

CASE REPORT

Patch testing a patient with allergic contact hand dermatitis who is taking infliximab

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We report the case of a patient who developed allergic contact hand dermatitis while receiving infliximab infusions for psoriasis and psoriatic arthritis. Patch testing showed multiple positive allergens. To our knowledge, this is the first case report of successful patch testing in a patient receiving tumor necrosis factor- α (TNF- α) blockade therapy. TNF- α blockers do not necessarily suppress allergic contact hypersensitivity and are not an absolute contraindication to patch testing. (J Am Acad Dermatol 10.1016/j.jaad.2008.02.016.)

A 51-year-old man presented with an 8-month history of dry, cracked, itchy hands. His dermatologic history was also significant for psoriasis and psoriatic arthritis since age 22. His psoriatic disease had been well controlled since 2001, when his rheumatologist instituted infliximab infusions (5 mg/kg) every 7 weeks. He had no history of hand dermatitis or breakthrough psoriasis until his current problem started 8 months before presentation.

His medications included infliximab, atenolol, and ibuprofen as needed. The patient worked at Gillette as a tool and die maker. His occupation involved exposure to coolants, metals, and oils. After his hand dermatitis began, he wore nitrile rubber gloves at work. He felt that his gloves offered only partial protection, and fluids would often get inside. He suffered significant distress due to pain, inability to work, and difficulty using his hands in everyday activities. The patient stopped working 2 months before presentation because of the severity of his condition. His hands improved while away from work, but he did not experience a complete resolution of his dermatitis.

At presentation, the patient appeared to be well. The bilateral hands showed marked erythema, edema, desquamation, crusting, and fissures. There were no pustules or typical psoriatic scales. His nails were normal and he had no swollen joints. Findings of a 4-mm punch biopsy of the right hand were more consistent with lichen simplex chronicus than with active psoriasis as the specimen showed psoriasiform epidermal hyperplasia with hypergranulosis and compact hyperkeratosis/parakeratosis as well as dermal fibrosis and vascular dilatation with mild perivascular mononuclear cell infiltrates.

Given the patient's biopsy results and occupational history, allergic contact dermatitis was considered a likely cause of his hand dermatitis and patch testing was recommended. He was treated with betamethasone dipropionate 0.05% ointment twice daily, with occlusion under white cotton gloves each night. Vinyl gloves with white cotton liners were recommended for work, rather than nitrile rubber gloves. Recommendations were made for hypoallergenic personal care products, including soap, emollients, shampoo, and laundry detergent.

The patient presented for patch testing 3 weeks after receiving his last infusion of infliximab. He was tested to a modified North American Contact Dermatitis Group standard series, fragrance, preservative, metals, coolants, and rubber series (all allergens from Chemotechnique Diagnostics, Ontario, Canada) using Finn Chambers on Scanpore tape (Allerderm, Phoenix, Ariz). The patches were removed at 48 hours and readings were performed at 48 and 72 hours.

Blistering (3+) reactions to the following were observed: carba mix, thiuram mix, tetramethylthiuram disulfide, tetramethylthiuram monosulfide, tetraethylthiuram disulfide, zinc diethylthiocarbamate.

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The patient also showed strong (2+) reactions to the following: lanolin alcohol, bacitracin, nickel sulfate, formaldehyde, ethylenediamine dihydrochloride, dipentamethylenethiuram disulfide, and BIOBAN CS-1135.

Weak (1+) reactions were seen to the following: Amerchol L 101, paraben mix, fragrance mix, benzalkonium chloride, benzophenone-3, neomycin, potassium chromate, cobalt chloride, diazolidinyl urea, DMDM hydantoin, imidazolidinyl urea, and BIOBAN CS-1246.

The patient was given suggestions for skin care products without his proven allergens. He was also given information for a polyethylene liner glove (Barrier. Ansell Occupational Healthcare, Coshocton, Ohio) and an overglove suitable for exposure to his work chemicals in consultation with a specialist at Ansell Occupational Healthcare.

The patient has not returned for a follow-up appointment. However, over the telephone, he reports that he is significantly improved by using the recommended gloves. He says that if he ever accidentally gets coolants on his hands, itching and dermatitis develop several hours later.

