

Positive Patch Test Reaction in a Patient Taking Dupilumab

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PRECÍS

Patch testing sensitivity varies by immunosuppressive agent; we report a positive patch test reaction in a patient on dupilumab.

DISCUSSION

A 63-year-old woman with a 30-year history of atopic dermatitis with worsening over the past 5 years was started on dupilumab 300 mg every other week for severe atopic dermatitis. Six months after initiation of therapy, the patient's dermatitis had improved, but she was not clear. There was concern for allergic contact dermatitis, and patch testing was recommended. Her history included 2 previous patch tests: a positive patch test for formaldehyde at an outside clinic, and an "angry back" reaction at this institution when off immunosuppressants and in the setting of severe disease.

While the patient was taking dupilumab, 129 allergens were tested, including the North American Contact Dermatitis Group screening series, the corticosteroid series, and 50 additional allergens. Allergens were obtained from Chemotechnique Diagnostics (Vellinge, Sweden) and Allergeaze (SmartPractice, Calgary, Alberta, Canada) and were applied with Finn Chambers (SmartPractice, Phoenix, AZ) on Scanpor tape (Norgesplaster Alpha AS, Vennesla, Norway). Readings were completed on D2 and D5 and designated in accordance with the International Contact Dermatitis Research Group criteria.¹ Patch testing was positive with a 1+ reaction to methylisothiazolinone. She also had a +/– reaction to dimethylaminopropylamine 1% aqueous. There were several irritant reactions, including formaldehyde 2% aqueous.

The case provides evidence of the ability to mount a positive patch test reaction while concurrently immunosuppressed with dupilumab. On March 2017, dupilumab became the first biologic agent to gain U.S. Food and Drug Administration approval for the treatment of moderate to severe atopic dermatitis in adults. As an interleukin 4 (IL-4) receptor antagonist, dupilumab blocks the stimulatory effects of both IL-4 and IL-13.²

It is worth noting that the patient failed to mount a response to her previously reported formaldehyde allergy. Two possibilities

exist for this finding: (1) dupilumab inhibited the patient's ability to mount a response to formaldehyde, or (2) the previous reading was misinterpreted.^{3–5} Formaldehyde is a known irritant, and irritant reactions can be misinterpreted as positive by inexperienced patch testers. Formaldehyde was interpreted as an irritant reaction during this patch test; this supports misinterpretation of results during the previous patch test.

Patch testing was previously inconclusive in this patient because of an "angry back" reaction, which was likely related to her diffuse cutaneous involvement at that time. With active severe dermatitis lowering the yield of patch testing and patients improving on dupilumab, we will continue to see patients presenting for testing while immunosuppressed on dupilumab.^{3–5}

PEARL

Patients immunosuppressed on dupilumab can mount a positive patch test reaction.

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Allergic Contact Stomatitis Associated With Sweet Vermouth

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PRECÍS

We discuss allergic contact stomatitis (ACS) associated with sweet vermouth to increase awareness of this potential allergen.

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DISCUSSION

A 63-year-old woman presented with oral labial burning of 3 months' duration. She denied symptom onset with new medications or oral hygiene products and denied frequent use of mint or cinnamon, but reported symptoms were aggravated by acidic foods. She denied additional mucosal or cutaneous lesions. Amoxicillin, valacyclovir, nystatin, vitamin B₁₂ injections, and diphenhydramine rinses had been prescribed without benefit. Current medications included irbesartan, nebivolol, and vitamin D₃. Social history was positive for tobacco and alcohol use, and upon further questioning, the patient reported consuming 2 to 3 Manhattan cocktails nightly containing sweet vermouth.

On evaluation, the extraoral area was unremarkable. Intraoral examination revealed generalized erythema and striae on the bilateral buccal, lower labial, and palatal mucosa (Fig. 1). Differential diagnosis consisted of ACS, oral lichen planus, and lichenoid mucositis. The patient deferred biopsy, so an elimination of the vermouth was suggested, with the plan to patch test if there were no improvement. On her 1-month reassessment, she was noted to have substantial symptom improvement and almost complete resolution of the previous examination findings (Fig. 2).

