Repeat patch testing in a patient with allergic contact dermatitis improved on dupilumab

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INTRODUCTION

Dupilumab, the first monoclonal antibody approved by the US Food and Drug Administration for the treatment of moderate-to-severe atopic dermatitis (AD), inhibits interleukin (IL)-4 and IL-13 via blockade of IL-4Ra, inhibiting helper T cell (Th)2 signaling. Allergic contact dermatitis (ACD) has a complex and dynamic pathophysiology, in which at least 1 or more of the Th1, Th2, and Th17/22 pathways may mediate reactions. Patients with AD are at risk of ACD. Here we present a patient with AD and ACD who was patch tested before starting dupilumab and during therapy.

REPORT OF CASE

A 54-year-old man with lifelong history of AD presented with a 2-month history of acute hand and foot dermatitis. Previously, his AD was reasonably controlled with emollients and intermittent topical corticosteroids. He was a saxophone player and repairman, with frequent exposure to glues, varnishes, epoxies, and metals. Examination found hyperkeratotic eczematous plaques and distal onycholysis affecting the dorsal and volar fingers and toes. The following reactions were observed on his initial patch testing at 48 hours and 96 hours, respectively: 1+/2+ to nickel sulfate hexahydrate 2.5% pet (Ni), 3+/3+ to methylchloroisothiazolinone/methylisothiazolinone 0.02% aq (MCI/MI), 3+/3+ to methylisothiazolinone 0.2% aq (MI), 1+/1+ to 2-n-octyl-4-isothiazolin-3-one 0.1% pet, and 1+/1+ to 4,4-dithiodimorpholine 1% pet (Fig 1, *A* and *B*). He had definite exposure to MI and MCI/MI and probable exposure to Ni, 2-n-octyl-4-isothiazolin-3-one and 4,4-dithiodimorpholine. He partially responded to prednisone, but failed to respond to several months of allergen avoidance, desoximetasone ointment, and phototherapy. Adding acitretin to this regimen led to only slight

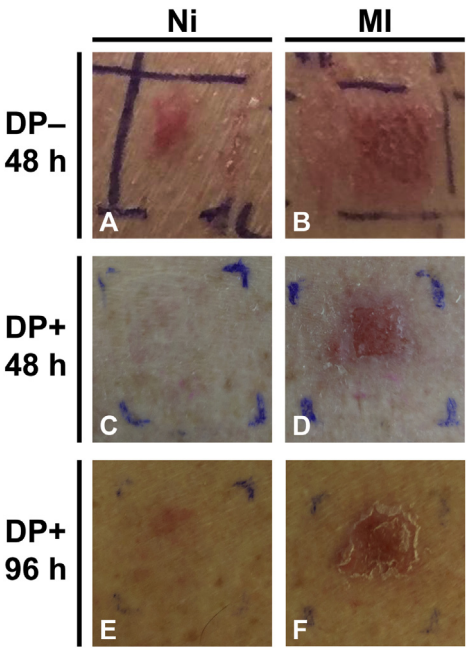

Fig 1. Positive patch testing reactions to Ni and MI on dupilumab (DP) therapy. Before dupilumab initiation, patch testing against (**A**) Ni and (**B**) MI was positive at 48 hours. At week 8 of dupilumab therapy, repeat limited patch testing to (**C, E**) Ni and (**D, F**) MI showed persistent reactions at 48 hours and 96 hours, respectively. All testing was performed on the upper back, and the same batch of allergens was used.

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Abbreviations used:

ACD: allergic contact dermatitis
AD: atopic dermatitis
Th: T helper cell
Ni: nickel
MCI: methylchloroisothiazolinone
MI: methylisothiazolinone

improvement of his hand and foot dermatitis; however, he had a scattered generalized eczematous dermatitis presumed to be AD. Dupilumab was initiated at standard dosing with significant improvement of both the generalized eruption and hand foot dermatitis within weeks (Fig 2). Repeat patch testing with Ni and MI on week 8 of dupilumab therapy showed ?/1+ reaction to Ni and 3+/3+ reaction to MI at 48 hours and 96 hours (Fig 1, *C-F*).

