

Generalized Eczematous Dermatitis from Imipenem after Topical Exposure

To the Editor:

A 57-year-old nonatopic woman had a 6-year history of venous insufficiency and associated ulcers of the right leg. For this reason, she had used a considerable number of topical products, obtaining variable results.

Two years earlier, following the advice of a vascular surgeon, her venous leg ulcers had been treated with an aqueous solution containing imipenem-cilastatin (Tienam, Merck Sharp & Dohme[Italia] SpA[in Rome, Italy]) and then covered with an occlusive dressing made of zinc oxide paste bandages. This type of treatment caused a partial healing of the ulcerative lesions on that occasion and was well tolerated. Ten days prior to our visit, because of the re-appearance of an ulcer on the right leg, the surgeon again applied the imipenem-cilastatin solution to the skin lesion and used the same type of dressing as described above, which had to be left on the leg for about 2 weeks. Five days later, the patient developed a pruriginous exanthema that progressively worsened over the subsequent days. No other previous or concomitant treatments were taken by the patient. On examination, the rash was characterized by erythematous vesicular lesions involving the entire body surface (including the scalp and auricles), with accentuation of erythema on skinfolds. There were no mucosal changes and no fever. The dressing was removed from the right leg, where more severe and exudative lesions were seen. Treatment with topical corticosteroids and oral antihistamines led to complete remission of the skin rash within 2 weeks.

The patient was subsequently patch-tested with the Italian Society of Allergologic, Occupational, and Environmental Dermatology standard series and with the Tienam powder (5% in petrolatum [pet]). Patch testing was performed according to the International Contact Dermatitis Research Group's guidelines, and the haptens

were applied to the back for 2 days with Finn Chambers (Epitest Ltd Oy, Tuusula, Finland) on Scanpor tape (Norgesplaster A/S, Vennesla, Norway). Readings were made after 48 hours (D2) and 96 hours (D4). The test results were positive (++) for nickel sulfate and Tienam at both D2 and D4. Therefore, the patient underwent patch testing with imipenem 5% pet and cilastatin 5% pet, along with the following β -lactams: meropenem 5% pet, penicillin G 5% pet, ampicillin 20% pet, amoxicillin 20% pet, and cefaclor 20% pet. Patch testing with imipenem caused a strong reaction (+++) at D2 and D4 whereas all the remaining test results were negative. The result of prick testing with Tienam (1 mg/mL) was negative.

Patients with leg ulcers are particularly prone to becoming sensitized to constituents of the topical treatments used on their skin ulcers. Substances recommended for parenteral use are sometimes improperly applied to the skin, as occurred in the case of our patient with imipenem-cilastatin (Tienam), an antibiotic drug that is available only as a formulation for parenteral administration. Our patient developed an exanthematous skin eruption after the application of a solution containing Tienam to her leg ulcers. The application to ulcerative skin lesions and the concomitant use of an occlusive dressing may have favored the systemic absorption of the sensitizer and consequently the occurrence of a particularly severe and widespread reaction. Alternatively, the development of diffuse lesions may have been the expression of an id reaction.

Contact allergy to carbapenems has rarely been reported.^{1,2} The contact sensitization potential of imipenem was confirmed in a guinea pig model of delayed-type hypersensitivity, which also disclosed a very low cross-reactivity between imipenem-cilastatin and other β -lactams.³ In a study carried out in 73 patients with cell-mediated allergy to β -lactams, patch testing showed that the rate of cross-reactivity between imipenem-cilastatin and other β -lactams was 5.5%.⁴ In the same study, the negative predictive value of patch tests with imipenem-cilastatin was 100% for patients with delayed-type allergy to β -lactams, as patients with negative patch-test reactions to imipenem-cilastatin did not experience any adverse reactions after intramuscular test dosing.⁴

Our patient presented a contact sensitization to imipenem without cross-reactivity to several β -lactams that include meropenem on patch testing, despite the structural similarity of these drugs. There is no detailed

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information about cross-sensitization among the carbapenems although isolated case reports have described the safe use of meropenem in patients with immediate or delayed hypersensitivity to imipenem.^{5,6} However, the negative predictive value of patch tests with meropenem and other β -lactams is not established, because a negative patch-test result with a drug does not exclude the risk of an adverse reaction after the systemic administration of that drug.

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