolimus in liver transplant recipients with recurrent psoriasis. Ann Transplant. 2014;19:427-433.
- 7. Brokalaki El, Voshege N, Witzke O, Kribben A, Schadendorf D, Hillen U. Treatment of severe psoriasis with etanercept in a pancreas-kidney transplant recipient. Transplant Proc. 2012;44: 2776-2777.
- 8. Collazo MH, Gonzalez JR, Torres EA, Etanercept therapy for psoriasis in a patient with concomitant hepatitis C and liver transplant. P R Health Sci J. 2008;27:346-347.
- 9. Hoover WD. Etanercept therapy for severe plaque psoriasis in a patient who underwent a liver transplant. Cutis. 2007;80: 211-214.
- 10. Mansouri B, Patel M, Menter A. Tumour necrosis factor-alpha inhibitor use in patients with psoriasis with organ transplantation. Br J Dermatol. 2013;169:481-483.