Concurrent Atopic Dermatitis and Psoriasis Vulgaris: Implications for Targeted Biologic Therapy

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PRACTICE **POINTS**

- Treatment of psoriasis vulgaris, a helper T cell T_H1/T_H17-mediated skin condition, with secukinumab may result in phenotypic switching to T_H2-mediated atopic dermatitis.
- Atopic dermatitis responds well to dupilumab but may result in phenotypic switching to psoriasis.
- Biologic therapies targeted at specific immunologic pathways may have unintended consequences on the T_H1/T_H2 immune axis.

Psoriasis vulgaris, a helper T cell T_H1/T_H17-mediated inflammatory dermatosis, may be effectively treated with biologic medications such as secukinumab, an IL-17A inhibitor. However, suppression of the T_H1-mediated axis may result in the paradoxical appearance of T_H2-mediated inflammatory skin conditions, such as atopic dermatitis (AD). Dupilumab, a biologic medication that inhibits IL-4/IL-13—cytokines involved in T_H2-mediated inflammation—has demonstrated efficacy in treating AD but may result in phenotypic switching to psoriasis. We describe a patient with psoriasis that was well controlled on secukinumab who developed severe AD that improved with dupilumab. After several months of effective treatment with dupilumab, he subsequently developed re-emergence of psoriatic lesions. This case highlights how pharmacologic interventions targeted at specific immunologic pathways, such as the T_H1/T_H2 axis, may have unintended consequences.

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Psoriasis vulgaris is a chronic inflammatory skin condition associated with notable elevation in helper T cell (T_H) production of T_H1/T_H17-mediated inflammatory cytokines, including IL-17A.[1] Upon binding of IL-17A to IL-17 receptors in the skin, an inflammatory cascade is triggered, resulting in the classic clinical appearance of psoriasis. Moderate to severe psoriasis often is managed by suppressing T_H1/T_H17-mediated inflammation using targeted immune therapy such as secukinumab, an IL-17A inhibitor.[2] Atopic dermatitis (AD), another chronic inflammatory dermatosis, is associated with substantial elevation in T_H2-mediated inflammatory cytokines, such as IL-4.[3] Dupilumab, which interacts with IL-4R, disrupts the IL-4 and IL-13 signaling pathways and demonstrates considerable efficacy in the treatment of moderate to severe AD.[4]

A case series has shown that suppression of the T_H1/T_H17-mediated inflammation of psoriasis may paradoxically result in the development of T_H2-mediated AD.[5] Similarly, a recent case report described a patient who developed psoriasis following treatment of AD with dupilumab.[6] Herein, we describe a patient with a history of psoriasis that was well controlled with secukinumab who developed severe refractory erythrodermic AD that resolved with dupilumab treatment. Following clearance of AD with dupilumab, he exhibited psoriasis recurrence.

Case Report

A 39-year-old man with a lifelong history of psoriasis was admitted to the hospital for management of severe erythroderma. Four years prior, secukinumab was initiated for treatment of psoriasis, resulting in excellent clinical response. He discontinued secukinumab after 2 years of treatment because of insurance coverage issues and managed his condition with only topical corticosteroids. He restarted secukinumab 10 months before admission because of a psoriasis flare. Shortly after

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resuming secukinumab, he developed a severe exfoliative erythroderma that was not responsive to corticosteroids, etanercept, methotrexate, or ustekinumab.

On initial presentation, physical examination revealed diffuse erythema and scaling with associated edema of the face, trunk, and extremities (Figure 1). A biopsy from the patient's right arm demonstrated a superficial perivascular inflammatory infiltrate composed of lymphocytes, histiocytes, and scattered eosinophils consistent with spongiotic dermatitis (Figure 2). Cyclosporine 225 mg twice daily and topical corticosteroids were started.

Over the next several months, the patient had several admissions secondary to recurrent skin abscesses in the setting of refractory erythroderma. He underwent trials of infliximab, corticosteroids, intravenous immunoglobulin, guselkumab, and acitretin with minimal improvement. He underwent an extensive laboratory and radiologic workup, which was notable for cyclical peripheral eosinophilia and elevated IgE levels correlating with the erythroderma flares. A second biopsy was obtained and continued to demonstrate changes consistent with AD.

