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Erythema Multiforme-like Rash in a Patient Sensitive to Ofloxacin

Eustachio Nettis, Daniela Giordano, Traetta Pierluigi, Antonio Ferrannini and Alfredo Tursi
Department of Medical Clinic, Immunology and Infectious Diseases, Division of Allergy and Clinical Immunology, University of Bari, Piazza Giulio Cesare, IT-70124 Bari, Italy. E-mail e.nettis@allergy.uniba.it
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Sir,

Ofloxacin is a widely used fluorinated quinolone antibiotic that is highly active against a wide spectrum of bacteria. The most commonly described adverse effects with ofloxacin are gastrointestinal disturbances, central nervous system reactions and skin reactions (1). Among cutaneous adverse drug reactions, ofloxacin has been reported as causing fixed drug eruption (2), toxic pustuloderma (3) and hypersensitivity vasculitis (4), but no systemic contact dermatitis. We report here a case of erythema multiforme-like rash in a patient with delayed hypersensitivity to ofloxacin.

CASE REPORT

A 27-year-old man with a personal history of atopy, using topical ofloxacin (Exocin® eye-drops 0.3%) for bacterial conjunctivitis, developed acute eyelid dermatitis associated with hyperaemia and conjunctival chemosis. His lesions improved rapidly with topical corticosteroids and avoidance of the ophthalmic preparation he had used in the past. Four months later, he contracted an infection of the urinary tract and was treated with oral ofloxacin 400 mg/day (Oflocin®). Several hours after taking 200 mg of ofloxacin on the first day of treatment, the patient presented erythema, oedema and exudation of both eyelids and zygomatic regions. Nevertheless, he showed a generalized pruritic maculopapular skin rash, which was successfully treated with steroids and antihistamines.

Two months later, after giving informed consent, the patient was subjected to allergologic *in vivo* tests. Prick tests and intradermal tests with ofloxacin (at 1 and 5 mg/ml in saline) were performed without eliciting any immediate reaction. Twenty-four hours later, the patient exhibited erythema, infiltration and vesicles in the area of the intradermal test. In the zone of the prick test with ofloxacin a papulo-erythematous lesion appeared at 36 h. Subsequently, patch tests were performed with the SIDAPA standard series (Chemotecnique Diagnostics AB, Sweden), Exocin® eye-drops (as is) and its active ingredients, including ofloxacin (5% and 25% pet.) and benzalkonium chloride (0.1% aq.). The patch preparations were applied with Finn Chambers on Scanpor following the International Contact Dermatitis Research Group recommendations. Patch tests were positive at days 2 and 4 for Exocin® as is (+ + +/+ + +), ofloxacin 5% (+/+) and ofloxacin 25% (+ +/+ + +). Prick, intradermal and patch tests with ofloxacin were negative in 15 controls.

The patient was also subjected to a single-blind placebo (talc) and to a controlled peroral challenge test with ofloxacin at gradually increasing doses, reaching a maximal dose of 200 mg. On the first day, 2 placebo capsules were administered, one every 2 h; after 7 days the patient received divided doses of ofloxacin: 50 mg initially and 150 mg 2 h later. The patient developed an erythema multiforme-like rash, localized particularly on the face, about 10 h after the administration of a total dose of 200 mg of ofloxacin. He was successfully treated with systemic corticosteroids and antihistamines.

DISCUSSION

This is the first time that oral administration of ofloxacin is reported to have caused an erythema multiforme-like rash, as a form of systemic contact dermatitis, in a patient with delayed contact hypersensitivity to this drug. Systemic contact dermatitis can appear only in previously contact sensitized subjects when the allergen is introduced systemically (5) and it shows itself with skin signs and often with systemic signs. Skin signs can be various types of reaction: relapse or aggravation of the primitive contact dermatitis or, more rarely, generalized various morphology eruptions. Our patient developed an erythema multiforme-like rash that, unlike classic erythema multiforme, presents neither evident bullous lesions nor mucous membrane involvement.