DISCUSSION

Infliximab is a chimeric mouse-human monoclonal antibody that inhibits TNF- α . Other TNF- α inhibitors include adalimumab and etanercept. TNF is involved in delayed-type hypersensitivity, the type of immune reaction involved in allergic contact dermatitis.¹

In mice deficient in TNF- α , there is an impaired contact hypersensitivity reaction and reduced production of vascular endothelial growth factor.² In a mouse model, interferon gamma (IFN- γ), TNF- α , and IFN- γ -inducible protein 10 mRNA were expressed after challenge of the antigen in urushiol-sensitized mice, but not in unsensitized mice.³ IFN- γ knockout mice and TNF- α knockout mice failed to elicit contact hypersensitivity with urushiol.

In one study, genetically susceptible mice exposed to ultraviolet B radiation had impaired induction of contact hypersensitivity.⁴ Contact hypersensitivity was restored upon adding anti-TNF- α antibodies, which the authors determined is mediated via the TNF-receptor 2. Therefore, while TNF- α is part of delayed-type hypersensitivity, it may also be involved in suppressing certain types of contact hypersensitivity.

In a study by Anveden et al⁵ who did a multicenter, randomized, double-blind, crossover study on patients with contact allergy to nickel, it was observed that the total number of positive nickel

patch-test reactions for patients taking prednisone, 20 mg, was significantly lower than patients receiving placebo treatment. However, those patients tested with nickel sulfate 5% while taking 20-mg prednisone still maintained 75% as many reactions as the placebo group.⁵ It has also been shown, in vitro, that costimulatory effects of interleukin 2 and CD28 can abrogate the suppressive action of dexamethasone on T-cell proliferation.⁶

As targeted biologic therapies become more prevalent, it is unclear what effect they have in altering the results of patch testing, if any. Recently, a patient taking etanercept was reported to develop contact dermatitis due to urushiol exposure.⁷

Our patient showed strong or extreme reactions to multiple allergens. Many of the patient's reactions confirmed each other and made an "angry back" syndrome unlikely. Specifically, he reacted to rubber mixtures, carba and thiuram mix as well as individual constituents of these mixes (zinc diethyldithiocarbamate, tetramethylthiuram disulfide, tetramethylthiuram monosulfide, tetraethylthiuram disulfide, dipentamethylenethiuram disulfide). He reacted to formaldehyde and formaldehyde releasers, diazolidinyl urea, DMDM hydantoin, and imidazolidinyl urea. He reacted to lanolin alcohol and a trade name product for alcohol, Amerchol L. He reacted to bacitracin and its co-reactor, neomycin. He reacted to the cooling fluid preservative, BIOBAN CS-1246 (4, 4 dimethyl oxazolidine), which is a component of BIOBAN CS-1135, to which he also reacted. His allergens were believed to be clinically relevant, given his work exposures.

His hand dermatitis had been so severe because he was allergic to rubber additives in the nitrile gloves he had initially worn to protect his hands (thiurams and carbamates). In addition, he had become sensitized to multiple preservatives (parabens, formaldehyde, benzalkonium chloride, BIOBAN CS-1135 and -1246), some of which could be used in coolants at work and in personal care products at home. This explains why he did not improve completely while away from work. He additionally showed reactions to chemicals potentially present in vinyl or plastic gloves (ethylenediamine and formaldehyde). These were likely contributing to the recalcitrant nature of his rash even after switching from nitrile to vinyl gloves.

One could hypothesize that the dose per unit area of allergens used for patch testing is high enough to abrogate the immunosuppressive effects of infliximab in a sensitized individual and will exceed the threshold necessary to generate a delayed-type hypersensitivity response.

Our case shows that patch testing reactions can be elicited in patients taking TNF- α blockers; however, the exact effects of TNF- α blockade on delayed-type hypersensitivity remains unknown. Certainly in an ideal setting, if patch-testing a patient taking infliximab is necessary, it is best to try to schedule testing the week before the next scheduled infliximab infusion, so as to minimize the possible suppressive effects from the medication. However, often there are work and scheduling constraints on both patients and physicians. Recent infliximab infusion is not an absolute contraindication for patch testing. Clearly more studies are needed to delineate the exact role of TNF- α and TNF- α blockers in allergic contact dermatitis.

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