Four months after the initial hospitalization, all psoriasis medications were stopped, and the patient was started on dupilumab 300 mg/2 mL every 2 weeks and an 8-week oral prednisone taper. This combination led to notable clinical improvement and resolution of peripheral eosinophilia. Several months after disease remission, he began to develop worsening erythema and pruritus on the trunk and extremities, followed by the development of new psoriatic lesions (Figure 3) with a biopsy consistent with psoriasis (Figure 4). The patient was continued on dupilumab, but cyclosporine was added. The patient self-discontinued dupilumab owing to injection-site discomfort and has been slowly weaning off oral cyclosporine with 1 to 2 remaining eczematous plaques and 1 to 2 psoriatic plaques managed by topical corticosteroids.

Comment

We present a patient with psoriasis that was well controlled on secukinumab who developed severe AD following treatment with secukinumab. The AD resolved following treatment with dupilumab and a tapering dose of

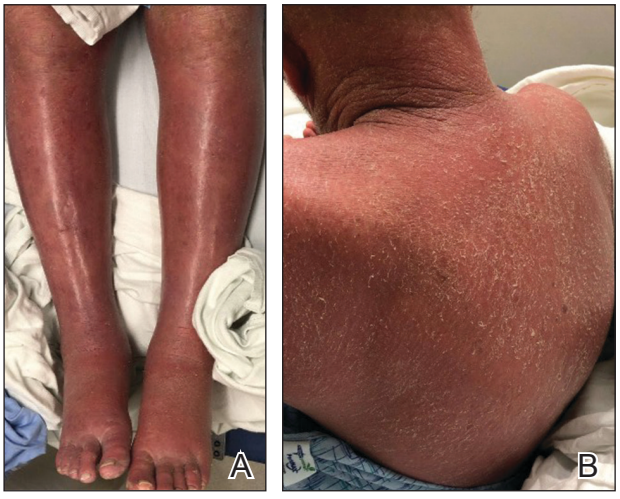

FIGURE 1. A psoriasis patient who was treated with secukinumab later developed atopic dermatitis. A, Diffuse erythema and edema of the lower extremities. B, Diffuse erythema and scaling of the back.

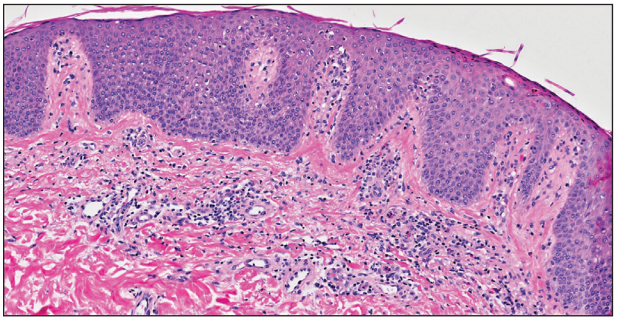

FIGURE 2. Histopathology of an erythroderma biopsy revealed a superficial perivascular inflammatory infiltrate composed of lymphocytes, histiocytes, and scattered eosinophils consistent with spongiotic dermatitis (H&E, original magnification ×40).

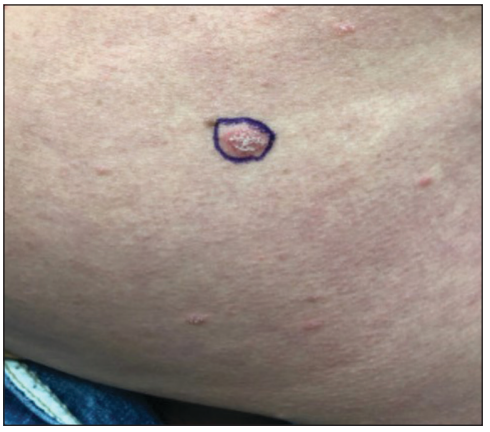

FIGURE 3. Following treatment of atopic dermatitis with dupilumab, psoriatic lesions recurred. Scattered erythematous plaques with overlying silvery scale were seen on the abdomen.

