SKIN

BRIEF ARTICLE

Bimekizumab-Induced Eczematous Eruption Treated Successfully with Sequential Upadacitinib and Dupilumab Therapy

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ABSTRACT

Bimekizumab, a selective IL-17A and IL-17F inhibitor, is FDA-approved for the treatment of adults with moderate-to-severe plaque psoriasis and psoriatic arthritis. While IL-17 inhibitors are generally well tolerated, there have been reports of eczematous eruptions after starting treatment with this medication class. Herein, we report a case of bimekizumab-induced eczematous eruption that partially cleared with upadacitinib (selective oral JAK 1 inhibitor), but ultimately required switching to dupilumab to achieve complete skin clearance.

INTRODUCTION

Bimekizumab is a humanized monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17A and IL-17F, and is currently FDA-approved for the treatment of adults with moderate-to-severe plaque psoriasis and psoriatic arthritis.[1,2] While IL-17 inhibitors are generally safe and well tolerated, there have been recent reports of eczematous eruptions after starting treatment with this class of medication.[3] Moreover, a recent real-world study with bimekizumab in an Italian cohort of 237 patients reported two cases of eczematous eruptions (0.8%) that led to treatment discontinuation.[4]

Eczematous drug eruptions (EDE) due to systemic therapies are typically managed with the discontinuation of the suspected medication combined with topical corticosteroids or topical immunomodulatory agents if needed.[5] However, some cases of EDE persist despite discontinuation of the causative medication, highlighting the need for specific management strategies for these types of eruptions.[6] Upadacitinib is a selective oral janus kinase (JAK) 1 inhibitor approved for the treatment of several immune-mediated inflammatory diseases, and has been used to treat EDE from IL-17 inhibitors.[7] Herein, we report a case of bimekizumab-induced eczematous eruption that partially cleared with upadacitinib but ultimately required switching to dupilumab to achieve complete skin clearance.

CASE REPORT

A 50-year-old morbidly obese white male with past medical history of hypertension and hyperlipidemia, but no prior history of atopy, presented for treatment of plaque psoriasis affecting the scalp, elbows, lower back, and nails. Prior treatments included clobetasol

0.05% solution, roflumilast 0.3% cream, methotrexate, apremilast, secukinumab, ixekizumab, brodalumab, guselkumab, and most recently risankizumab combined with deucravacitinib, which yielded the best results, but patient still had significant scalp disease (elbows, lower back, and nails had cleared).

Due to inadequate response, the patient was switched to bimekizumab 320mg every 4 weeks. Four weeks into treatment, patient reported an intensely pruritic follicular eruption on the chest and upper back (**Figure 1**). Histopathology showed psoriasiform hyperplasia with diffuse spongiosis covered by broad parakeratosis. PAS stain was negative for any fungal organisms, including pityrosporum (**Figure 2**).

The decision was made to hold his next bimekizumab dose and was treated with oral doxycycline and fluconazole. At his 6-week follow-up, patient reported no improvement in his rash and was switched to upadacitinib 15mg daily. Four weeks into treatment, patient reported complete resolution of his itch and had barely perceptible erythema on the chest and back (**Figure 3**), but he still had persistent scalp disease. Risankizumab 150mg SC every 12 weeks was restarted with upadacitinib 30mg daily but patient failed to show appreciable improvement after 16 weeks of treatment. Therefore, it was decided to switch upadacitinib to dupilumab 300mg every 2 weeks after a loading dose of 600mg. At his 12 week follow-up, patient's scalp had completely cleared and he remains on risankizumab and dupilumab as of today's writing.

