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A Subtle Historical Clue Unlocks a Contact Puzzle

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PRECÍS

A case of allergic contact dermatitis to ketotifen-containing eye drops highlights the significance of conjunctivitis evolving into periorbital dermatitis in solidifying the diagnosis.

DISCUSSION

A 61-year-old woman with inflammatory bowel disease and ankylosing spondylitis, treated with infliximab infusions, presented with a several-year history of episodic red eyes and periorbital rash. Three years ago, she underwent patch testing that was reportedly positive for gold and lanolin. The patient continued wearing gold jewelry but avoided wool alcohol products, with resolution of symptoms. However, several weeks before presentation, she again had conjunctival injection and pruritus that progressed to involve the periorbital skin. Repeated oral prednisone tapers resulted in moderate improvement of eye redness only. A month before presentation, she discontinued use of contact lenses, antihistamine eye drops, sunscreen, and cosmetics but continued to use shea butter on the face.

She had seen an ophthalmologist who advised her to avoid gold, discontinue ophthalmic solutions, and apply only petrolatum to the skin. She was then seen at our dermatology clinic, where patch testing was performed with the North American Contact Dermatitis Group 80 series (Chemotechnique) and her personal cosmetic products and eye drops. To minimize the potential of infliximab masking patch test results, we conducted the procedure at a time point most distal to her next infliximab infusion.

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Patch testing revealed a single positive reaction, to Alaway eye drops, which contained ketotifen, benzalkonium chloride, and glycerin. Pertinent negative reactions included lanolin, gold, and benzalkonium chloride, as well as her other ophthalmic products, including contact lens solutions. Since avoiding Alaway eye drops, she has remained symptom-free.

The positive reaction to Alaway eye drops, coupled with a negative reaction to benzalkonium chloride, led us to conclude that ketotifen in the eye drops was the relevant causative agent. The progression of her symptoms from conjunctivitis to periorbital dermatitis plus resolution of the eruption after avoidance of the offending eye drops validates this conclusion. For more definitive patch testing, we requested a sample of ketotifen used by Alaway's manufacturer, but the company refused.

Ketotifen is a recognized contact sensitizer, with 9 previous cases reported. One retrospective review of 49 patients from Japan with documented sensitivity to ophthalmic drops found 8 cases due to products containing ketotifen fumarate, although only 6 confirmed causality with patch testing.¹ Aschenbeck and Warshaw² documented the first case of allergic contact dermatitis due to ketotifen-containing eye drops in North America. Smets et al³ reported a case of isolated conjunctivitis without involvement of surrounding skin due to ketotifen, and Niizeki et al⁴ described a case of bilateral periorbital erythema without eye involvement.

Ketotifen has both antihistaminic and mast cell-stabilizing properties. It is available over-the-counter in topical ophthalmic form in the United States for allergic conjunctivitis, and the oral form is available in a limited number of countries for asthma.⁵ In our patient, previous positive testing to lanolin and gold were historical confounders that delayed correct management, especially because neither gold nor lanolin was a suitable cause of the initial conjunctivitis.

PEARL

Subtle historical clues (eg, conjunctivitis preceding periorbital dermatitis) can assess relevance of patch test–positive allergens. Inclusion of personal products in testing can clinch the diagnosis.

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