Allergic contact stomatitis is a hypersensitivity reaction often presenting as a diagnostic dilemma.¹ Patients with ACS frequently complain of nonspecific symptoms, such as burning, paresthesia, and dysgeusia.^{1,2} Allergic contact stomatitis typically has a lichenoid appearance with varying degrees of erythema, edema, desquamation, and/or ulceration² and may present with similar clinical findings and/or symptoms to aphthous stomatitis, oral lichen planus, lichenoid mucositis, pemphigus vulgaris, mucous membrane pemphigoid, and burning mouth syndrome.^{1,2}

Dental restorative materials, such as mercury-containing amalgam, resin, and various metals, such as gold and palladium, have



Figure 1. Lichenoid lesions with erythema on the left buccal mucosa of a 63-year-old woman using sweet vermouth.

been associated with ACS.^{1,2} Toothpaste is commonly associated with ACS and contains several potential allergens, such as flavoring agents, cocamidopropyl betaine, and propylene glycol.³ Elimination or removal of identified allergens typically results in resolution of ACS. In many cases, allergens are not identified, and topical corticosteroids are usually effective for symptom management.²

Vermouth is derived from a white base wine, fortified and infused with bark, seeds, and fruit peels collectively termed *botanicals*.⁴ The term *vermouth* is derived from the German word meaning "wormwood," which was thought to have powerful medicinal and psychoactive qualities.⁴ *Myroxylon pereirae* is the hapten most commonly positive on patch testing done for reactions to sweet vermouth. The temporal relationship, frequency of exposure to vermouth, and improvement upon withdrawal are highly suggestive of ACS.⁵ Dry (French) and sweet (Italian)

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Figure 2. Nearly complete resolution of lichenoid lesions and erythema on the left buccal mucosa after cessation of sweet vermouth.

varieties of vermouth differ substantially in alcohol and sugar content, as well as color. The sweet variety typically has lower alcohol content, higher sugar content, darker color, and more herb and spice extract compared with the dry variety.⁴ Sweet vermouth is used in many cocktails consumed in the United States.⁴

ZEBRA

Clinicians should be aware of the potential for sweet vermouth to be a causative agent in ACS. Diagnosis of ACS and identification of specific causative agent(s) remain challenging.

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Contact Allergy to Cocamide Diethanolamine and Cross-reactions

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Cocamide DEA (diethanolamine or diethanolamide) (CDEA) and other related compounds appeared together as contact allergens in our patch testing center. Given structural similarities, we consider the possibility of cross-reaction (CR).

When counseling contact allergy patients about allergen avoidance, it is essential to identify chemical CR. For uncommonly tested

allergens, it is especially difficult to identify CR. However, when positive patch test reactions are identified between 2 closely related uncommonly tested allergens, the probability that this would occur by chance is unlikely. It is important that all CRs between less commonly tested allergens are reported.

Cocamide DEA is used as a foam booster in soap and shampoo products.¹ In our center between January 2014 and January 2016, positive patch test reactions were seen in 0.4% of 1128 patients tested to CDEA. Of these 1128 patients, 335 were simultaneously tested with lauramide DEA (LDEA) and cocamide MEA (monoethanolamine) (CMEA). Two of these patients tested 3+ to CDEA and 2+ to LDEA. One of these patients also tested 2+ to CMEA.

Cocamide DEA consists of DEA linked to a mixture of coconut fatty acids of various lengths (between 8 and 18 carbon) including 48.2% lauric acid (12 carbon), 18% myristic acid (14 carbon), 8.5% palmitic acid (16 carbon), 8% caprylic acid (8 carbon), 7% capric acid (10 carbon), 6% oleic acid (18 carbon), and small amounts of stearic and linoleic acids.²

Lauramide DEA consists of lauric acid plus diethanolamine, and therefore CDEA contains 48.2% LDEA. Thus, it is logical that CR would be found between these 2 substances. Cocamide MEA consists of a mixture of coconut fatty acids of various lengths linked to MEA. The cases previously mentioned suggest that individuals allergic to CDEA may cross-react with CMEA and have concomitant reactions with LDEA; however, the low frequency (0.6% and 0.3% of 335 patients, respectively) suggests that this level of CR may not be clinically significant. The low frequency of patients allergic to CDEA who have CRs with LDEA is especially surprising because they are 48.2% homologous. It appears that some patients allergic to CDEA are not allergic to the lauric acid fraction. On the other hand, both patients allergic to LDEA and the 1 patient allergic to CMEA tested positive to CDEA. If future data are comparable, this may indicate unidirectional cross-reactivity.

In a previous study of 25 patients allergic to CDEA, 11 were tested to MEA and DEA. Two of these patients tested positive to DEA and MEA.³ These data suggest that ethanolamines may be the allergens in this subgroup of patients allergic to CDEA. Combined with our reports of CRs among CDEA, LDEA, and CMEA, it is reasonable to consider that CR may occur among all ethanolamines. Future data will be needed to determine whether some or all of these CRs occur frequently enough to be clinically significant.

Our data suggest that patients allergic to CDEA may have CRs with LDEA and CMEA, but these CRs may not be common enough to be clinically relevant. However, it is possible that CR in the opposite direction may be more common, which would indicate unidirectional CR. The lack of data on less commonly tested allergens makes it difficult to assess CRs between them. Patch testing related chemicals that are less commonly tested can provide insight into less common contact allergy cross-reactors.

With more data on this potential CR, we can better counsel patients on allergen avoidance.

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