

THERAPEUTIC HOTLINE: SHORT PAPER

A case series of dupilumab-treated allergic contact dermatitis patients

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Abstract

Atopic dermatitis is characterized by skin barrier abnormalities and immune dysregulation with increased T_H2 signaling playing a central role. Investigations of allergic contact dermatitis suggest that certain allergens may also activate particular T cell signatures such as T_H2 -dominant responses to fragrance and rubber. We present a case series of patients with allergic contact dermatitis who were successfully treated with dupilumab, a biologic developed for atopic dermatitis that dampens T_H2 signaling. In our cohort of three patients, two had extensive allergic contact dermatitis on their torso and extremities primarily due to textile and rubber allergens. The third was a hairdresser with severe hand dermatitis due to occupational allergens. Two of the three patients had no history of atopic dermatitis during childhood. Each patient experienced at least 90% improvement in body surface area involvement and continues to maintain their clinical response on dupilumab (range 6–13 months). Our hypothesis that dupilumab suppressed contact allergic reactions is supported by the identification of clinically relevant contact allergens on patch testing, acute onset and/or worsening of dermatitis in adulthood, and absence of childhood atopic dermatitis in two cases. Further, larger investigations to understand which factors affect responses of allergic contact dermatitis to dupilumab are warranted.

KEYWORDS

allergic contact dermatitis, dupilumab

1 | INTRODUCTION

Atopic dermatitis (AD) is characterized by skin barrier abnormalities and immune dysregulation with increased T_H2 signaling playing a central role. Investigations of allergic contact dermatitis (ACD) also indicate that specific contact allergens may activate particular T-cell signatures such as T_H2 -dominant responses to fragrance and rubber (Dhingra et al., 2014). Therefore, for certain allergens eliciting ACD, immunomechanisms may more closely overlap those of AD than for other allergens. We present a case series of patients with ACD who were successfully treated with dupilumab, a biologic developed for AD that dampens T_H2 signaling (Simpson et al., 2016).

2 | MATERIALS AND METHODS

Patch testing was performed using allergens (Chemotechnique Diagnostics, Malmö, Sweden) placed in Finn Chambers® (Smart

Practice, Phoenix, Arizona) on Scanpore® tape. Allergens were adhered to the skin for 48 hr. A first read was performed at the time of patch removal followed by a delayed read 1–3 days later. Reactions were graded using the International Contact Dermatitis Research Group (ICDRG) classification. Given that each patient's severe ACD was insufficiently improved with allergen avoidance or other standard therapies, dupilumab was initiated administered as a 600 mg loading dose followed by 300 mg every 2 weeks thereafter.

3 | RESULTS

Our three patients were women, 20, 52, and 53 years-of-age (Table 1). Two had no history of AD during childhood. Patch testing demonstrated at least two categories of clinically relevant allergens for each patient. Clinical relevance was determined by factors such as patient's occupation, dermatitis distribution, ingredients in personal care products, and response to allergen avoidance. All received topical

TABLE 1 Demographic and clinical data for patients treated with dupilumab

	Patient 1	Patient 2	Patient 3
Age	20	53	52
Gender	Woman	Woman	Woman
Dermatitis location	Under elastic in textiles/bra/bathing-suit, chest, back, generalized	Torso, extremities	Hands > face, back, extremities
Dermatitis acute worsening/onset	6 months	7 years	6–7 years
Occupation	Student and lifeguard	Speech therapist	Hairdresser
Atopy	Seasonal allergies, childhood AD	Seasonal allergies	Seasonal allergies, hay fever
Treatments			
Prior systemic(s)	Multiple courses of prednisone	Azathioprine, multiple courses of prednisone	Cyclosporine, two courses of prednisone
Current systemic	Dupilumab for 13 months	Dupilumab for 12 months	Dupilumab for 6 months
BSA improvement with Dupilumab	>90%	>90%	>90%
Contact allergens on patch testing			
	Rubber Accelerators ^a	Rubber Accelerators ^a	Hairdresser/Dyes ^a
	? –> black rubber mix	+++ Thiuram mix	+++ Disperse orange 3
	Dyes/formaldehyde resin ^a	++ Tetraethylthiuram disulfide	+++ Ammonium persulfate
	++ Reactive black 5	+ Tetramethylthiuram disulfide	++ 2,5-diaminotoluene
	+ Reactive red 238	+ Tetramethylthiuram monosulfide	+ PPD ^b
	+ Dimethylol dihydroxyethyleneurea	+ Dipentamethylenethiuram disulfide	+ 4-aminophenol
	Cosmetic/preservatives/adhesives ^a	+ Diphenylguanidine	+ Disperse blue 35
	+++ Methylisothiazolinone	Dyes ^a	+ Disperse yellow 9
	++/+ Diazolidinyl urea	+ Disperse blue 106	+ Disperse red 17
	++ Amidoamine	Cosmetic/preservatives/adhesives	Cosmetic/preservatives/adhesives ^a
	++ Resorcinol (<i>also a dye</i>)	+ Methyl methacrylate	+++ Methylisothiazolinone
	Fragrances	Fragrances	+ MCI/MI
	+ Tea tree oil	+ Cinnamyl alcohol	+ Amidoamine
			+ HEMA ^b
			+ Ethyl acrylate ^b
			+ Methyl methacrylate ^b
			Fragrances ^a
			+ Fragrance mix I
			+ Fragrance mix II
			+ Linalool
			Topical antibiotics
			+ Neomycin ^b

