Patch Testing on Dupilumab: Reliable or Not?

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PRACTICE **POINTS**

- Allergic contact dermatitis is an important diagnostic consideration in patients with refractory or persistent dermatitis.
- Patch testing is important to help determine a possible allergic contactant, but there is confusion about its accuracy in patients taking dupilumab.
- Patients with residual dermatitis while on dupilumab are likely to benefit from patch testing.

In patients with persistent atopic dermatitis (AD) who are taking dupilumab, is there benefit of patch testing to determine if allergic contact dermatitis (ACD) also is contributing to their disease? Results of patch testing are likely be influenced by the immunomodulatory effects of dupilumab. Similar to the recommendation for patients to refrain from using topical or systemic corticosteroids for 1 week or more prior to patch testing to eliminate false negatives, we reviewed the literature to create practice guidelines for dermatologists regarding patch testing while a patient is taking dupilumab.

Pathophysiology and Pathomechanism

Dupilumab functions through the blockade of T helper 2 (T_H2) cells; ACD is propagated through the T helper 1 (T_H1) cellular pathway. However, patients with ACD that is unresponsive to allergen avoidance and traditional therapies, such as topical and oral corticosteroids, have responded to dupilumab. The more common reports of this responsiveness are with fragrances; multiple case series described patients with ACD to fragrance mix I[1] and balsam of Peru[1,2] who improved on dupilumab when other treatments failed. There also are reports of response when ACD was secondary to nickel,[2,3] *p*-phenylenediamine,[1] Compositae,[4] and non–formaldehyde-releasing preservatives (non-FRPs).[5] Therefore, not all ACD is propagated through the T_H1 cellular pathway.

As noted in these cases, ACD can be a response to an allergen whose pathogenesis involves the T_H2 pathway or when patient characteristics favor a T_H2 response. It has been suggested that AD patients are more susceptible to

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T_H2-mediated contact sensitization to less-potent allergens, such as fragrances.[6]

Patch Test Results

Positive patch test results for allergens have been reported while patients are on dupilumab therapy, including a few studies in which results prior to starting dupilumab were compared with those while patients were on dupilumab therapy. In a retrospective chart review of 48 patients on dupilumab for AD with persistent disease, 23 patients were patch tested before and during dupilumab therapy. In these patients, the majority of contact allergies were persistent and only 10% (13/125) of patch test–positive results resolved on dupilumab therapy.[7] Contact allergies that resolved included those to emulsifiers (propylene glycol, Amerchol L101 [lanolin-containing products found in cosmetics and other goods], dimethylaminopropylamine), fragrances (fragrance mix I, balsam of Peru), sunscreens (sulisobenzone, phenylbenzimidazole-5-sulfonic acid), and metals (vanadium chloride, phenylmercuric acetate).[7] The following results observed in individual cases demonstrated conflicting findings: persistence of allergy to non-FRPs (methylisothiazolinone [MI]) but resolution of allergy to formaldehyde[8]; persistence of allergy to corticosteroids (budesonide and alclometasone)[9]; persistence of allergy to an antibiotic (neomycin sulfate) but resolution of allergies to a different antibiotic (bacitracin), glues (ethyl acrylate), bleach, and glutaraldehyde[9]; persistence of nickel allergy but resolution of allergies to fragrances (cinnamic aldehyde, balsam of Peru) and non-FRPs (methylchloroisothiazolinone or MI)[10]; and persistence of allergies to non-FRPs (MI) and FRPs (bronopol) but resolution of allergies to nickel, fragrances (hydroperoxides of linalool), and Compositae.[11] Additional case reports of positive patch test results while on dupilumab but with no pretreatment results for comparison include allergies to rubber additives,[12-14] nickel,[14] textile dyes,[14] cosmetic and hair care additives,[12,14,15] corticosteroids,[15] FRPs,[15] fragrances,[15,16] emulsifiers,[16] and non-FRPs.[17]

An evident theme in the dupilumab patch-testing literature has been that results are variable and case specific: a given patient with ACD to an allergen will respond to dupilumab treatment and have subsequent *negative* patch testing, while another patient will not respond to dupilumab treatment and have persistent *positive* patch testing. This is likely because, in certain individuals, the allergen-immune system combination shifts ACD pathogenesis from a purely T_H1 response to at least a partial T_H2 response, thus allowing for benefit from dupilumab therapy. T helper 1 cell–mediated ACD should not be affected by dupilumab; therefore, reliable results can be elucidated from patch testing despite the drug.

Final Thoughts

We propose that AD patients with residual disease after taking dupilumab undergo patch testing. Positive results indicate allergens that are not inhibited by the drug. Patients will need to follow strict allergen avoidance to resolve this component of their disease; failure to improve might suggest the result was a nonrelevant positive.

If patch testing is negative, an alternative cause for residual disease must be sought. We do not recommend stopping dupilumab prior to patch testing to avoid a disease flare from AD or possible T_H2-mediated ACD.

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