

Sensitization from ketotifen fumarate in eye drops presenting as chronic conjunctivitis

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Contact allergy resulting from the use of ophthalmic preparations usually presents as eyelid eczema. However, it can also manifest as conjunctivitis without involvement of the surrounding skin. In the following case report, we provide an example of chronic conjunctivitis resulting from sensitization to an ophthalmic preparation.

Case Report

A 32-year-old woman was referred to our outpatient clinic by her ophthalmologist in March 2016 because of a 3-year history of chronic conjunctivitis. The patient suffered from a burning sensation in the eyes and on the eyelid margins, sometimes accompanied by a feeling of pressure in the eyes; however, she had never experienced eczematous lesions. For the past 1.5 years, there had been a continuous need to use local corticosteroids. When she stopped applying these for 1 week in January 2016, watery eyes and some irritation on the cheeks, most probably caused by tears, were noted. The personal history for atopy was positive in terms of eczema and cow's milk allergy as a baby. Currently, she suffered from hay fever, and was found to be allergic to cats, dogs, and tree pollen.

The patient was using a day cream, no make-up, and perfumes only rarely. She had never experienced any axillary reactions following the use of deodorants, or problems when wearing costume jewellery or other metal accessories. She always wore goggles for swimming. As a teacher, she handled different colours of chalk (white, green, and yellow) on a daily basis, which she suspected of causing the eye symptoms; however, she had never experienced any skin problem on the fingertips;



Fig. 1. Patch test readings (day 4) showing a positive reaction to Altribak® eye drops.



Fig. 2. Positive patch test reactions to ketotifen fumarate 2.5% pet. (top) and 0.7% aq. (bottom) observed on day 4.

moreover, the symptoms were also present when she avoided contact with chalk.

Previous local treatments included eye drops containing dexamethasone and nepafenac, and a non-steroidal anti-inflammatory drug; for systemic therapy, the anti-histamine desloratadine had been used. Currently, the patient was using eye drops containing ketotifen fumarate

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(Altriabak®; Théa Pharma, Wetteren, Belgium), natrium hyaluronate (Visionlux®; Meda Pharma, Brussels, Belgium), and dexamethasone (Monofree Dexamethason®; Théa Pharma). Clinical investigation showed hyperaemic conjunctivae, but no eczema on the eyelids.

Patch tests were performed with the European baseline series, the topical drugs, the patient's day cream, and chalk (the materials provided by the patient were tested 'as is'), by the use of IQ Ultra® chambers (Chemotechnique Diagnostics, Vellinge, Sweden) covered with Mefix® (Mölnlycke Health Care, Göteborg, Sweden). A semi-open test with mascara 'as is' was also performed. Patch tests were read according to the ESCD guideline (1) at day (D) 2 and D4. Positive reactions were observed to nickel (+ on D2; ++ on D4) and cobalt (– on D2; + on D4), but these were not considered to be relevant (a nickel test on the chalks remained negative). Moreover, a positive reaction was observed to the Altriabak® eye drops (– on D2; + on D4) (Fig. 1), which contained ketotifen hydrogen fumarate, glycerol, sodium hydroxide, and purified water. The active ingredient was later kindly provided by the company, and additional patch tests were performed, resulting in positive reactions to ketotifen hydrogen fumarate 2.5% pet. (+ on D2; ++ on D4) and 0.7% aq. (+ on D2 and D4) (Fig. 2). Twenty control subjects did not react to these two ketotifen fumarate preparations.

The patient was advised to avoid contact with the eye drops containing ketotifen, and this resulted in complete clearance of the conjunctivitis. We contacted her again 4 months later, and since she had stopped using the eye drops, she had no longer needed to apply corticosteroids. She occasionally suffered from 'red eyes', which, according to the ophthalmologist, were caused by hay fever, and that were successfully treated with topical disodium-cromoglycate eye drops and desloratadine orally.

Discussion

Ketotifen (hydrogen fumarate) is a second-generation non-competitive H1-antihistamine and mast cell stabilizer. The topical ophthalmic form is mostly used for the prevention and treatment of allergic conjunctivitis, whereas the orally administered drug is used for the prevention and treatment of asthma (2). The literature also describes its effectiveness in the treatment of childhood atopic eczema (3), or as a treatment option for chronic urticaria (4).

Cutaneous side-effects of ketotifen fumarate, apart from occasional dryness of the skin and mouth, have rarely been described (5, 6). Gail et al., when comparing the bioequivalence of two eye drop formulations of this compound, also did not detect any significant cutaneous side-effects (7). However, one case of sensitization resulting from continuous use of ketotifen fumarate-containing eye drops, which only presented as bilateral periorbital erythema with well-circumscribed margins, has been reported (8). Allergic contact dermatitis on the eyelids in association with conjunctivitis following the use of ophthalmic preparations is a common feature (9, 10), whereas conjunctival involvement alone is a rare finding (11). However, this has already been described for other allergens, for example contact lens solutions (12), and also following airborne exposure to acrylic monomers in ultraviolet-cured paint (13) and epoxy resins (14).

Our case report emphasizes that conjunctivitis without involvement of the surrounding skin may indeed be attributable to contact allergy to ophthalmic preparations. In view of the scarcity of published reports, ketotifen fumarate can probably be considered to be a weak sensitizer. The pet. preparation chosen here is suggested for patch testing.

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