AD = atopic dermatitis; BSA = body surface area; MCI/MI = methylchlorisothiazolinone/methylisothiazolinone; HEMA = hydroxyethylmethacrylate.

Strength of patch test reactions were graded using the International Contact Dermatitis Research Group (ICDRG) classification [IR], ?, +, ++, +++. The 0, IR, and ? reactions are not listed. All patients were tested to our standard, cosmetic/preservative/adhesive, fragrance, rubber, textile, and bakery series. Patient 3 was also tested to our hair and shoe series.

^a These allergen categories were considered the most clinically relevant ones in each case.

^b These allergens were positive on prior patch testing, and were not retested in our clinic.

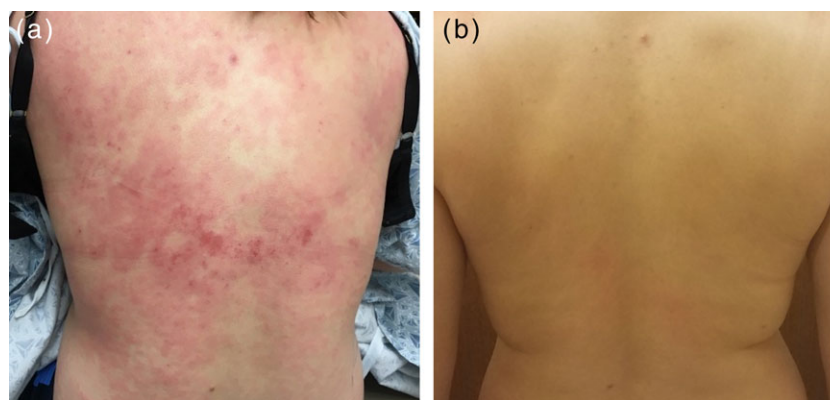


FIGURE 1 Dermatitis of the back secondary to rubber accelerators suggested by more marked involvement underneath the patient's bra elastic (left) with resolution following dupilumab treatment (right)

corticosteroids and at least one other systemic therapy prior to dupilumab.

Each patient had at least 90% improvement in body surface area (BSA) with dupilumab. Patient 1, a lifeguard, presented with a BSA over 80%. Her dermatitis was most severe in a bathing suit distribution and under the bra elastic (Figure 1). Within 6 weeks of starting dupilumab, she experienced dramatic improvement in her dermatitis and continues to be clear on dupilumab after 13 months. Patient 2, who previously required azathioprine and numerous prednisone tapers due to the severity of her dermatitis on the torso and extremities, began to improve after 3–4 weeks of starting dupilumab. She reported near complete resolution of her dermatitis within 3 months, and at follow-up 12 months later, her BSA of 40% had decreased to 2%. Patient 3, a hairdresser diagnosed with severe, occupational, diffuse, and fissuring hand dermatitis, was treated with cyclosporine for 6 weeks before transitioning to dupilumab. For 6 months she has remained nearly clear on dupilumab alone while continuing to work.

4 | DISCUSSION

Dupilumab may be a therapeutic option for patients with ACD who have not adequately responded to allergen avoidance strategies and other traditional treatments. It can be difficult for certain patients, such as those with numerous contact sensitizations and/or challenging occupational exposures, to adequately avoid allergens. Targeted biologic therapy may be particularly beneficial in improving outcomes for these cases.

Prior reports of severe, recalcitrant hand dermatitis responding to dupilumab, either noted no relevant allergens on patch testing (Zirwas, 2018) or no improvement with allergen avoidance (Oosterhaven, Romeijn, & Schuttelaar, 2018). Characteristics of the three patients presented here support the hypothesis that for our cases dramatic clinical improvement was based on dupilumab

suppressing ACD reactions. These include clinically relevant allergens found on patch testing, such as textile and rubber allergens for two patients and multiple occupational allergens for another, acute onset and/or worsening of dermatitis in adulthood, and absence of childhood atopic dermatitis in two cases. Further, larger investigations to understand which factors affect responses of ACD to dupilumab are warranted.

CONFLICT OF INTEREST

No conflict of interest.

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