

Allergic contact dermatitis due to ripasudil in eye drops

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Case Report

A 60-year-old Japanese woman with glaucoma was treated using Glanatec[®] (ripasudil 0.4%; Kowa, Tokyo, Japan) eye drops 5 months prior to presentation. One month later, she developed itchy erythema on her eyelids (Fig. 1A). The lesions resolved upon discontinuation of Glanatec[®] and topical corticosteroid treatment.

As allergic contact dermatitis was suspected, patch tests (with and without tape stripping) were performed with Glanatec[®] (as is) 2 months after its discontinuation. For patch testing, Finn Chambers[®] on Scanpor[®] 8 mm (SmartPractice, Phoenix, AZ) was used and the occlusion time was 2 days. Readings were performed on days (D) 2, 3, and 7 according to ICDRG guidelines. As erythema was also observed on the non-chamber area, skin irritation due to sweat was unable to be excluded and it was difficult to judge potential positivity to Glanatec[®]. However, on D3, flare-up phenomenon, i.e. a relapse of the periocular dermatitis, developed (Fig. 1B). Moreover, 5 weeks later, when the patient re-used Glanatec[®] only in the right eye, she again developed itchy erythema on that side the day after (Fig. 1C). Therefore, contact allergy to (a component of) Glanatec[®] was suspected, and patch tests (with and without tape stripping) were performed for the eye drops and their components 3 months later. Positive reactions (+) to Glanatec[®] and ripasudil (10% pet., 1% pet.) were noted, whereas the other ingredients (benzalkonium chloride 0.01% and 0.1% aq., glycerin 1% and 10% aq., and anhydrous sodium dihydrogen phosphate 1% aq.) yielded negative reactions (Fig. 1D). No reactions to ripasudil were observed in the 3 healthy control subjects, consistent with the previous report.¹⁾ The patient was thus diagnosed with allergic contact dermatitis due to ripasudil and she remained free of symptoms by avoiding contact with the eye drops.

Discussion

Ripasudil, a Rho-associated protein kinase (ROCK) inhibitor, is the active ingredient of Glanatec[®], which is used to treat glaucoma worldwide. One other case of allergic contact dermatitis caused by this drug was previously reported .¹⁾

To the best of our knowledge, this is the first reported case of flare-up phenomenon during the patch testing of eye drops. The possible mechanisms of such flare-up reactions depend either on persisting local allergen or T-cell retention at the skin sites.²⁾ Allergen-specific T-cells may persist for several months or longer in the skin, and they may be activated by allergen entry from the systemic circulation. On the other hand, allergen retention in loco is considered not to exceed 2 weeks. In our case, the flare-up reaction was probably caused by T-cell retention at the involved skin sites. ROCK inhibitors also induce vasorelaxation and this may have facilitated allergen (ripasudil) penetration from the skin into the circulation, being further promoted by tape stripping and occlusion during the patch procedure.³⁾

Although the initial patch test reaction to Glanatec[®] was difficult to evaluate, the flare-up phenomenon, use test, and repeated patch test enabled us to confirm the diagnosis.

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Figure Legend

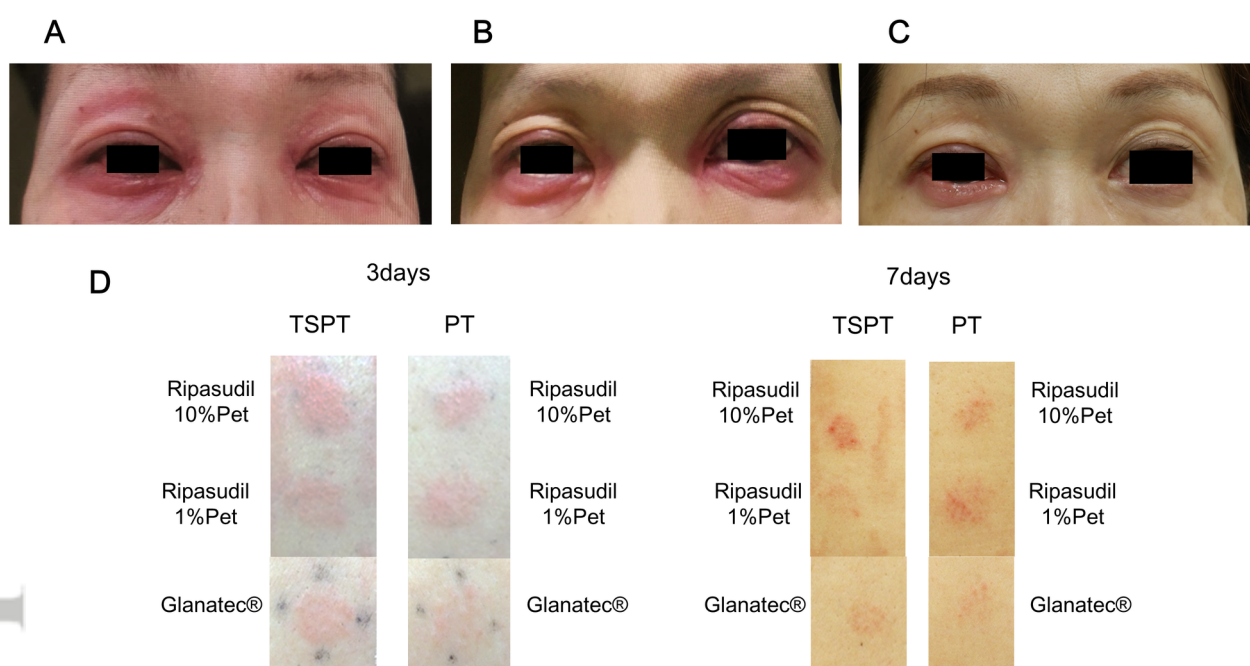
Fig 1.

A. Clinical findings of the patient's eyelids one month after starting the use of Glanatec® eye drops.

B. Flare-up phenomenon observed on the 3rd day after initial patch testing.

C. Clinical findings of the patient's eyelids when she re-applied Glanatec® only in the right eye.

D. Patch test reactions to ripasudil 10% pet. (upper), 1% pet. (middle), and Glanatec® 'as is' (lower) on days (D) 3 and 7. TSPT; tape stripping patch test, PT; patch test.



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