Dupilumab for Treatment of Severe Atopic Dermatitis in a Heart Transplant Recipient

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PRACTICE **POINTS**

- Chronic tacrolimus use in solid-organ transplant recipients may increase intestinal permeability to allergens and is a potential cause for development of atopic dermatitis (AD).
- Dupilumab has the potential to provide relief from particularly tenacious cases of AD.
- History of solid-organ transplant should not be cause for exclusion from consideration for dupilumab therapy.

To the Editor:

Solid-organ transplant recipients can develop a range of dermatologic consequences due to chronic immunosuppression, including frequent skin infections and malignancies. Atopic dermatitis (AD) and psoriasis are relatively rare in this population because many immunosuppressive therapies, such as mycophenolate mofetil and tacrolimus, also are used to treat inflammatory dermatoses.[1] In a large renal transplant population, the prevalence of AD was 1.3%.[2] The pathogenesis of posttransplantation AD is poorly understood, and standard treatment regimens have not been defined. Dupilumab is a novel biologic medication that has demonstrated efficacy in the treatment of AD.[3] Reports of dupilumab use for AD management in solid-organ transplant recipients are limited in the literature.

A 29-year-old woman with a history of a heart transplant 4 years prior presented to our dermatology clinic with an itchy rash over the entire body. Since the transplant, she had been on long-term immunosuppression with prednisone, mycophenolate mofetil, and tacrolimus. The rash appeared after she switched from brand-name to generic versions of the medications. Physical examination revealed erythematous scaly plaques on the lateral face, back, chest, arms, and legs covering approximately 10% of the body surface area. The patient's total serum IgE level was elevated at 711,500 µg/L (reference range, 0–1500 µg/L). Outside biopsies revealed changes consistent with spongiotic dermatitis, and patch testing performed by an outside physician was positive for sensitivity to the preservative bronopol.

The patient was switched back to brand-name tacrolimus, but the rash did not improve. Topical steroids, phototherapy, and omalizumab were ineffective. The itching was primarily managed with desoximetasone spray, mometasone cream, and loratidine. With approval from the patient's transplant team outside of our hospital system, she was started on dupilumab 300 mg once every 14 days. Complete clearance of the rash was noted within 3 months of treatment. Besides bilateral conjunctivitis, which was treated with ophthalmic prednisolone and moxifloxacin solutions, dupilumab was well tolerated. No issues related to immunosuppressant levels or graft-related issues, including rejection, were reported at 6-, 12-, and 18-month follow-up visits.

Atopic dermatitis is characterized by activation of type 2 immune responses, skin barrier defects, and increased *Staphylococcus aureus* colonization.[4] A potential mechanism for the development of AD in transplant recipients relates to their use of tacrolimus for chronic immunosuppression. Tacrolimus increases intestinal permeability and therefore allows greater absorption of allergens. This influx of allergens promotes hypersensitivity reactions, resulting in elevated IgE levels and eosinophilia. Tacrolimus also facilitates predominance of helper T cells (T_H2 cytokines) through selective inhibition of the T_H1 cytokine IL-2.[5]

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Dupilumab is a human monoclonal antibody that blocks IL-4 and IL-13, which are key drivers of T_H2-mediated inflammation. In addition to downregulation of inflammatory mediators, dupilumab also increases production of epidermal barrier proteins, resulting in skin repair. It has demonstrated rapid, dose-dependent efficacy in patients with moderate to severe AD.[6] Dupilumab boasts a good safety profile with no increase in risk for skin infections compared to placebo[6]; however, its safety has not yet been verified in transplant recipients.

Our case is notable for the severity of the patient's AD despite considerable immunosuppression with transplant medications. Development of AD was associated with a switch from brand-name to generic drugs, which is not commonly reported. Her condition was refractory to a litany of treatments prior to a trial of dupilumab. The rapid clearance observed with this novel biologic medication highlights its potential to provide relief to patients who have particularly tenacious cases of AD. Prior to starting dupilumab, we do recommend more extensive laboratory testing in immunosuppressed patients including transplant recipients and patients with human immunodeficiency virus. We illustrate that a history of solid-organ transplant need not exclude patients from consideration for dupilumab therapy.

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