

Contact sensitization to metronidazole from possible occupational exposure

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Jakob Torp Madsen, Henrik Frank Lorentzen and Evy Paulsen

Department of Dermatology, Odense University Hospital, University of Southern Denmark, Sdr. Boulevard 29, DK-5000 Odense, Denmark

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Contact dermatitis to topically applied metronidazole is a rare side effect, especially considering the large number of patients using it on a daily basis. We report two cases of possible occupational sensitization.

Case 1

A 67-year-old female community nurse was referred with rosacea. She had no history of allergy but had a long history of basal cell carcinoma

caused by insufficient protection when working with X-rays when she was young. After 2 days of treatment with topically applied Rozex[®] cream (Galderma Nordic AB, Bromma, Sweden), she developed a weeping, vesicular, and erythematous facial dermatitis. The metronidazole cream was discontinued, and she was treated with systemic tetracycline.

Prior to patch testing, the patient made a use test by applying Rozex cream on the volar aspect of her wrist. There was a positive reaction within 1 day and persisted for more than 1 month.

Diagnostic patch testing with the Rozex cream 0.75% (Galderma Nordic AB, preserved with benzyl alcohol) 'as is' and metronidazole 5% in pet. (Central Pharmacy of Odense University Hospital) showed a +++/++ reaction on D3 (Fig. 1) and +/+++ on D7. Testing with the European baseline series elicited positive reactions to thimerosal, epoxy resin, methyldibromo glutaronitrile, and methylchloroisothiazolinone and methylisothiazolinone (MCI/MI) (+++ D3 and ++ D7) without any known relevance. The patient had been working for many years as a community nurse handling metronidazole tablets for patients. She had been treated with metronidazole (in a pessary) once without any adverse effects.

Case 2

A 40-year-old nurse whose history was previously published in a series of three cases of metronidazole contact allergy (1) was referred with rosacea and developed facial dermatitis with erythema, swelling, and itching after a few days of treatment with metronidazole cream (Alpharma, Gentofte, Denmark). Use tests with metronidazole cream (1% metronidazole) and Rozex gel (0.75% metronidazole) showed acute vesicular dermatitis after six applications on D3. Diagnostic patch testing with the European baseline series, selected ingredients, the metronidazole cream, and metronidazole 5% pet. showed positive reactions to the Rozex cream (++) at D3 and a weaker response to metronidazole 5% pet. (+) at D3 and to metronidazole 5% in pet. (+) at D7.

The patient had been working for years in a gastroenterology department and handled metronidazole as a parenteral medicine and tablets. She had taken metronidazole tablets

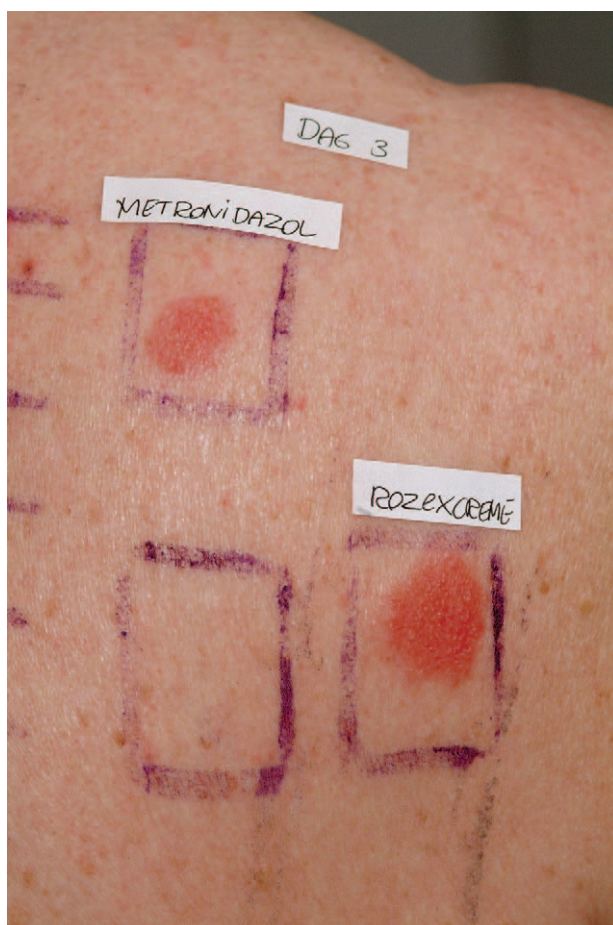


Fig. 1. Positive patch test with Rozex[®] cream 0.75% (Galderma Nordic AB) and metronidazole 5% in pet. on D3 in a 67 years old former community nurse with possible occupational sensitization.

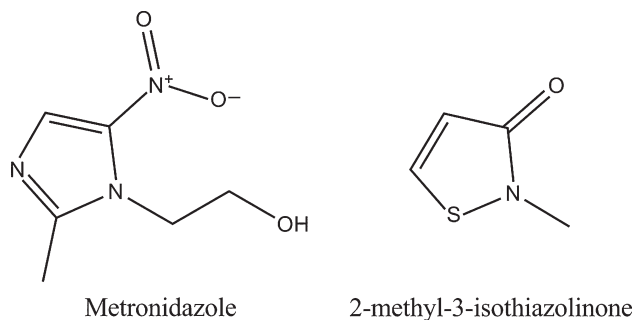


Fig. 2. Molecular structure of metronidazole and methylisothiazolinone.

herself several times without any adverse reactions.

Discussion

The rapid onset of the facial dermatitis after topically applied metronidazole cream in both patients suggests a previous sensitization most likely from an occupational exposure due to less stringent protective measures in nurses in the past. Only six cases of contact dermatitis to topically

applied metronidazole have been published (1–4). All were women aged 26–68 years old. Unfortunately, we do not know their occupation or the time from the first topical metronidazole application to development of facial dermatitis except in one case in whom the facial contact dermatitis developed after only 1 day of metronidazole use (4). This patient also reacted to a mixture of MCI/MI and was suspected to have a cross-reaction between metronidazole and

MCI/MI, believed to be caused by the similarity of the molecular structures of these substances (Fig. 2). MCI/MI was suggested as the primary sensitizer due to the fact that the patient reacted after 1 day of metronidazole use and, therefore, could not be sensitized from that substance (4). In case 1, concomitant patch test positivity to MCI/MI and metronidazole was also found. Whether the primary sensitizer is MCI/MI or the patient was sensitized to both substances on separate occasions is impossible to clarify. However, if the cross-reactivity indeed exists, it is not a reciprocal reaction because our patient in case 2 tested negative to MCI/MI.

As disposable gloves are nowadays used on a routine basis, we do not expect to see many more cases in nurses in the future.

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Address:

Jakob Torp Madsen
Department of Dermatology
Odense Universitetshospital
University of Southern Denmark
Sdr. Boulevard 29
DK-5000 Odense
Denmark
Tel: +4565413239
Fax: +4566123819
e-mail: jakobtorp@dadlnet.dk