SKIN

BRIEF ARTICLE

Treatment of Severe Recalcitrant Atopic Dermatitis with Dupilumab in a Kidney Transplant Patient

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ABSTRACT

This case report highlights the successful treatment of refractory atopic dermatitis (AD) in an immunosuppressed patient using dupilumab, a biologic agent that selectively targets cytokines crucial in the pathogenesis of AD. The patient had a history of failed treatment with numerous topical and systemic immunomodulating agents, including corticosteroids and immunosuppressive drugs for organ transplant. Dupilumab treatment resulted in significant improvement of symptoms, including reduced pruritus, and ultimately achieved disease control. Importantly, the patient experienced no adverse effects apart from one COVID-19 infection over three years of co-administration of dupilumab with immunosuppressive transplant rejection treatment. The safety of dupilumab in immunocompromised and transplant patients has been a concern, but studies have shown its safety and efficacy in these patient populations. This case highlights the potential for dupilumab as a safe and effective treatment option for patients with severe AD who are immunocompromised or have undergone solid organ transplantation.

INTRODUCTION

Atopic dermatitis (AD) is a chronic inflammatory skin condition that affects both children and adults. Clinical symptoms of AD include severe itching, redness, and dry skin. AD relapse is driven by genetic predisposition and includes altered skin barrier function associated with filaggrin gene mutation and filaggrin deficiency.[1] Type 2 cytokines such as interleukin (IL)-4 and IL-13 play a significant role in the pathogenesis of AD. IL-4 has been shown to initiate the Th2 response while IL-13 maintains the response.[1] Although topical corticosteroids are the first line treatment for AD, systemic immunomodulating agents such as mycophenolate mofetil or prednisone may be used in patients who do not respond well to topical therapy or have severe refractory AD.[2] These systemic agents aim to reduce cutaneous inflammation and achieve long-term disease control by disrupting disease pathways, leading to reduced lymphocyte proliferation; however, these treatments are related to notable adverse effects, such as an increased risk of infections and the occurrence of rebound flares.[3,4] This case report highlights the unique specificity and safety of dupilumab, a biologic agent that selectively targets cytokines (IL-4 and IL-13) that are crucial in the pathogenesis of AD, in

successfully treating an immunosuppressed patient with refractory AD.

CASE REPORT

A 30-year-old male first presented to us with severe atopic dermatitis in the context of an atopic triad. His past medical history included congenital kidney dysplasia and end-stage renal disease for which he received three kidney transplantations. Of note, he was on oral tacrolimus 1.5 mg twice daily, mycophenolate mofetil 1000 mg twice daily, and prednisone 5 mg daily for transplant immunosuppression. His atopic dermatitis was inadequately controlled with fluocinonide cream and clobetasol, evidenced by the presence of pigmented patches, xerosis, excoriations, and mild to moderate, generalized pruritus throughout the body. Over the next year, the patient was treated with phototherapy and various topicals, such as pimecrolimus, tacrolimus, mometasone, and methylprednisolone. Notably, his oral transplant anti-rejection medications did not adequately treat his AD symptoms.

The following year, the patient presented with exacerbation of his AD, asthma, and allergies. At this time, his Eczema Assessment Severity Index (EASI) score was 37 and he was initiated on dupilumab therapy. The dupilumab treatment consisted of an initial 600 mg dose, followed by 300 mg dose every two weeks thereafter. Within two weeks of his initial treatment, the patient reported that his skin had improved considerably, and the general level of pruritus had reduced significantly.

Physical examination during the patient's follow-up appointment three months later showed that his skin was clear, and the symptoms of AD had largely disappeared. His use of topical treatments for AD is minimal, with rare flares controlled with topical ruxolitinib. The patient's EASI score was reduced to 0, and he reports a dramatic increase in quality of life. Importantly, the patient experienced no adverse effects apart from one COVID-19 infection over three years of co-administration of dupilumab with immunosuppressive transplant rejection treatment.

DISCUSSION

Dupilumab is a monoclonal antibody that selectively inhibits the signaling of both IL-4 and IL-13, key drivers of the inflammatory response in atopic dermatitis, by binding to their shared receptor alpha subunit.[5] This blocks downstream signaling and ultimately decreases the Th2-driven inflammatory response to help reduce skin inflammation and improve skin barrier function.[5] Dupilumab is approved for the treatment of moderate to severe atopic dermatitis.[5] Patients in the dupilumab clinical trials reported 75% or greater improvement from their baseline EASI score over the course of sixteen weeks, relief from pruritus, and enhanced quality of life.[5]

Although our patient was on an immunosuppressive organ transplant regimen, his AD remained uncontrolled. Mycophenolate mofetil inhibits the proliferation of T and B cells thereby, reducing the production of cytokines that contribute to inflammatory pathways.[6] Similarly, oral tacrolimus functions by forming a complex with FKBP-12 to inhibit the downstream effects of calcineurin, a key enzyme responsible for T-cell activation.[7] Prednisone, a corticosteroid, broadly suppresses the immune system.[8] However, despite a robust combination of immunosuppressive therapies, our patient's AD failed to respond.

The safety of dupilumab in immunocompromised and transplant patients has been a concern due to the potential risk of infections and impaired immune function. However, Lukac et al. conducted a study which demonstrated the safety of dupilumab in these patient populations.[9] Other studies have also reported successful use of dupilumab in patients with AD and underlying primary immunodeficiency disorders, such as X-linked agammaglobulinemia and hyper IgE syndrome.[10,11] The risk of infections with dupilumab appears to be similar to that of placebo, and there have been no reports of opportunistic infections or reactivation of latent infections.[12] Demonstrated by our patient, dupilumab can be considered as a safe and effective treatment option for patients with severe AD who are immunocompromised or have undergone solid organ transplantation.

Conflict of Interest Disclosures: Vivian Li and Sophie Guenin have no conflicts of interest. Mark Lebwohl is an employee of Mount Sinai and receives research funds from: Abbvie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Cara Therapeutics, Dermavant Sciences, Eli Lilly, Incyte, Inozyme, Janssen Research & Development, LLC, Novartis, Ortho Dermatologics, Regeneron, and UCB, Inc. Dr. Lebwohl is also a consultant for AnaptysBio, Arcutis, Inc., Arena Pharmaceuticals, Aristea Therapeutics, Avotres Therapeutics, BioMX, Boehringer-Ingelheim, Brickell Biotech, Castle Biosciences, Corevitas, Dermavant Sciences, Evommune, Inc., Facilitatation of International Dermatology Education, Forte Biosciences, Foundation for Research and Education in Dermatology, Hexima Ltd., Meiji Seika Pharma, Mindera, National Society of Cutaneous Medicine, New York College of Podiatric Medicine, Pfizer, Seanergy, SUN Pharma, Verrica, and Vial.

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