Dupilumab in the management of topical corticosteroid withdrawal in atopic dermatitis: A retrospective case series

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INTRODUCTION

Topical corticosteroid (TCS) withdrawal, or steroid addiction, is a poorly understood, distinct adverse effect of inappropriate TCS use. It occurs most commonly in adult women applying mid- or high-potency TCS to the face or genital region and is associated with increased frequency and duration of treatment.[1-3] TCS withdrawal should be suspected when confluent erythema appears within days to weeks of discontinuing therapy, stinging and burning are prominent symptoms, and history is consistent with the at-risk population described above. This condition can be divided into 2 subtypes with distinct clinical presentations. The erythematoedematous variant is characterized by erythema, scaling, papules and nodules, desquamation, and edema, with symptoms including burning, pruritus, pain, and decreased tolerance for emollients. The papulopustular type is distinguished by the prominence of pustules, papules, and nodules and the less common presence of edema and burning.[4]

Although the mechanism of this phenomenon is not well understood, it is theorized to be caused by the effects of TCS on the local immune system and cutaneous blood vessels.[5] TCSs decrease production of nitric oxide (NO), thereby inhibiting its vasodilatory action and depleting mast cells, which are regulated by NO.[6-8] In the absence of TCS use, a rebound effect may occur in which NO levels increase, leading to exaggerated vasodilation.[5] Similarly, sparse data exist to guide definitive diagnosis or therapy. In most reported cases, the first step in treatment is to discontinue TCS use. Other reported therapeutic modalities include medications such as tetracycline antibiotics, antihistamines, and calcineurin inhibitors. Ultraviolet therapy was described in 1 case report.[4] Because rebound of underlying disease may occur and may be indistinguishable from TCS withdrawal when steroid therapy is halted, some investigators suggest initiation of oral corticosteroids or a TCS taper in an effort to circumvent flares.[9] However, evidence to support the use of systemic immunosuppressants in the management of this condition is lacking.

Abbreviations used:

BSA: body surface area
IGA: Investigator's Global Assessment
TCS: topical corticosteroid

We performed a retrospective chart review of adult patients with suspected TCS withdrawal treated with dupilumab for atopic dermatitis at a single center from March 2017 to March 2018. Effectiveness was measured by decrease in body surface area (BSA) involved and decrease in Investigator's Global Assessment (IGA) score. Case summaries are presented in Table I.

CASE 1

The patient in case 1 was a 25-year-old woman with neck, arm, and severe facial involvement by erythematous eczematous plaques. She had previously used topical desonide and desoximetasone,

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Table I. Characteristics of patients with TCS withdrawal treated with dupilumab

Patient	Gender	Age	IGA start*	BSA (%) start*	IGA final†	BSA (%) final†	Treatment duration (wk)
1	F	25	4	60	3	25	13.6
2	F	32	4	70	2	15	13.6
3	M	35	4	70	2	20	14.7
4	F	26	3	60	1	10	8.7
5	M	22	3	45	1	10	31.3
Mean	—	28	3.6	61	1.8	16	16.4

BSA, Body surface area; *F*, female; *IGA*, Investigator's Global Assessment; *M*, male; *TCS*, topical corticosteroid.
*IGA and BSA start are respective values at the time of dupilumab initiation.
†IGA and BSA final are respective values at the time of the most recent office visit.

which were discontinued 6 months before initiation of dupilumab. She initially did not respond to a trial of cyclosporine, 100 mg twice a day, and crisaborole, 2% twice a day. Her respective affected BSA and IGA at time of dupilumab initiation were 60% and 4. After 13.6 weeks of dupilumab therapy with a 600-mg loading dose followed by 300 mg every 2 weeks, her affected BSA improved to 25% and IGA to 3.

CASE 2

The patient in case 2 was a 32-year-old woman with erythematous eczematous plaques of the scalp, cheek, neck, and arms. Her disease had an affected BSA of 70% and IGA of 4 at time of dupilumab initiation. She previously used triamcinolone, hydrocortisone 2.5%, fluocinonide, and clobetasol. Additionally, she did not respond to a month-long trial of tacrolimus 0.1% twice a day before dupilumab therapy. She had an excellent clinical response to dupilumab, with improvement to 15% BSA and IGA of 2 after 13.6 weeks of treatment with a 600-mg loading dose followed by 300 mg every 2 weeks.

CASE 3

The patient in case 3 was a 35-year-old man with erythematous eczematous plaques involving his face, hands, legs, and trunk who had used triamcinolone and did not respond to multiple treatment modalities before dupilumab. He did not improve with 24 sessions of narrowband ultraviolet B therapy, mycophenolate mofetil, 1000 mg twice a day, or cyclosporine, 100 mg twice a day. Evaluation at the time of dupilumab initiation found an affected BSA of 70% and IGA of 4. After 14.7 weeks of treatment with a 600-mg loading dose followed by 300 mg every 2 weeks, affected BSA improved to 20% and IGA to 2.

CASE 4

The patient in case 4 was a 26-year-old woman with erythematous eczematous plaques of the face, arm, and hands who had most recently been applying desonide. She experienced worsening of symptoms with topical pimecrolimus and similarly was started on cyclosporine, 50 mg twice a day, without lasting improvement. At the time of dupilumab initiation, examination found an affected BSA of 60% and IGA of 3. After receiving dupilumab for 8.7 weeks with a 600-mg loading dose followed by 300 mg every 2 weeks, her affected BSA decreased to 10% and IGA to 1.

CASE 5

The patient in case 5 was a 22-year-old man with diffuse erythematous eczematous plaques who had previously been on triamcinolone and mometasone, which were discontinued 3 months before his initial visit. He tried tacrolimus 0.1% 3 times a day and 22 treatments of narrowband ultraviolet B without improvement. Evaluation at the time of dupilumab initiation found an affected BSA of 45% and IGA of 3, which improved to 10% and 1, respectively, after 31.3 weeks of treatment with a 600-mg loading dose followed by 300 mg every 2 weeks.

DISCUSSION

This case series sheds light on dupilumab as a potential novel therapy for TCS withdrawal. Our patient population is aligned with previously reported cases of this phenomenon, suggesting it may be representative of patients affected by TCS withdrawal. Most patients are women who used TCS for treatment of atopic dermatitis, similar to what was shown in a systematic review of reports of TCS withdrawal.[4] As would be expected from previous case reports, most of these patients were using mid- to high-potency TCS, although in 1 case the patient most recently used low-potency TCS.

Although underaddressed in the literature, TCS withdrawal is a pressing concern for some patients and is garnering increasing attention in social media. Further, consistent with what was observed in our patient population, most cases are self-diagnosed rather than identified by a physician, and no gold

standard diagnostic approach has been defined.[10] Counseling patients appropriately regarding this phenomenon and identifying at-risk patients is essential to promoting adherence to therapy. Considering the wariness of corticosteroids that often accompanies TCS withdrawal, it is important to identify effective treatments that these patients also find acceptable. Our experience suggests that dupilumab may be of value in the treatment of TCS withdrawal in the context of moderate or severe atopic dermatitis and merits further investigation. High-quality studies are needed to better inform our understanding of this phenomenon and guide clinical management.

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