First Case of Symmetric Drug-Related Intertriginous and Flexural Exanthema Induced by Meropenem

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Symmetric drug-related intertriginous flexural exanthema syndrome (SDRIFE) is a cutaneous reaction that symmetrically affects skin folds and intertriginous areas, without systemic involvement and with a benign prognosis. It has to be related to a systemic drug administration, appearing from one hour to several days from the intake. This type IV hypersensitivity reaction was first described as Baboon syndrome by Andersen *et al*. in 1984 and later named with the acronym of SDRIFE[1,2]. The diagnosis, is based on five clinical criteria: exposure to a systemically administered drug either at the first or repeated dose (excluding contact allergens), sharply demarcated erythema of the gluteal/perianal area and/or V-shaped erythema of the inguinal/perigenital area, involvement of at least one other intertriginous/flexural localization, symmetry of affected areas, and absence of systemic symptoms and signs [2]. Even though SDRIFE induced by β-lactam antibiotics [3], specially aminopenicillins, have been the most frequently reported, no cases related to meropenem have been described to the date.

We report the case of a 36-year-old, non-atopic woman, with morbid obesity and medical history of giant cells tumor in the sacrum with spinal canal affection, treated with radiotherapy and chemotherapy, actually receiving a mensual dose of denosumab with good tolerance who was admitted to the hospital with cellulitis in the left lower limb. At that moment, laboratory findings only showed leukocytosis (13 x 10^9/L) with peripheral neutrophilia (9 x 10^9/L). Antibiotic therapy with meropenem and linezolid was started. On the second day of treatment, several hours after the administration of meropenem, she developed pruriginous erythematous maculopapular lesions on the buttocks and body flexures (neck, armpits, arm flexures, groins and the inframammary area). No other systemic symptoms or signs were observed. The exanthema remitted in a week as a result of removing the meropenem and treatment with dexclorpheniramine and topic corticosteroids. No residual lesions were observed. Subsequently, she tolerated linezolid.

Skin biopsy, from one macular lesion, showed superficial perivascular dermatitis of unspecific characteristics with a lymphocytic perivascular seep limited to the epidermis. Eight weeks later, despite strict recommendations about avoiding β-lactams, she took amoxicillin-clavulanic acid for a week without any adverse reactions.

Once in the Allergy's service, a detailed medical history was compiled and did not show any latex allergy or atopic disease. After signing a written informed consent, epicutaneous tests were performed with penicillin (10%), meropenem, ertapenem and imipenem (5%) with readings at 48 and 96 hours with negative results. Skin prick (SPT) and intradermal tests (IDT) with immediate and delayed readings with benzylpenicilloylocta-L-lysine, benzylpenilloate, penicillin, imipenem, and ertapenem showed negative results. SPT to meropenem (100 mg/ml) was negative whereas IDT to

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meropenem (1 mg/ml) resulted positive at 48 hours reading [Figure]. All skin tests were performed within an area of previously inflamed skin.

Given that our patient gathered the five clinical criteria [2] and the positivity of skin testing to meropenem, the diagnosis of meropenem-induced SDRIFE was established, so carbapenems were forbidden.

The positive result on IDT in delayed reading, as well as histopathological findings, suggest that a type IV hypersensitivity mechanism is implicated as it has been already described [4,5].

In our best knowledge, this is the first case of meropenem-related SDRIFE reported. In addition, it is worth to point out the lack of sensitization to the β-lactam ring, as the patient could tolerate amoxicillin-clavulanic acid.

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Conflicts of interest

IGM: Advisory boards/ speaker/ investigator: Novartis, AstraZeneca, Teva, GSK, Chiesi, Allergy Therapeutics, Leti, Stallergenes, ALK-Abelló, Mundipharma, Pfizer, Orion Pharma.

DBGG, RB, VV and MCDP declare that they have no competing interest.

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Figure: ID to meropenem: positive result at delayed reading