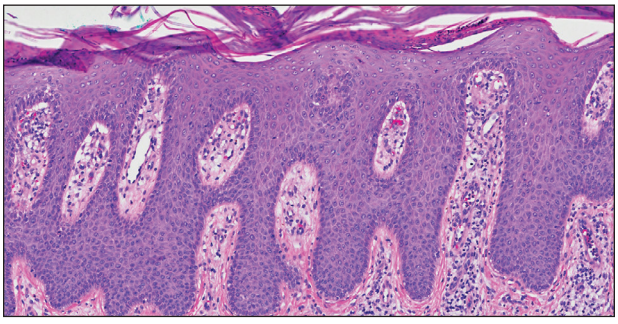

FIGURE 4. Histopathology revealed new psoriatic lesions following treatment of atopic dermatitis with dupilumab (H&E, original magnification ×20).

prednisone. However, after several months of treatment with dupilumab alone, he began to develop psoriatic lesions again. This case supports findings in a case series describing the development of AD in patients with psoriasis treated with IL-17 inhibitors[5] and a recent case report describing a patient with AD who developed psoriasis following treatment with an IL-4/IL-13 inhibitor.[6]

Recognized adverse effects demonstrate biologic medications' contributions to both normal as well as aberrant immunologic responses. For example, IL-17 plays an essential role in innate and adaptive immune responses against infections at mucosal and cutaneous interfaces, as demonstrated by chronic mucocutaneous candidiasis in patients with genetic defects in IL-17–related pathways.[7] Similarly, in patients taking IL-17 antagonists, an increase in the incidence of *Candida* infections has been observed.[8] In patients with concurrent psoriasis and inflammatory bowel disease (IBD), treatment with IL-17 inhibitors is contraindicated due to the risk of exacerbating the IBD. This observation is somewhat paradoxical, as increased IL-17 release by T_H17 cells is implicated in the pathogenesis of IBD.[9] Interestingly, it is now thought that IL-17 may play a protective role in T-cell–driven intestinal inflammation through induction of protective intestinal epithelial gene expression and increased mucosal defense against gut microbes, explaining the worsening of IBD in patients on IL-17 inhibitors.[10] These adverse effects illustrate the complicated and varied roles biologic medications play in immunologic response.

Given that T_H1 and T_H2 exert opposing immune mechanisms, it is uncommon for psoriasis and AD to coexist in a single patient. However, patients who exhibit concurrent findings may represent a unique population in which psoriasis and AD coexist, perhaps because of an underlying genetic predisposition. Moreover, targeted treatment of pathways unique to these disease processes may result in paradoxical flaring of the nontargeted pathway. It also is possible that inhibition of a specific T-cell pathway in a subset of patients will result in an immunologic imbalance, favoring increased activity of the opposing pathway in the absence of coexisting disease. In the case presented here, the findings may be explained by secukinumab's inhibition of T_H1/T_H17-mediated inflammation, which resulted in a shift to a T_H2-mediated inflammatory response manifesting as AD, as well as dupilumab's inhibition of T_H2-mediated inflammation, which caused a shift back to T_H1-mediated inflammatory pathways. Additionally, for patients with changing morphologies exacerbated by biologic medications, alternative diagnoses, such as cutaneous T-cell lymphoma, may be considered.

Conclusion

We report an unusual case of secukinumab-induced AD in a patient with psoriasis that resolved following several months of treatment with dupilumab and a tapering dose of prednisone. Subsequently, this same patient developed re-emergence of psoriatic lesions with continued use of dupilumab, which was eventually discontinued by the patient despite appropriate disease control. In addition to illustrating the underlying pathophysiologic mechanisms of 2 common inflammatory dermatologic conditions, this case highlights how pharmacologic interventions targeted at specific immunologic pathways may have unintended consequences. Further investigation into the effects of targeted biologics on the T_H1/T_H2 immune axis is warranted to better understand the mechanism and possible implications of the phenotypic switching presented in this case.

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