

Occupational Airborne Allergic Contact Dermatitis to Olanzapine

To the Editor:

Occupational allergic contact dermatitis (ACD) due to drugs is long known, and there are several cases reported in the literature. In this setting, drug exposure occurs usually by epidermal application or inhalation (nebulization or dust exposure), leading to a high risk of sensitization.¹ Professionals at major risk are those working for chemical or pharmaceutical companies, who participate in the drug manufacturing. The potential exposure can occur during the drug synthesis, packaging, or loading of the final product. Also at risk are technicians or cleaning employees and professionals who deal with the drugs in the therapeutic field.

Sensitization may occur to precursors, intermediate components, and final products and also to other agents used during the synthesis process, such as accelerators, enzymes, catalysts, fillers, and stabilizers, because all of these substances can act as allergens. The diagnosis of these skin conditions is occasionally difficult because it requires collaboration with the pharmaceutical company to provide the necessary information regarding the drug manufacturing process and the diluted chemical compounds for patch testing.²

We present a pharmacist who developed an airborne ACD because of a drug in the occupational setting.

It was a 43-year-old man, with pre-existing history of atopy and chronic hand eczema for 20 years, who attended to our department complaining of 1-year history of sporadic episodes of periorbital edema along with severe itching (Fig. 1). He worked as a pharmacist, preparing drugs for an important pharmaceutical company, namely, olanzapine, raloxifene, and tadalafil. He stated that his skin lesions subsided spontaneously in 3 days of leaving his work place, without requiring treatment. In addition, he associated the episodes when preparing olanzapine. A total of 15 employees worked preparing the same drugs, and no one else presented skin complaints.

The patient was patch tested with the Spanish Contact Dermatitis Society baseline series (True Test®, Mekos Laboratories, Hillerød, Denmark, and Chemotechnique Diagnostics®,



Figure 1. Edema affecting the eyelids.



Figure 2. Patch tests with positive reactions to olanzapine 1% and 5%.

Vellinge, Sweden), and with olanzapine, raloxifene, and tadalafil in petrolatum at 1% and 5%. Allergens were applied using Curatest® (Lohmann and Rauscher, Rengsdorf, Germany). Readings at day 2 and day 4 showed positive reactions to olanzapine at both concentrations, more intense at 5% dilution (Fig. 2). Patch tests in 10 healthy controls with olanzapine at 1% were all negative.

Occupational ACD to olanzapine was diagnosed, and changing work place resulted in symptomatic improvement.

Exposure to drugs in the occupational setting can originate skin reactions with different clinical patterns, such as irritant or ACD, airborne, dermatitis, photo-induced reactions, contact urticaria, or other dermatologic conditions.³ It can also trigger respiratory symptoms. There are several reports in the literature of occupational contact allergy to drugs but few to antipsychotic agents.

Olanzapine, a thienobenzodiazepine, is an atypical antipsychotic agent that is Food and Drug Administration–approved for the treatment of schizophrenia and other psychotic disorders and bipolar syndrome. Off-label uses include its uses for anxiety, eating disorders, and depression.

Safety data sheets include potential of contact allergy, but so far, there are only 3 cases of occupational sensitization to olanzapine reported in the literature.^{4,5} All of those patients presented with episodes of facial and hand lesions when preparing olanzapine, and the misuse of the personal protective equipment was considered determinant to the sensitization. In our case, the patient had similar lesions and reported to use an individual, nonshared sealed air-fed mask and latex gloves during all steps of the drug manufacture and taking them off, but not always, in a different building facility. The point of drug exposure was possibly when dumping and mixing olanzapine with the other drug components because it remained in the environment because of a poor ventilation system. Potential exposure at other different stages of the drug fabrication could not be

ruled out. This justifies the airborne mechanism of the ACD in the present case and in the other case reports of the literature.

The present case emphasizes the role of olanzapine in the development of occupational contact dermatitis, even when using appropriate personal protective equipment. In this situation, it is major to educate employees in following proper protective measures in their workplace. In addition, it is recommended to inspect the local facilities of the patient's workplace to ensure that these measures are pursued. When sensitization occurs, avoidance of the allergen is fundamental for the resolution of the skin condition. In more serious cases, it is necessary to provide the patient a job relocation or even changing profession.

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Effects of Immunomodulatory Agents on Patch Testing: Expert Opinion 2012

To the Editor:

Experience over the last century or so has suggested that patch testing (PT) is best performed on the back in individuals who are currently free of dermatitis and who are not taking any medications or treatments that may reduce cutaneous immunoresponsiveness. In practice, however, we are sometimes called upon to perform PT on patients who need systemic immunomodulating medications for control of their skin disease or for a variety of other conditions such as prevention

of transplant rejection, treatment of autoimmune disease, treatment of malignancy, and so on. Although small case surveys have been published, except for systemic corticosteroids, there is little concrete data on the likelihood of having false-negative PT results in patients who may be immunosuppressed. The members of the North American Contact Dermatitis Group (NACDG) collectively have significant PT experience and are often asked to render opinions on this matter. The NACDG is undertaking a prospective survey to attempt to shed more light on this question.

The members were asked the following questions:

1. What is the minimum withdrawal time before PT for (a) topical corticosteroid or calcineurin exposure to the test site, (b) natural or artificial UV light, (c) systemic corticosteroid (prednisone) intake, and (d) intramuscular corticosteroid (triamcinolone acetate)?
2. What is the highest dose of prednisone acceptable during PT to minimize the chance of false-negative results?
3. Which of the following drugs are likely to impair PT responsiveness: methotrexate, azathioprine, mycophenolate mofetil, cyclosporine (CSA), tacrolimus, tumor necrosis factor α (TNF- α) inhibitors (etanercept, adalimumab, infliximab, golimumab, etc), and ustekinumab?

RESULTS

TABLE 1. Results of Poll of NACDG Members Regarding Effects of Various Agents on PT Reactions

Agent	Range of Recommendations	Consensus Opinion
Topical corticoids on test site	Avoid for 3–7 d	Evenly split between 3 and 7 d
UV exposure at test site	Avoid for 0 d to 2 wk	Avoid for 1 wk
Oral prednisone—maximum dosage	OK to test on 10–20 mg/d	OK to test on 10 mg, but best if able to DC
Oral prednisone withdrawal time	Avoid for 1–14 d	Avoid for 3–5 d
40 mg IM triamcinolone	Wait between 3 and 4 wk	Wait until 4 wk after injection
Methotrexate	Unknown to little/no effect	Little to no effect
TNF- α inhibitors	Unknown to little/no effect	Little to no effect
Ustekinumab	Unknown to little/no effect	Little to no effect
Azathioprine	Dose-dependent inhibition	Dose-dependent inhibition
Cyclosporine	Dose-dependent inhibition	Dose-dependent inhibition
Mycophenolate mofetil	Dose-dependent inhibition	Dose-dependent inhibition
Tacrolimus(systemic?)	Dose-dependent inhibition	Dose-dependent inhibition

DC indicates discontinue; IM, intramuscular; UV, ultraviolet.

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