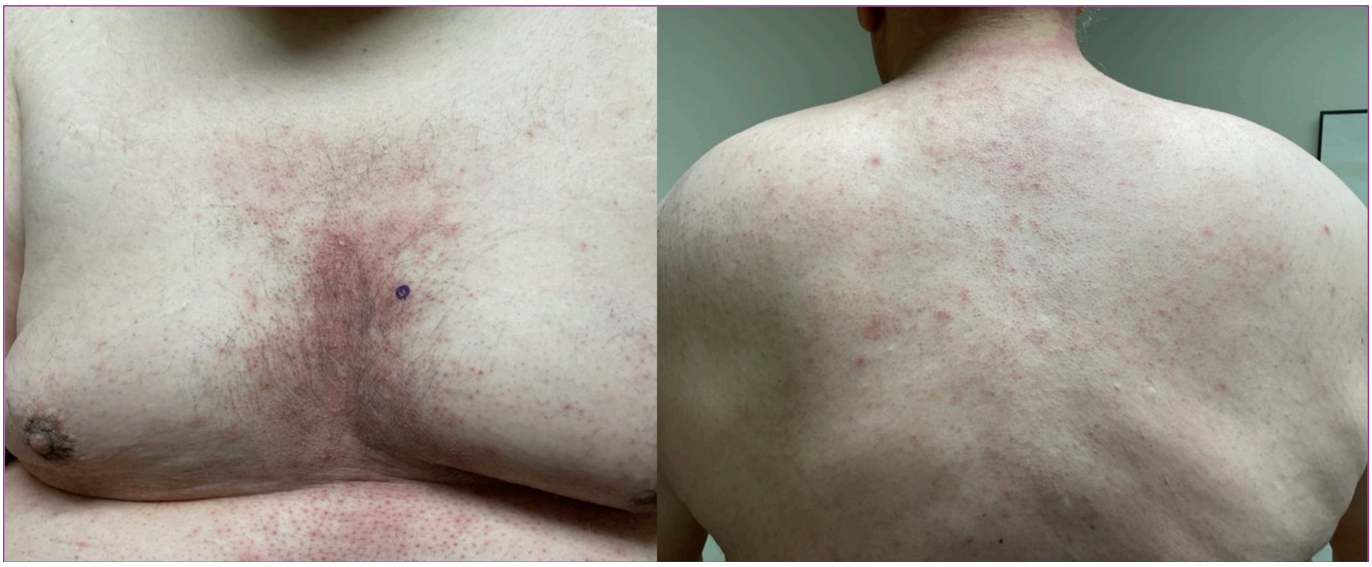

Figure 1. Intensely pruritic follicular eruption 4 weeks into bimekizumab on the chest (A) and back (B)

DISCUSSION

While psoriasis is largely driven by activation of the IL-17 pathway, atopic dermatitis is strongly associated with Th2 activation.[8] Although the mechanism of EDEs is unclear, the inhibition of the Th1 pathway by IL-17 inhibitors is thought to induce an imbalance between the Th1/Th2 immune response, leading to overactivation of the Th2 pathway.[9] Gene expression analyses of individuals who experienced EDEs following treatment with anti-IL17A medications found a

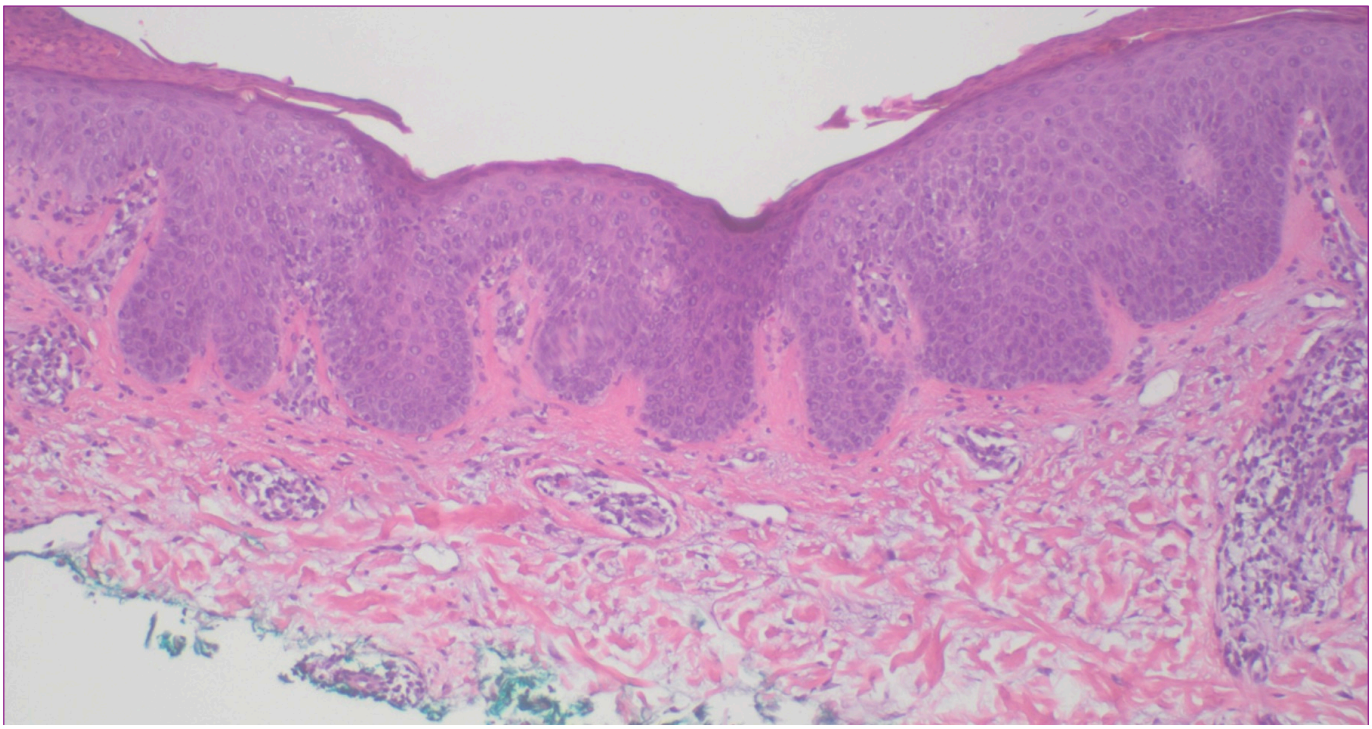

Figure 2. Histopathology showing psoriasiform hyperplasia with diffuse spongiosis covered by broad parakeratosis at 10x magnification

