

Contact urticaria syndrome caused by sulfamethoxazole sodium contained in eye drops

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There have been only a few reports of contact urticaria syndrome (CUS) resulting from an allergic reaction to eye drops that developed into anaphylaxis, although eye drops often cause contact dermatitis. We report an interesting case of CUS caused by sulfamethoxazole sodium in eye drops.

Case Report

A 31-year-old woman was referred to our hospital because she had suffered from two intolerance reactions immediately after applying eye drops. Just after applying the over-the-counter eye drops (Shinganryo®; Hisamitsu Pharmaceutical, Tokyo, Japan) for allergic conjunctivitis for the fourth time, she developed conjunctival congestion, lacrimation, eye pruritus, sneezing, and nasal discharge. Four months later, she applied the same eye drops. Immediately, she developed the same symptoms as before, and also throat swelling, wheezing, dyspnoea, generalized urticaria, and abdominal pain.

To investigate the causative allergen of the anaphylactic reactions, prick tests were performed with the eye drops and their ingredients (Table 1) on the volar forearm according to standard procedures (1). The skin was pricked through the allergen drop with the tip of a prick lancetter (EWO CARE, Gislaved, Sweden), and the responses were read 15 min following application. The response elicited by prick tests was considered to be

Table 1. Results of skin prick test with ingredients of the causative eye drops

Ingredient of the eye drops	Test concentration*	Largest wheal diameter (mm)
Dipotassium glycyrrhizinate	0.25 mg/ml Ns	1
Chlorpheniramine maleate	0.03 mg/ml Ns	0
Aminoethylsulfonic acid	1 mg/ml Ns	1.7
Sulfamethoxazole sodium	4 mg/ml Ns	8.3
L-menthol	0.002 mg/ml Ns	1.4
Glycerin	0.5 mg/ml Ns	2.1
Benzalkonium chloride solution, 50%	0.01 mg/ml Ns	1.3
Polysorbate 80	0.03 mg/ml Ns	0
Monoethanolamine†	–	ND
Disodium edetate hydrate†	–	ND
Hydrochloric acid†	–	ND
Sodium hydroxide†	–	ND
Histamine	10 mg/ml	8.9
Saline	–	3.7

ND, not done; Ns, normal saline.

*The ingredients were used at the concentration in the eye drops.

†Indicates ingredients not tested, because they can induce skin irritation.

positive when the largest diameter of wheal induced by the allergen was ≥ 3 mm. The prick tests with the relevant eye drops and their ingredients were also carried out on 4 control subjects. The prick tests showed positive reactions to the eye drops at a 10-fold dilution and to sulfamethoxazole sodium (Figs. 1 and 2). Furthermore, in basophil activation tests, the sulfamethoxazole extract enhanced basophil CD203c expression (Fig. 2); an assay for quantification of specific IgE was not available. On the basis of these results, the patient was diagnosed with CUS stage 3 caused by sulfamethoxazole sodium in eye

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Fig. 1. The skin reaction in a prick test with sulfamethoxazole.

drops according to the staging proposed by von Krogh and Maibach (2).

Discussion

Four cases of CUS resulting from a reaction to eye drops that developed into anaphylaxis, including the present case, were reported up to April 2016. In 2 Japanese patients, the causative allergens in eye drops were the antibiotics levofloxacin (3) and sulfamethoxazole, whereas those for the other 2 patients reported in other countries were carboxymethylcellulose (4) and hydroxypropyl methylcellulose.

The mechanism of CUS caused by eye drops is currently unknown. In the present case, as the mucosal

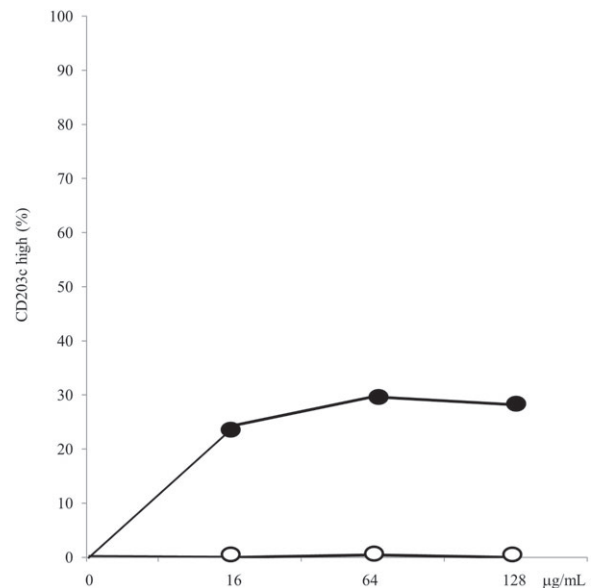


Fig. 2. The results of basophil activation tests (BATs) with sulfamethoxazole. Closed circles indicate BAT results obtained with peripheral blood mononuclear cells (PMBCs) from the patient, and open circles indicate the mean values of BAT results obtained with PMBCs from 3 healthy control subjects without sulfamethoxazole allergy. In BATs using an Allergen Kit (Beckman Coulter, Fullerton, CA, USA), a whole-blood BAT showed 29.7% CD203c-positive cells at a sulfamethoxazole extract concentration of 64 μg/ml, indicating that the sulfamethoxazole extract enhanced basophil CD203c expression. The results of BATs with a positive control (anti-IgE) showed 43.6% and 75.6% CD203c-positive cells in the patient and healthy controls, respectively.

barrier was disrupted because of allergic conjunctivitis, the ingredients in eye drops could easily have caused sensitization via the conjunctival mucosa. In addition, the surfactant in the eye drops might promote barrier perturbation in the conjunctivae.

This case emphasizes the importance of considering all medications, even eye drops, given to patients as possible causes of anaphylactic reactions.

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