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Allergic contact dermatitis to shoes induced by dimethylfumarate: A new allergen imported from China

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Abstract

Background: In the last two years several cases of severe contact dermatitis related to newly acquired sofas and armchairs originating from China have been published. The responsible allergen is dimethylfumarate (DMF), an extremely potent sensitizer and irritant found in sachets inside the furniture. Recently, cases of contact dermatitis related to shoes and riding helmets have also been described. **Methods:** We evaluated two patients with allergic contact dermatitis related to shoes manufactured in China that were contaminated by dimethylfumarate found in sachets placed inside the shoeboxes. **Results:** Patch tests with DMF extracted from the sachets inside the shoeboxes showed positive reactions. Postitive reactions were also obtained using small fragments of the shoes and tissue of the ñMouldProofò sachet. The patients were instructed to avoid the suspected shoes and were treated with topical corticosteroids. **Conclusions:** Contact dermatitis induced by dimethylfumarate should be suspected in appropriate cases. It is important to remember that this allergen is not included in most series for patch testing.

Background

In 2007 and 2008 a ñsmall epidemicò emerged in the North of Europe and England. Susitaival [1] and Rantanen [2] illustrated severe cases of contact dermatitis of the back and buttocks that were related to newly acquired sofas and armchairs originating from China. Later, a relationship was established with dimethylfumarate (DMF) after the isolation by chromatography of this allergen placed in sachets inside furniture. Subsequently, this was confirmed by epicutaneous tests when these patients reacted positively to DMF [1, 2, 3, 4, 5].

Other cases have been published in other areas of Europe that were related also to furniture [4, 6, 7] and, more recently, to shoes [8, 9, 10] and riding helmets [11].

Dimethylfumarate is an ester of fumaric acid that is usually commercially available as a crystalline powder or white granules. The chemical is placed in sachets inside furniture or clothes, as well in shoeboxes, which evaporates and impregnates the products, protecting them from mold. It also prevents deterioration during storage and shipping in warm and humid climates [2, 6, 9, 12].

Dimethylfumarate has also been a systemic therapeutic option in moderate to severe psoriasis (Fumaderm® in German) since 1994 [13] and in multiple sclerosis [14].

We describe two cases of allergic contact dermatitis that was induced by DMF presence in shoes and summarize the available information concerning this new allergen.

Case reports

In April and May 2009 we studied two female patients at our Allergology Unit.

Case 1

The first patient, a 19-year-old massage therapist, presented with a bilateral acute dermatitis localized to the dorsal aspects of the feet and ankles, in the area of contact with a new pair of boots.

Lesions appeared on the third occasion that she wore the boots and presented with an intense burning sensation and itching. She was treated with potent topical steroids; when she stopped wearing the boots the lesions slowly regressed with desquamation.

Figure 1

Figure 2

Three weeks later at the time epicutaneous tests were performed, a well-circumscribed dermatitis was present on the dorsal feet (Figure 1). She had bought the leather boots in a non-Chinese shop and they were kept within their shoebox that still contained two types of sachets, 3 designated ñSilica gelò and 5 others designated ñMouldProofò (Figure 2). The latter contained a variable amount of a white powder that corresponded to the descriptions of what we supposed to be DMF.

Case 2

The second patient, a 44-year-old employee in a textile fabrication plant, reported to the emergency department with an acute inflammatory dermatitis on both feet thought to be associated with recently acquired plastic shoes that were bought in a Chinese shop. She could not remember if the shoes were in a box when she bought them.

Although she was treated with systemic and topical steroids, but within 3-4 weeks, she presented with fissured, erythematous-exudative, and pruriginous lesions, predominantly on the toes and adjacent dorsum of the feet, sparing the interdigital spaces and soles. (Figure 3)

Figure 3

Both patients had no previous history of atopy, contact allergy, or other skin diseases.

