doi:10.36849/JDD.9249

Atopic Dermatitis Flare Following Initiation of Nemolizumab

Olivia M. Burke BS, Jacob Beer MD, Scott A. Elman MD
Dr. Phillip Frost Department of Dermatology & Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL

ABSTRACT

Background: Atopic dermatitis (AD) is a chronic inflammatory skin disorder marked by intense pruritus and episodic flares. While nemolizumab, an interleukin-31 (IL-31) inhibitor, has demonstrated efficacy in reducing itch severity, its broader effects on skin inflammation are not fully understood.

Case Presentation: We describe a 49-year-old male with longstanding, treatment-resistant AD who began off-label therapy with nemolizumab. Within weeks of initiation, he developed a new pruritic vesiculobullous eruption localized to the palms, clinically and histologically consistent with dyshidrotic eczema. His prior AD lesions remained stable, but the new eruption prompted temporary discontinuation of nemolizumab.

Intervention and Outcome: The patient was treated with intravenous corticosteroids, resulting in significant improvement of the dyshidrotic eczema.

Conclusion: This case highlights the potential for nemolizumab to exacerbate AD in some patients, emphasizing the need for caution and further research on its inflammatory effects and safety in real-world settings.

J Drugs Dermatol. 2026;25(8): doi:10.36849/JDD.9249

INTRODUCTION

Atopic dermatitis (AD) is a chronic inflammatory skin condition characterized by intense pruritus and recurrent flares 1Despite advances in biologic therapies targeting key cytokines involved in AD, treatment challenges remain for patients with refractory disease. Nemolizumab, an interleukin-31 (IL-31) inhibitor, has shown promise in reducing pruritus in AD by targeting a cytokine central to the itch-scratch cycle.2 However, the broader inflammatory consequences of IL-31 inhibition, particularly in patients with active AD, are still being evaluated.

Case Report

A 49-year-old male with a longstanding history of AD presented with a significant flare following the initiation of nemolizumab, an IL-31 inhibitor, **which at the time was** an off-label treatment of AD. The patient had previously responded to dupilumab, though the efficacy diminished over time. Subsequent treatments with tralokinumab, upadacitinib, abrocitinib, cyclosporine, and methotrexate were ineffective in managing his symptoms.

One day after his first injection of nemolizumab, the patient experienced a severe flare of AD necessitating admission to the dermatology inpatient service for further management. On presentation, he had widespread erythema and edema affecting the eyelids, face, and entire body, along with numerous small vesicles on the bilateral hands and feet, consistent with dyshidrotic eczema - a new clinical manifestation for him (Figure 1A and Figure 1B). He reported worsening pruritus, discomfort, and malaise.

FIGURE 1. Clinical Imaging. (A) Generalized erythema and edema on the face and (B) Erythematous papules on plantar aspect of left hand.

(A) (B)

Laboratory findings were notable for elevated glucose levels, mild anemia (Hb 12.1 g/dL), leukocytosis (WBC 12.6 x10³/µL), and eosinophilia (9.7%), consistent with systemic inflammation and possible allergic or drug-induced reactions during the flare

The patient was treated on the same day of admission with intravenous methylprednisolone 40 mg every 8 hours for its anti-inflammatory effect and received cefazolin for 2 days to address possible bacterial superinfection. With steroid therapy, the patient's symptoms gradually improved over the course of three days, and he was discharged on a prednisone taper

DISCUSSION

To our knowledge, there have been no previously published cases describing a case of a severe AD flare, including a new manifestation of dyshidrotic eczema, following the initiation of nemolizumab. While nemolizumab shows promise for managing chronic itch, this patient's rapid flare—mar ed by widespread erythema, swelling, and dyshidrosis raises concerns about its effects in AD.

IL-31, a cytokine central to pruritus in AD, is primarily produced by T-helper type 2 (Th2) cells and binds to its receptor, IL-31RA, on sensory neurons, stimulating ion channels that transmit itch sensations.[3] The resultant scratching exacerbates skin barrier dysfunction and perpetuates inflammation [4] Given its mechanism, nemolizumab would logically be expected to alleviate pruritus in AD. However, reducing scratching alone may not fully address the underlying inflammation or barrier dysfunction and subsequent clinical manifestations of AD. AD is driven by an overactive Th2 response, with cytokines like IL-4, IL-13, and IL-31 playing key roles in inflammation [1,4] While nemolizumab targets IL-31, it does not affect IL-4 or IL-13, and blocking IL-31 may lead to a compensatory increase in these cytokines, further driving inflammation and potentially triggering an AD flare [5] Clinical trials investigating nemolizumab in AD have reported successful reductions in pruritus and inflammation, however, worsening of AD was the most reported adverse effect in both studies.[2,6] This patient's severe, distinct flare underscores how nemolizumab might not adequately address broader inflammatory pathways in certain individuals. Additionally, disrupting IL-31 signaling might interfere with immune regulatory feedback, worsening inflammation. More real-world data on the treatment of atopic dermatitis with nemolizumab are warranted.

DISCLOSURES

The authors have no conflicts of interest to disclose

REFERENCES

1. Silverberg JI. Atopic dermatitis in adults. *Med Clin North Am.* 2020; 104: 157-76.
2. Silverberg JI, Wollenberg A, Reich A et al. Nemolizumab with concomitant topical therapy in adolescents and adults with moderate-to-severe atopic dermatitis (ARCADIA 1 and ARCADIA 2): results from two replicate, double-blind, randomised controlled phase 3 trials. *Lancet.* 2024; 404: 445-60.
3. Nakahara T, Furue M. Nemolizumab and atopic dermatitis: the interaction between interleukin-31 and interleukin-31 receptor as a potential therapeutic target for pruritus in patients with atopic dermatitis. *Current Treatment Options in Allergy.* 2018; 5: 405-14.
4. Yamamura Y, Nakashima C, Otsuka A. Interplay of cytokines in the pathophysiology of atopic dermatitis: insights from Murin models and human. *Front Med (Lausanne).* 2024; 11: 1342176.
5. Masuyuki R, Sato E, Imafuku S. A case of bullous pemphigoid following administration of anti-IL31 receptor A antibody. *J Dermatol.* 2024; 51: 1252-5.
6. Kabashima K, Matsumura T, Komazaki H et al. Trial of nemolizumab and topical agents for atopic dermatitis with pruritus. *N Engl J Med.* 2020; 383: 141-50.

AUTHOR CORRESPONDENCE

Scott A. Elman MD
E-mail:..... Selman@med.miami.edu