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A case of contact dermatitis caused by timolol in anti-glaucoma eyedrops

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The side-effects of eyedrops employed for glaucoma treatment may first manifest after years of use, and can be localized [dermatitis, conjunctivitis (1), and nail pigmentation (2)] or generalized [bullous pemphigoid (3), toxic epidermal necrolysis (4), and anaphylactic reactions (5)].

Case Report

A 70-year-old man with glaucoma was treated with eyedrops containing timolol maleate and brimonidine tartrate for > 2 years. The patient presented with erythematous and oedematous pruritic lesions on both cheeks (Fig. 1a). Patch testing was performed with the Spanish Contact Dermatitis Research Group baseline series (TRUE Test®; Stallergenes Ibérica, Madrid, Spain; Brial Allergens GmbH, Greven, Germany; and Chemotechnique, Vellinge, Sweden), commercial eyedrop formulations containing timolol maleate 0.5% (Timofitol®; Merck Sharp & Dohme, Clermont-Ferrand, France), brimonidine tartrate 0.2% (Alphagan®; Allergan Inc., Irvine, CA, USA), and the patient's own eyedrops containing timolol maleate 0.5% and brimonidine tartrate 0.2% (Combigan®; Allergan Inc.), all 'as is', with Curatest® chambers (Lohmann & Rauscher International GmbH & Co., Rengsdorf, Germany), fixed with Micropore® (3M Health Care, Borken, Germany). All readings were negative at day (D)2 and D4, except for Combigan® (+) and Timofitol® (+) (Fig. 1b).

We contacted the manufacturer (Allergan España SA, Tres Cantos, Madrid, Spain), who provided the active

principles, so we further patch tested the patient with timolol maleate 1% aq. and 2%, 5% and 10% pet., brimonidine tartrate 0.2%, 0.4%, 1% aq., 1% pet., and 10% pet., and benzalconium chloride 0.1% aq. Results were positive for timolol maleate 5% pet. (+) and 10% pet. (+) on D2 and D4. Five patients under follow-up by the Contact Allergy Unit were patch tested as controls with the two preparations yielding positive reactions in our patient, with negative results.

The patient was diagnosed with allergic contact dermatitis caused by timolol maleate and, possibly, irritant dermatitis caused by brimonidine tartrate. Performance of a repeated open application test with brimonidine tartrate and switching to other β -blocker eyedrops were not considered, because of the patient's moderate intellectual disability. Hence, he was prescribed eyedrops containing travoprost, a prostaglandin analogue, which he has since been using for 18 months, with complete resolution of the lesions.

Discussion

Recommendations for timolol patch testing propose a concentration of 0.5–1% aq. (6). In our opinion, which is shared by some authors (7), this should be increased to at least 10% pet. In our patient, only timolol 5% and 10% pet. elicited weak positive reactions (+). Recommendations concerning the patch test concentration for brimonidine tartrate vary. In a recent case, it was tested from 0.2 to 0.0002% pet., with negative results (8), and other authors have tested the commercial preparation as is (9). In our patient, it was tested at 0.2% (the commercial concentration), 0.4% and 1% aq. and pet. and 10% pet. with negative results. Nevertheless, we are inclined to think that this does not fully exclude a possible allergic contact dermatitis.

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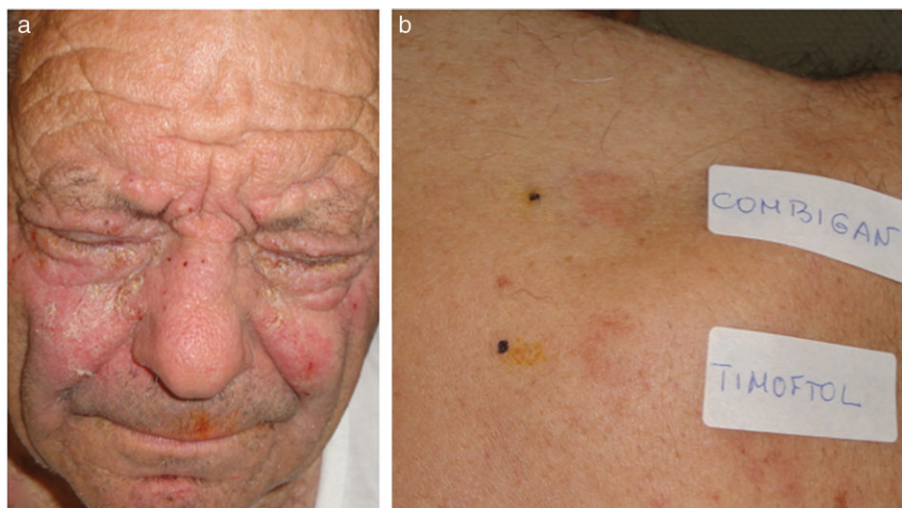


Fig. 1. (a) Erythematous and oedematous plaques on the face with some excoriations and crusting. (b) Weak positive reactions to Combigan® and Timofтол® eyedrops on D4.

Pitfalls in the diagnostic work-up of patients with suspected dermatitis caused by ophthalmic preparations include the lack of standardized allergens, false-negative test results because of lower penetration of allergen into the back, and the lack of reliable information concerning

the most suitable concentration and vehicle for each allergen. In the case of commercial preparations with more than one active principle, patch testing with eyedrops with a single active principle is a pragmatic approach and has proven very helpful.

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