

Local reaction to ocular disodium cromoglycate

A 36-YEAR-OLD man, a bricklayer, was treated for 4 years in our outpatient allergy clinic for grass pollen-induced asthma and rhinoconjunctivitis. His symptoms were controlled with salbutamol, terfenadine, budesonide nasal spray, and disodium cromoglycate (DSCG) ophthalmic solution (Cusicrom Oftálmico Fuerte®). Three days after starting treatment with disodium cromoglycate ophthalmic solution, he experienced an acute exacerbation of his ocular symptoms. It appeared immediately after administration of the eye-drops and was followed by an eczematous lesion on the eyelids some days later. The symptoms improved when the treatment was discontinued and worsened when he resumed the medication. When the patient visited our outpatient clinic, he was challenged with the commercial ophthalmic solution and within 5 min he reacted with intensive conjunctival redness, pruritus, and tearing eyes.

A standard skin prick test was performed with Cusicrom Oftálmico Fuerte (40 mg/ml DSCG, and 0.1% benzalkonium chloride [BAC] as preservative) resulted in a typical flare-and-wheal reaction. Subsequent skin prick tests with serial 10-fold dilutions of BAC were negative, while pure DSCG (Fisons Ibérica, SA) tested in the same fashion yielded a positive reaction with a concentration of 10 mg/ml. Epicutaneous tests were carried out with Cusicrom Oftálmico Fuerte and the European standard series (True-Test, Pharmacia) and with BAC at 0.1%. All of them were negative at 48, 72, and 96 h.

An open conjunctival challenge test was then performed with different dilutions of BAC (0.001, 0.01, and 0.02%) and 7 days later with serial 10-fold dilutions of pure DSCG (0.001, 0.01, 0.1, 1, and 10 mg/ml). Only DSCG at 10 mg/ml yielded a positive challenge test.

Finally, we performed the same SPT and an open conjunctival provocation in 10 atopic patients who had been treated with DSCG previously with negative results.

The total serum IgE of the patient was 578 UI/ml. We tried to detect specific IgE to DSCG with the RAST technique (Pharmacia) by binding the substance to epoxy-activated Sepharose (2), but we could not detect it.

■ For more than two decades, DSCG has been widely used as a treatment of allergic disorders, very few adverse effects being reported. Most of the observed side-effects are mild, often transient, and usually they do not require cessation of therapy. More severe manifestations of adverse reactions appear rarely (6). Thus, DSCG has been reported to cause polymyositis, pericarditis associated with pulmonary infiltrates and eosinophilia, urticaria, and anaphylaxis (1, 4, 7, 8).

Specific IgE to DSCG should be detected *in vivo* in a few cases. In one case, this was detected after passive transfer of the patient's serum to her mother (1) and in three cases by positive skin prick test (4, 5, 8).

In our patient, allergic ocular symptoms worsened immediately after administration of eye-drops. Positive SPT and conjunctival provocation with DSCG support the hypothesis that a type I IgE-mediated hypersensitivity reaction to DSCG was responsible in this case.

In 1988, Wass et al. detected DSCG-specific IgE antibodies in serum from a patient with a systemic immediate hypersensitivity reaction after administration of DSCG eye-drops (8). In our case, *in vitro* techniques failed to detect specific IgE to DSCG.

BAC can cause hypersensitivity reactions when it is used as a preservative in nose-drops (3). However, we excluded the possibility that the symptoms in our patient were caused by BAC.

We were not able to prove that a type IV mechanism was responsible for the development of eczematous lesions on the eyelids of our patient. One plausible explanation is a late-phase response elicited in the wake of repeated exposure to DSCG eye-drops.

In conclusion, we report a case of immediate allergic reaction to DSCG confirmed by positive SPT and conjunctival provocation. Adverse reaction to benzalkonium chloride was excluded.

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Delayed hypersensitivity to penicillin

ADVERSE reactions to penicillin and its derivatives are well known. They affect 0.7–10% of the patients who take these antibiotics. The delayed-type reaction includes allergic contact dermatitis (ACD). This mechanism has also been invoked in maculopapulous exanthema, erythema multiforme-like rash, toxic epidermal necrolysis, pruritus *sine materiae*, and some erythrodermas (1).

Delayed hypersensitivity is often studied by patch test and/or challenge tests. However, immediate hypersensitivity used to be studied by prick tests or intradermal tests.

There are isolated references to patients with drug reactions to β -lactams who present prick or intradermal reactions with delayed onset (2–6).

We report the new case of a patient whose hypersensitivity to β -lactams was shown by prick and intradermal tests with delayed onset.

■ In October 1993, a 49-year-old housewife with personal and familial antecedents of atopy came to our hospital. Twenty-five years before, before treatment with antibiotics, a nurse had performed an intradermal test with penicillin on her. She then developed an erythematous nodule which persisted for a month without leaving a residual lesion.

SPT reactions to β -lactams delayed more than 24 h are rare but clinically relevant.

Nevertheless, she had taken different betalactams at least three times. In the last 8 years, she had had three episodes of generalized, erythematous, and edematous cutaneous lesions coinciding with the administration of, respectively, ampicillin, cefalotone, and kefloridine.

■ Prick tests and intradermal tests were performed with penicilloyl polylysine (PPL), minor determinant mixture (MDM), benzylpenicillin, ampicillin, and amoxicillin. The reading at 15–20 min was negative; 24 h later, some erythematous and warm nodules of firm consistency and vesiculous surface appeared in the area of the intradermal tests with MDM, benzylpenicillin, ampicillin, and amoxicillin. In the zone of the prick tests with benzylpenicillin, amoxicillin, and ampicillin, papuloerythematous lesions with smooth surface appeared at 36 h. The lesions persisted for 3 weeks in the case of the intradermal tests and 6–7 days in the case of prick tests.

We have excluded sensitization to gentamicin, tetracycline, trimetoprim, and sulfamethoxazole by skin test or by simple-blind oral or parenteral challenge.

Epicutaneous tests were done with the GEIDC standard battery, the textile battery, and penicillin G (10 000 and 50 000 UI/g). They were read at 48 and 96 h, according to the recommendation of the International Contact Dermatitis Research Group. They were positive only to penicillin G (48 h: ++; 96 h: ++).

The cutaneous biopsy from the patch test showed an epidermis with acanthosis, papillomatosis, spongiosis, and suprapapillary exocytosis. On the dermis, there was focal edema along with superficial perivascular mix infiltrate composed of eosinophils, lymphocytes, and neutrophils.

The intradermal test biopsy displayed an epidermis with focal spongiosis and minimal acanthosis. The bulk of the lesion consisted of dermal edema with massive infiltration of eosinophils, both interstitial and angiocentric. Moreover, multiple dermal "flame figures" composed of extruded eosinophilic granules aggregated on collagen fibers were found. These characteristic flame figures were partially surrounded by a palisade of histiocytes and a few multinucleated giant cells.

■ Adverse reactions to β -lactams which are associated with immediate hypersensitivity are the most numerous. The delayed hypersensitivity reactions due to these drugs have been invoked in some cases of maculopapulous exanthemas, itchiness without cutaneous lesions, local reactions of prolonged nodular type (2–6), toxic epidermal necrolysis, and all ACD.

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