Allergic contact dermatitis to topical metronidazole – 3 cases

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Jakob Torp Madsen[1], Jens Thormann[2], Stefan Kerre[3], Klaus E. Andersen[1] and An Goossens[4]

[1]Department of Dermatology, Odense University Hospital, University of Southern Denmark, Odense, Denmark, [2]Skin Clinic, Vejle, Denmark, [3]Skin Clinic, Aarschot, Belgium, and [4]Department of Dermatology, University Hospital, K.U. Leuven, Belgium

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Contact dermatitis to topically applied metronidazole is a rare side effect. We report 3 cases in this study.

Case I

A 40-year-old woman with acne rosacea and no previous history of allergy or skin diseases developed facial dermatitis with erythema, swelling and itching, after a few days of treatment with metronidazole cream (Alpharma® Copenhagen, Denmark). The patient is a hospital nurse and had administered metronidazole systemically to patients for many years, and had been treating herself with metronidazole tablets without any adverse reactions. The topical metronidazole treatment was discontinued and rosacea was treated successfully with systemic erythromycin and a short course of topical hydrocortisone cream. A use test on forearm skin with metronidazole cream (1% metronidazole; Alpharma®) and Rozex® gel (0.75% metronidazole; Laboratoires Galderma, Alby-sur-Chéran, France) showed acute vesicular dermatitis after 6 applications on D3 (Fig. 1). Diagnostic patch testing with the European standard series, selected ingredients, the metronidazole cream and metronidazole 5% pet. showed positive reactions only to the metronidazole cream (++) and a weaker response to metronidazole 5% pet. (+).

Case II

A 47-year-old atopic woman developed an infected weeping dermatitis on her chin and both cheeks, with the spreading of erythematous papules on the neck, following the application of Rozex® gel (Galderma® Belgilux N. V., Bornem, Belgium). The gel was applied to treat an acne rosacea she had developed a few weeks earlier. It was primarily treated with topical corticosteroids and systemic minocycline (100 mg/day). She had already been patch tested twice because of eczema on the face, hands and feet and had tested positive to potassium dichromate and cobalt chloride (found to be relevant for shoe dermatitis), formaldehyde, paraphenylenediamine, benzocaine, and diaminodiphenylmethane, as well as to wool alcohols (relevant to the lipstick and a facial cream she had used). Patch tests were performed with the patient's own products which showed a positive reaction (+ on D2 and ++ on D3) to Rozex gel® and to its ingredient, metronidazole 2% in pet. (+? on D2 and ++ on D4). The patient's lesions quickly healed upon application of a local corticosteroid and she was referred for laser therapy for treatment of her acne rosacea.

Case III

A 57-year-old woman developed facial dermatitis that had been present for about 2 years. Previous therapy had consisted of topical application of metronidazole 2% in cetomacrogol cream (cetostearylalcohol 7.2 g, cetomacrogol 1000 1.8 g, white pet. 15 g, liquid paraffin 6 g, potassiumsorbate 0.27 g, a buffer containing sodium dihydrogen phosphate dihydrate 0.30 g, diluted with phosphoric acid, and water added up to 100 g), associated with minocycline 100 mg/day (Klinotab®, Wyeth Lederle and AHP Pharma®, Louvain-La-Neuve, Belgium). As the lesions had not healed, Fucicort® cream (Leo Pharmaceutical Products®, Wilrijk, Belgium), containing both fusidic acid and betamethasone valerate as the active components, was continuously applied during a 1-year period. According to the patient, the lesions had improved considerably. She had been advised to stop this treatment and to continue with the metronidazole cream. However, this

Fig. 1. Use test showing vesicular reaction to metronidazole Alpharma® cream and Rozex® gel.

resulted in the development of sharply demarcated papular eczema around the nose, upper lip and chin (Fig. 2). Previous patch tests with the standard series, a cosmetic series, as well as several cosmetic products used, did not show any positive reactions except for nickel without any relevance. Another patch test was performed with the standard series as well as with the metronidazole preparation; the latter produced a clear positive reaction (+ on D2 and ++ on D3; Fig. 3). Testing with metronidazole and several azole derivatives, that is, miconazole, econazole, isoconazole, bifonazole, ketoconazole, clotrimazol, and sulconazole, all diluted 2% in pet., showed a positive reaction to metronidazole only (+ on D2 and D4).

Discussion

We have reported 3 cases of allergic contact dermatitis due to topical metronidazole. In the first case, the topical pharmaceutical drugs gave much stronger test reactions than metronidazole 5% pet., both at patch testing and use tests, probably related to better bioavailability from the cream and gel base. Metronidazole used as a topical agent is generally well tolerated, and contact dermatitis to topically applied metronidazole is rare and only two cases have been published previously (1, 2). There have been isolated reports of immediate allergic reactions and urticaria (3–5), fixed drug eruptions (6–13) and acute generalized exanthematous pustulosis (14) due to topical metronidazole. Vincenzi et al. (1) investigated their patient for possible cross reactions to other imidazole derivatives, but did not find any, in accordance with our finding in case III.

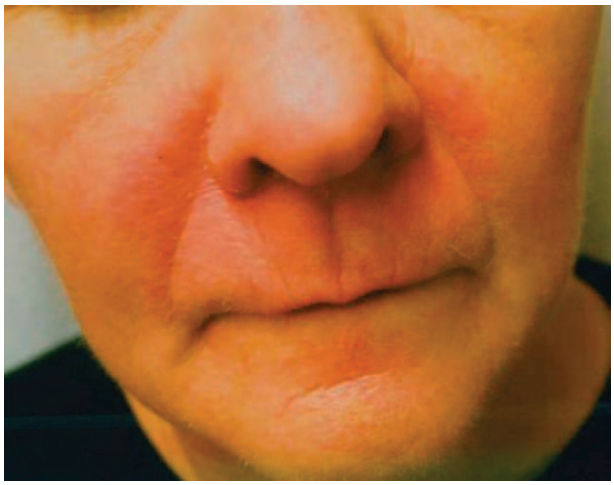

Fig. 2. Facial dermatitis due to metronidazole cream.

Fig. 3. Patch test reaction to metronidazole.

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Address:
Jakob Torp Madsen
Department of Dermatology
Odense Universitetshospital
Sdr. Boulevard 29, DK-5000 Odense
Denmark
Tel: +45 6541 2700
Fax: +45 6612 3819
e-mail: jakobtorp@dadlnet.dk