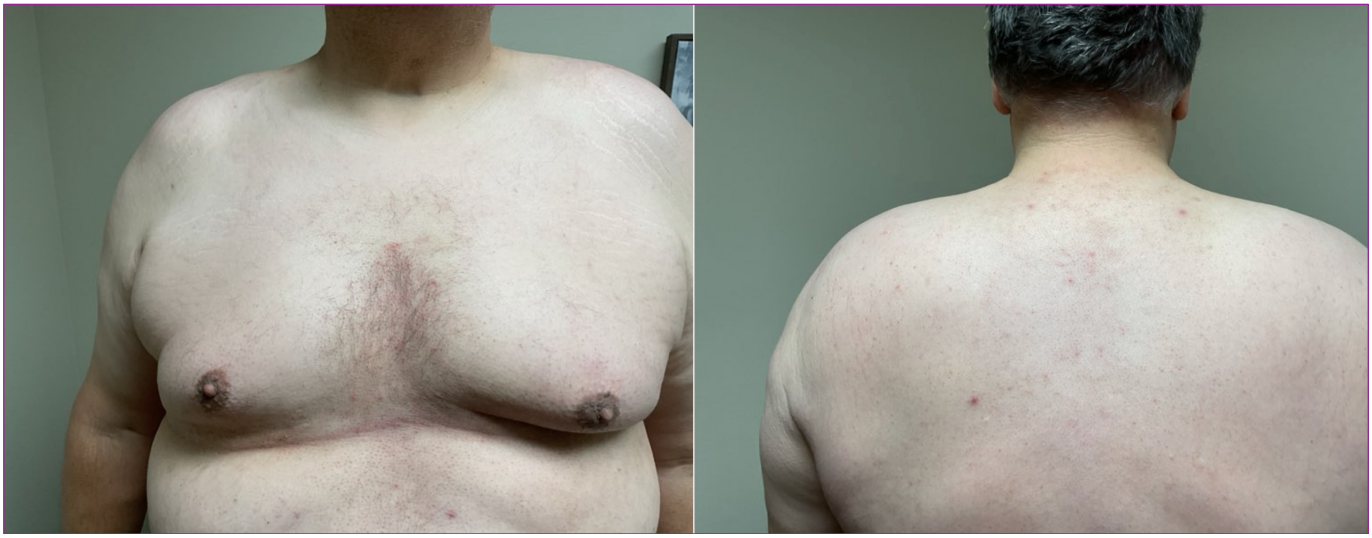

Figure 3. Chest (A) and back (B) showed significant clearance 4 weeks into upadacitinib 15mg daily

predominance of Th2/Th22 cytokines in EDE lesions compared to healthy skin.[6]

Although eczematous eruptions due to IL-17 inhibitors may resolve following the discontinuation of the causative medication, many cases persist, and alternative treatment options are needed. Barry et al. published a case series of successful combination therapy with dupilumab and guselkumab in patients with concomitant psoriasis and eczema.[10] However, dual biologic treatment is costly and insurance approval is often difficult. Given the broader immunoregulatory effects of JAK inhibition, this class of medication is well-suited to treat

concomitant inflammatory skin disorders, including atopic dermatitis and psoriasis.

Our case highlights a few important points. First, bimekizumab can induce an eczematous eruption even in patients who did not develop one on a prior IL-17A inhibitor. Second, bimekizumab-induced eczematous drug eruptions can be treated with a selective JAK1 inhibitor, as has been published with other IL-17A inhibitors.[7] Third, we provide additional histopathological (mixed psoriasiform and spongiosis) and clinical information (pruritic follicular eruption) on this entity, which can have variable findings. Lastly, our case demonstrates that patients with predominant scalp psoriasis may have a distinct immunophenotype from psoriasis vulgaris, given the lower response to highly effective biologic therapies for psoriasis. Furthermore, these patients may have higher levels of Th2 signaling, as evidenced by the dramatic response to dupilumab, and may be more susceptible to EDEs from IL-17 inhibition. Interestingly, our patient's scalp disease did not respond to upadacitinib which underscores the heterogeneity of this particular patient population.

Conflict of Interest Disclosures: NB: None; AS: None; EJS: BMS, AbbVie, Eli Lilly, Janssen, Novartis, UCB, Pfizer, Amgen, Dermavant, Arcutis, Incyte, SUN, Boehringer Ingelheim, Sanofi & Regeneron, LEO, Alphyn, Galderma, Ortho-Dermatologics

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