

Allergic contact dermatitis in response to ketotifen fumarate contained in eye drops

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Ketotifen (as hydrogen fumarate) is a second-generation non-competitive H1-antihistamine with a strong effect on stabilizing mast cells, and it is available on the market in topical and oral formulations. Besides its anti-histaminic activity, it is also a functional leukotriene antagonist and a phosphodiesterase inhibitor.¹ Nowadays, ketotifen eye drops are available without medical prescription (over-the-counter), and are thus widely used as medication to treat allergic ocular diseases, such as seasonal and perennial allergic conjunctivitis. Rarely, topical ketotifen contained in ophthalmic solutions has been described as sensitizing.²⁻⁵

CASE REPORT

A 69-year-old nonatopic woman presented with eczema on her eyelids associated with itching and burning (Figure 1). The history revealed that the skin lesions had appeared about 1 month after starting a new therapy with Ketoftil eye drops (Farmigee, Pisa, Italy), containing ketotifen fumarate (0.05 mg/mL) and benzalkonium chloride as preservative. Eye drops were prescribed by the general practitioner to treat her seasonal allergic conjunctivitis. The patient denied any previous intake of oral ketotifen. Ketoftil was immediately stopped and dermatitis healed within 2 weeks with mometasone furoate ointment (once daily).

Allergic contact dermatitis was suspected, and 1 month after complete healing, patch tests with the SIDAPA (Società Italiana di Dermatologia Allergologica, Professionale e Ambientale) baseline series (Euromedical, Calolziocorte, LC, Italy) and Ketoftil "as is" were performed. Patch tests were applied on the upper back and occluded for 2 days by the use of the AI Test (Euromedical) on Scanpor Tape (Norgesplaster, Venesla, Norway). Readings were performed on day (D)2, D4, and D7.⁶ On D4, positive reactions with past relevance to methylchloroisothiazolinone/

methylisothiazolinone (++) and methylisothiazolinone (++) and fragrance mix I (++) were observed. Moreover, Ketoftil "as is" was positive (++) on D4. Patch testing with Ketoftil "as is" in 20 healthy subjects was negative. Subsequently, ketotifen hydrogen fumarate (Sigma Aldrich, Milan, Italy) 2.5% pet., as previously suggested,⁵ and benzalkonium chloride (0.1% in saline solution) were patch tested in the patient, with positive result on D4 to ketotifen (++) (Figure 2).

DISCUSSION

We report a case of contact allergy to ketotifen fumarate, a medication available as eye drops with dual activity as antihistamine and mast cell stabilizer. It produces an effect within minutes after administering the drops, with rapid improvement of allergic conjunctivitis symptoms and signs.

The incidence of cutaneous adverse reactions caused by oral ketotifen is very low,^{7,8} apart from sporadic skin and mouth dryness. Among ketotifen hypersensitivity, allergic contact dermatitis caused by ketotifen-containing eye drops is rare, as for ophthalmic products containing other ingredients.⁹ Ketotifen hypersensitivity was described as bilateral erythema with well-circumscribed margins around eyes,² periorbital erythema and edema,⁴ and chronic conjunctivitis without eczematous periorbital lesions.⁵ Most patients are from Japan,^{2,3} probably owing to the more common use of ketotifen eye drops in this country.

However, with ketotifen eye drops being widely used as an over-the-counter medication, we may speculate that the real prevalence of contact allergy to this second-generation H1-antihistamine might be underestimated. Our case highlights that physicians must be aware of this risk and remember the importance of performing patch tests with the patient's own eye drops to avoid a false-negative patch test outcome.



FIGURE 1 Eczematous eruption on the eyelids caused by Ketoftil eye drops



FIGURE 2 Positive patch test to ketotifen 2.5% petrolatum at day 4

CONFLICTS OF INTEREST

All authors have no conflicts of interests to report.

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