Allergens responsible for systemic contact dermatitis are especially drugs, but also metals, food additives, formaldehyde and mercury. Although few experimental data are present in the literature, it has been suggested

that systemic contact dermatitis is a delayed, cell-mediated hypersensitivity reaction; some reports have demonstrated the usefulness of a positive patch test in its diagnosis (6). In the present case, this pathogenic mechanism is suggested by clinical findings, delayed skin tests, patch test and challenge positivity with ofloxacin.

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Gabapentin-induced Bullous Pemphigoid

C. O. C. Zachariae
Department of Dermatology, Gentofte Hospital, University of Copenhagen, Niels Andersens Vej 65, DK-2900 Hellerup, Denmark.
E-mail: cz@dadlnet.dk

Sir,

Gabapentin is a new antiepileptic drug that is being used increasingly in the treatment of chronic pain of different origins. It is generally considered a safe agent for patients with a history of allergic reactions (1). In more than 2000 patient exposures, only 2 cases of mild rash developed during preclinical trials in the USA (2). Since approval, only a few cases of rash associated with gabapentin have been reported, among them two cases of gabapentin-induced Stevens-Johnson syndrome (3, 4). We present a case of bullous pemphigoid presumably triggered by gabapentin.

CASE REPORT

A 61-year-old women suffering from epilepsy for 11 years, treated with oxcarbazepine 900 mg twice a day, developed an exanthema and slight hair loss during treatment with lamotrigine. The patient had previously had a rash following rofecoxib. She was given gabapentin because of neurogenic pain in the legs. After 2 weeks of increasing doses she developed an itching maculopapular rash on the abdomen with further spreading to the upper legs and arms. She was treated with betamethasondipropionate supplemented with oral loratadine with moderate effect. After a month, the elements became more nummular and gabapentin was discontinued.

A punch biopsy showed distinct acanthosis and hyperkeratosis along with hydrophic basal cell degeneration within the epidermis, and a perivascular oedema and interstitial cellular infiltration with eosinophils within the papillary dermis.

The patient was then referred to a dermatological department. Treatment with gabapentin was reinstituted in incremental doses of 300 mg as a result of the good clinical response to the neurogenic pains in the legs. After 1 week, an itching erosive bullous eruption developed on the trunk (Fig. 1). Treatment with gabapentin was stopped.

A new punch biopsy showed a subepidermal blister and a perivascular inflammation dominated by eosinophils and a few lymphocytes. Direct immunofluorescence of a perilesional biopsy displayed a distinct deposit of C-3 along the basement-membrane zone. Circulating IgG autoantibodies against the epidermal basementmembrane zone in a dilution of 1:100 were demonstrated by indirect immunofluorescence. Guinea-pig lower lip was used as antigen. The white blood cell count was 15.500 (90% neutrophils). No other abnormalities were found. The patient was treated with prednisolone 15 mg per day in combination with azathioprine

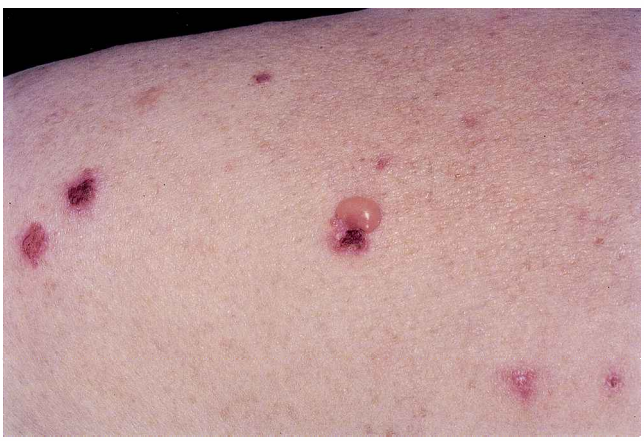

Fig. 1. Bullous eruption on the upper extremity of a 61-year-old woman.