Methods: Epicutaneous Tests

Epicutaneous tests were applied on the upper back using FinnÊ Chambers on Scanpor tape® (Epitest Ltd Oy) during 2 days using allergens from ChemotechniqueÊ (Malmö, Sweden) or Bial-AristeguiÊ (Oporto, Portugal). Readings were done on day2 (D2) and day3 (D3) according to ICDRGC guidelines.

Patients were tested with the European baseline series (with additions from the Portuguese Contact Dermatitis Study Group) and a shoe series, including chromate, plastic, rubber allergens, glue allergens, some preservatives, and textile dyes.

The white powder extracted from ñMouldProofò sachets (presumed to be DMF) was individually prepared at 0.1 percent petrolatum (pet.) in the first patient and also at 0.001 percent in the second patient. Fragments of shoes were tested ñas is,ò moistened with 0.9 percent saline in both patients. Small fragments of the external tissue of the ñMouldProofò sachets were also tested ñas isò in the first patient.

Results

In the first patient at D2 and D3, positive patch tests were exclusively seen with DMF at 0.1 percent pet. (+++); boot fragment (+) and sachet fragment (+) (Figure 4).

The second patient, at D2

and D3, had exuberant positive results with DMF at 0.1 percent pet. (+++, with an extensive area of eczema on her back) and a bullous reaction to the shoe fragment (+++) (Figures 5 and 6). A month later, testing with a dilution of 0.001 percent of DMF still induced a ++ reaction. This patient also reacted to nickel (+), diazolidinylurea (++) and perfume mix I (+).

Figure 4

Figure 5

Figure 6

In both patients the shoe series was negative.

The patients were instructed to avoid the suspect shoes and a total resolution of the lesions was seen in a few weeks.

Discussion

Topic application of fumaric acid derivatives causes important adverse effects such as irritation, rash, and non-immunologic contact urticaria [10, 15, 16]. Dimethylfumarate was the derivate that presented more irritant properties and was also classified as a moderate contact sensitizer in animal models [14]. Its commercialization as a topical drug was not possible, mainly due to its sensitizing properties. However, fumaric acid esters mainly composed of DMF (Fumaderm®) are being prescribed systemically in Germany [10].

Because of the high risk of irritant reactions and active sensitization, some authors recommend that DMF should be tested at low concentrations [2, 6]. In the Rantanen [2] report, the 3 patients tested had positive reactions to DMF in aqueous solution at 0.01 percent to 0.001 percent (including one patient with positive reactions down to 0.0001%). Our second patient also reacted to a similar concentration of the ñwhite powder,ò presumed to be DMF, in similarly low concentrations. So, Rantanen [1] recommended concentrations of 0.003 percent or 0.005 percent as an upper limit. Another report [7] described a patient with a lichenoid dermatitis localized at the left shoulder with positive tests to fumarate (Fumaderm®) 10 percent pet.; this patient showed an intense reaction (+++). However, it is agreed that more studies are necessary to ascertain the proper concentration of DMF to be used in epicutaneous tests [2, 6].

Similarly to our findings, other investigators have reported positive epicutaneous tests with samples of tissues contaminated by DMF [2, 4, 7], as well as fragments of the sachets called ñMouldproofò [8]. We have not studied the sachets named ñSilica gel,ò but Lamas et al. [12] warned that many sachets named ñSilica gelò contain also significant amounts of DMF.

Since 1998, DMF is not legally available for use in industry. However, there are manufactures outside the European Union that can use this non-authorized biocide and export their products (Directive 98/8/EC). In March of 2009 the European Commission published a communication [17] that banned importation of products contaminated with DMF such as sofas, shoes, and toys (maximum limit of 0.1 mg/Kg). They proposed that contaminated products in the marketplace should be seized; consumers should be informed of the risks.

Rapid Alert System For Dangerous Consumer Products (RAPEX) is an instrument of the European Commission that has proven to be useful in reporting new cases of irritant or allergic contact dermatitis associated with DMF [17].

Conclusion

The knowledge of this newly described contact dermatitis, as well as the responsible cause is essential in clinical practice, as DMF is not included in most series for patch testing.

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