Granuloma annulare arising under systemic psoriasis therapy successfully treated with adalimumab

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INTRODUCTION

Granuloma annulare (GA) is a granulomatous dermatosis characterized by dermal papules and annular plaques. GA is thought to result from a T helper (Th)1-mediated delayed-type hypersensitivity reaction, which elicits connective tissue degradation. A variety of events are thought to predispose to GA, including trauma, diabetes, and medications. Generalized GA can persist for decades despite therapy and has a severe impact on quality of life. In many cases, biological therapy is required to achieve therapeutic success.[1] Conversely, biologic treatment for unrelated skin diseases such as psoriasis have been suspected to trigger GA, in particular anti–interleukin (IL)-17 antibodies.[2,3]

Here we describe a psoriasis patient who had localized GA under apremilast treatment. Because of inefficient control of psoriasis, therapy was switched to secukinumab under which GA generalized. Both psoriasis and GA were then successfully treated with adalimumab.

CASE REPORT

A 62-year-old man presented with a 20-year history of severe plaque psoriasis (Fig 1, *A*). His medical history was known to include metabolic syndrome, such as diabetes. Previous conventional topical and systemic psoriasis treatments were ineffective, leading to the introduction of apremilast treatment. Shortly thereafter, limited annular plaques developed on the dorsal side of the hands for the first time. Histology findings showed a granulomatous dermatosis with deposition of mucin (Fig 1, *C* and *D*). Thus, clinical presentation and histology were consistent with GA, although other forms of drug-induced granulomatous dermatitis could not be ruled out completely. Topical treatment with clobetasol propionate led to complete remission of GA within weeks.

Eighteen months thereafter, his psoriasis worsened despite continuous apremilast treatment. The antipsoriatic therapy was, therefore, switched to secukinumab, an anti–IL-17 antibody, leading to a rapid and sustained improvement of the psoriasis. Psoriasis Area and Severity Index and Granuloma Annulare Severity Index were the tools used to measure the severity of the psoriasis and granuloma annulare (Fig 2).[4] However, 2 months later, the patient had multiple annular, pruritic plaques on the dorsal hands and distal arms (Fig 1, *B*), consistent with a relapse and dissemination of GA. This time, GA remained resistant to topical clobetasol propionate treatment. Because secukinumab has been

Abbreviations used:

GA:	Granuloma annulare
IL:	interleukin
PASI:	Psoriasis Area and Severity Index
Th1:	T helper 1
Th:	T helper
TNF:	tumor necrosis factor

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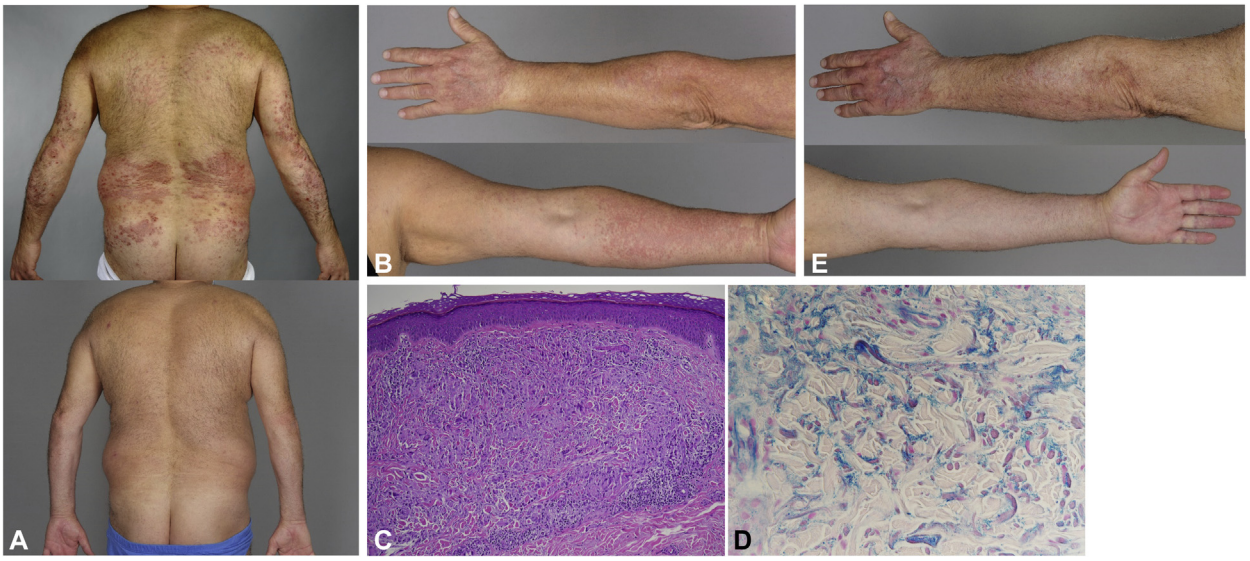

