Dupilumab for allergic contact dermatitis and implications for patch testing: Irreconcilable differences

To the Editor: Patch testing (PT) patients on systemic immunosuppression or immunomodulation has been a point of complexity and even controversy, and guidelines are not well established. Features of the patient, the immune-modulating agent, and the allergen in question must be considered, and independent effects are difficult to untangle.

Allergens appear to elicit unique inflammatory cascades. Cellular and molecular studies of PT reactions have demonstrated that cytokine responses are not generalizable across allergens, and instead are hapten-specific, with T-helper cell (Th) 1 and Th2 responses both observed.[1] Nickel, for example, is a known potent inducer of innate and adaptive immunity, with the latter predominately involving Th1- and Th17-mediated pathways. In contrast, fragrance and rubber are thought to predominately activate a Th2-mediated pathway.

Moreover, the "strength" of a PT reaction can also vary widely across allergens. Thus, the same dose of immunosuppression can inconsistently affect a positive signal on PT. For example, prednisone at 20 mg daily has been shown to allow positive reactivity to urushiol, a potent sensitizer[2] but appears to suppress reactivity to nickel.[3]

Dupilumab, specifically, is theorized to preferentially reduce allergic contact dermatitis (ACD) caused by allergens with a Th2 bias, such as fragrance and rubber. As a corollary, one would expect a false-negative reaction for these allergens among patients on dupilumab undergoing PT. With similar immunologic rationale, dupilumab is expected to have little to no effect on allergens with Th1-mediated effects, such as nickel, minimizing false-negative risk in PT for these allergens in individuals on dupilumab.

Contrary to these expectations, a recent retrospective study by Raffi et al[4] examining PT before and after dupilumab initiation, demonstrated a sustained positive reaction in 73.1% (19 of 26) of fragrance test sites. The authors reported a reaction loss rate (false-negative rate) of 10.4% across allergens tested and concluded that dupilumab does not appear to exert a dampening effect on PT results. In contrast to this conclusion, however, a recent case report demonstrated a significant reduction in ACD caused by nickel allergy after dupilumab initiation, with the authors suggesting treatment benefits of dupilumab in the management of ACD.[5] The seemingly contradictory clinical evidence for dupilumab to be both a minimal threat to PT results and a treatment for ACD is difficult to rationalize with any biologic plausibility.

Beyond mechanism, the varied pharmacokinetics of immune-modulating medications add further complexity to the PT approach, such as the decision of drug discontinuation lead time. Upon discontinuation of dupilumab, for example, the median time to nondetectable concentrations is up to 13 weeks, depending on dose (after reaching steady state).

Because our precise understanding of these reactions on a patient level remains limited, our approach to PT in patients on immune-modulating therapies becomes a matter of clinical judgment rather than of protocol guidance. Although dupilumab may prove itself a worthy ACD treatment option, the literature is currently contradictory and insufficient. Dupilumab may in fact be helpful in cases where allergen avoidance is not possible or when the dermatitis is particularly debilitating; however, where feasible, first-line therapy should still be the effective, safer, and far less expensive option of allergen avoidance.

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