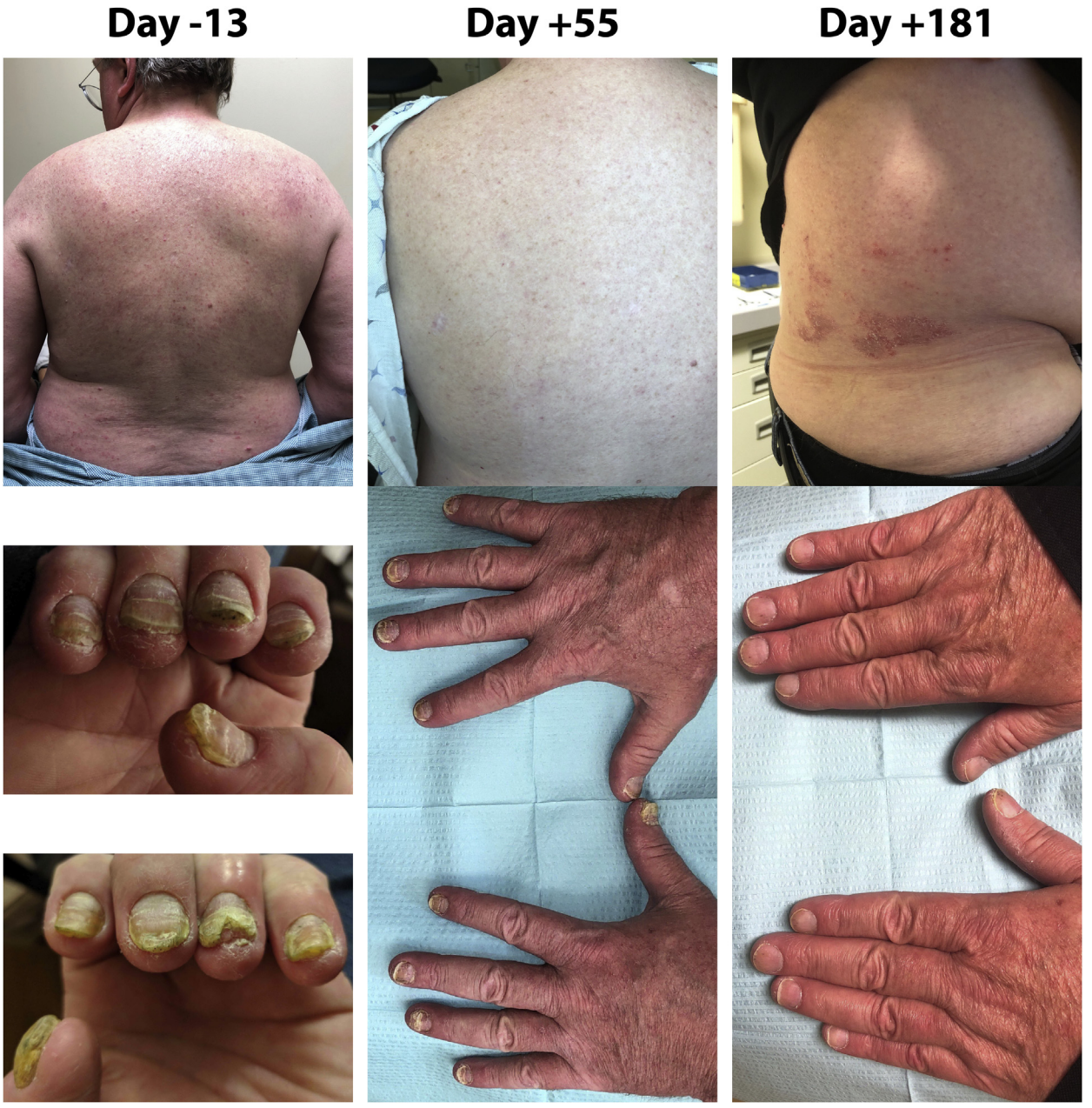

Fig 2. Improvement of truncal and hand dermatitis on dupilumab therapy. Before dupilumab initiation (**left panel**), he had 40% body surface area involvement. He had approximately 2% body surface area involvement after approximately 2 months (**center panel**) and less than 1% body surface area involvement after approximately 6 months (**right panel**).

DISCUSSION

ACD is elicited in sensitized individuals upon allergen re-exposure, leading to innate and adaptive immune activation. The inflammatory milieu during the elicitation phase is historically thought to be Th1 predominant, although recent work also implicates Th17 and Th22 cytokines.[1] These reactions are likely hapten specific[1]; for instance, contact allergy to nickel correlates with a mixed Th1/Th2 response.[1,2] After prolonged and repeated allergen exposure, a Th2-predominant response is observed in chronic lesions of ACD.[3]

Positive patch test reactions while receiving dupilumab have been reported, showing that these patients are capable of mounting an acute reaction upon allergen exposure; however, it is possible that patients with chronic ACD might benefit from dupilumab therapy despite remaining competent to elicit acute ACD on patch testing.[4,5] Our patient experienced significant clinical improvement on dupilumab but continued to have positive patch test reactions to Ni and MI. The slightly attenuated reaction to Ni on repeat patch testing (Fig 1) may represent expected variation on retesting; however, the possibility of attenuation due to IL-4/IL-13 blockade with dupilumab should be investigated. Although the immunology of ACD elicitation is complex, IL-4 and IL-13 are found to be released from peripheral blood mononuclear cells of Ni-sensitive patients after in vitro antigen challenge,[2,6] lending support to this hypothesis.

This case highlights the results of patch testing before and during treatment with dupilumab in the setting of a patient who had significant improvement of his ACD and AD, suggesting potential benefits of dupilumab in the management of chronic ACD. If proven beneficial, dupilumab could complement but not replace allergen avoidance strategies in patients with chronic ACD to ubiquitous allergens that are often not fully avoidable. More investigation is necessary to assess the potential therapeutic role of dupilumab in chronic ACD and also to assess the validity of patch testing during therapy.

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