Fig 1. **A**, Severe plaque psoriasis before and after therapy. **B**, Generalized granuloma annulare 2 months after start with secukinumab. **C**, Hematoxylin-eosin staining of histology. **D**, mucin stain of granulomatous skin lesions. **E**, Rapid improvement of erythematous and pruritic component after treatment with adalimumab.

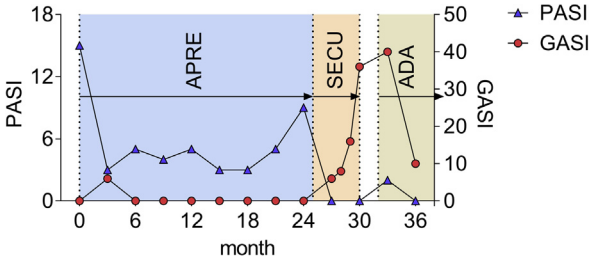

Fig 2. Timeline in relation to Psoriasis Area Severity Index (PASI) and Granuloma Annulare Severity Index (GASI). *ADA*, Adalimumab; *APRE*, apremilast; *SECU*, secukinumab.

associated with triggering of GA,[2,3] it was discontinued. To therapeutically address both the psoriasis and the extensive GA, therapy with adalimumab, a tumor necrosis factor (TNF)-α inhibitor, was initiated. Within 2 months, both the psoriasis and the generalized GA showed an almost complete regression (Fig 1, *C*). Adalimumab was well tolerated and is currently being continued.

DISCUSSION

Our case is in line with 2 previous reports of new-onset of GA in association with anti—IL-17 treatment.[2,3] It adds to these observations while also presenting 2 novel features.

First, the de novo development of GA under apremilast and the secondary exacerbation under secukinumab suggest a pathomechanistic link between antipsoriatic drugs, especially those blocking the Th17 pathway, and GA. Because both apremilast and secukinumab mediate their antipsoriatic effects via inhibition of the Th17 pathway, it can be speculated that a disturbance of the balance between different Th cell axes might be related to GA onset.[5] In fact, reciprocal counter-regulation of the Th1 and Th17 axes has been described; thus, blockade of IL-17 might enhance the activity of the Th1 axis and lead to GA in predisposed individuals.[6] Our patient suffered from metabolic syndrome and diabetes, both of which are considered predisposing risk factors for GA.[7]

Second, our case shows that the broad spectrum of currently available immunomodulatory treatments may allow us to select appropriate alternative drugs that treat both the underlying psoriasis as well as the treatment-associated GA. In our case, GA developed under treatments inhibiting the Th17 pathway, thus we chose a TNF-α inhibitor (adalimumab). Further, TNF-α inhibition is a well-established treatment for psoriasis, and up to 80% of patients with GA may show a clinical response to TNF-α inhibition.[1,8] Thus, TNF-α appears to have an integral role in the pathogenesis of GA in addition to its known role in psoriasis. To the best of our knowledge, this is the first case report of a rapid successful treatment of both plaque psoriasis and GA with the anti—TNF-α inhibitor, adalimumab.

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