

LETTER TO THE EDITOR

Case of phenylephrine hydrochloride-induced periorbital contact dermatitis with fulminant keratoconjunctivitis causing pseudomembrane formation

Dear Editor,

Phenylephrine, a selective α_1 -adrenergic receptor agonist, which is used as an ophthalmic solution for mydriasis inspection and treatment of uveitis, is a well-known contact allergen,¹ however, inflammation is usually limited to the skin. Herein, we report a previously unreported unusual case of phenylephrine hydrochloride (PH)-induced periorbital contact dermatitis with severe conjunctival involvement including ocular pseudomembrane formation. This study alerts readers that acute pseudomembrane formation is not limited to Stevens–Johnson syndrome² and ocular mucous membrane pemphigoid.

A 51-year-old Japanese woman with severe blepharitis was referred to our institute. She had been treated for uveitis with various ophthalmic solutions. Twelve days after the treatment with 0.5% PH solution (Mydrin-P[®]; Santen Pharmaceutical, Osaka, Japan) was initiated, an intense burning sensation in and around the eyes appeared and lasted for more than 18 days. Her medical history was not remarkable, except for vitiligo vulgaris.

On physical examination, well-demarcated erythemas on the periorbital areas and severe swelling with erosions on both eyelids were noted (Fig. 1a). Ophthalmological examination

revealed extensive conjunctival injection, pseudomembrane formation and symblepharon (Fig. 1b). Immunochromatography testing for adenovirus conjunctivitis was negative. Laboratory examinations were grossly within normal limits.

Histopathological investigation of the eyelid skin detected spongiosis and perivascular lymphocytic infiltration in the upper dermis, but not epidermal necrosis (Fig. 1c). Direct immunofluorescence was negative.

Immunoblotting analyses using various autoimmune blistering disease antigens, including laminin-332, and enzyme-linked immunoassays for desmogleins 1 and 3, BP180 and 230 were all negative.

Based on these findings, dermatological diagnosis of contact dermatitis was suggested and PH was terminated. However, because ophthalmological findings could not exclude Stevens–Johnson syndrome, i.v. corticosteroid pulse therapy was conducted. The skin lesions and ocular involvements improved, although minimal symblepharon and shortening of the conjunctival fornix were seen in both eyes.

Patch tests of previously used eye drops were all negative except 0.5% PH solution (Mydrin-P[®]) (data not shown). A

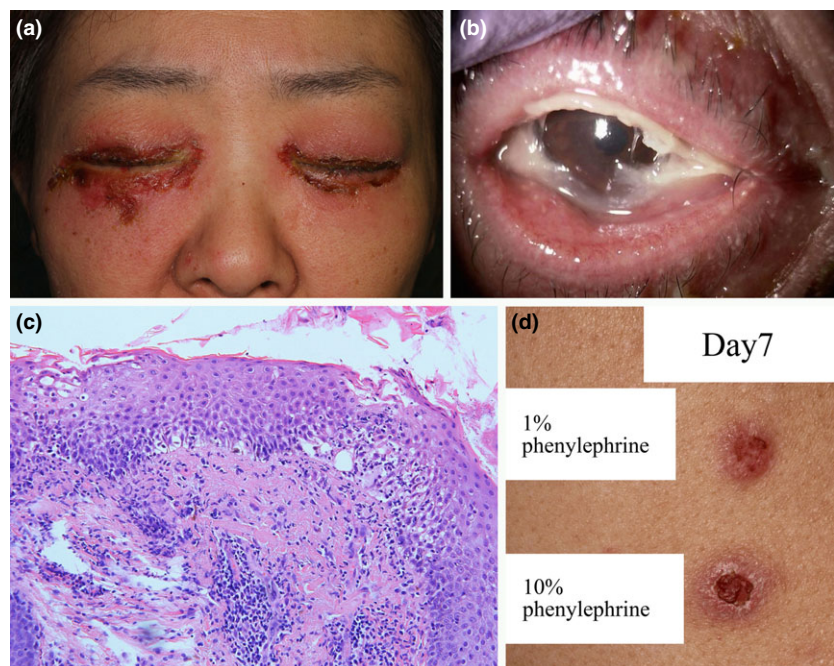


Figure 1. (a) Symmetrical erythemas and erosions on the eyelids and the periorbital areas. (b) Pseudomembrane formation, conjunctival injection and symblepharon on the conjunctivae. (c) Histopathological investigation of the eyelid skin detected spongiosis, exocytosis of lymphocytes and perivascular lymphocytic infiltration in the upper dermis, however, epidermal necrosis was not observed (hematoxylin-eosin, original magnification $\times 200$). (d) Positive patch test (3+) reaction to 1% and 10% phenylephrine hydrochloride on the back at day 7.

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confirmatory patch test using 1% and 10% PH³ following the International Contact Dermatitis Research Group criteria yielded a strongly positive reaction, which persisted from day 2 to 7 (Fig. 1d). Additional patch tests of the components of the causative eye drop other than PH were all negative. Finally, the diagnosis of PH-induced contact dermatitis was made.

Villarreal reported that the reagent elicited some allergic reactions in 93.5% of acute conjunctivitis patients.⁴ The resultant dermatitis could be very severe, however, ophthalmological symptoms have been reported to be mild, represented by pruritus, lacrimation.⁴ Thus, the diagnosis of similar cases with ocular involvement alone would be challenging.

The ocular pseudomembrane formation is a characteristic sign for Stevens-Johnson syndrome, mucous membrane pemphigoid, viral or bacterial infection and chemical burns. However, the ocular pseudomembrane formation can be observed in severe ocular damage producing necrotic cells and fibrin-rich exudates covering the conjunctival surfaces.⁵ We speculate that long-term repetitive use of the causative agent potentially contributed to the severe symptom. This report alerts that contact dermatitis can also cause an acute pseudomembrane formation and ophthalmological examination is indispensable in cases with severe blepharitis or contact dermatitis.

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REFERENCES

- 1 Barber KA. Allergic contact eczema to phenylephrine. *Contact Dermatitis* 1983; **9**: 274–277.
- 2 Sotozono C, Ueta M, Nakatani E *et al.* Japanese research committee on severe cutaneous adverse reaction. Predictive factors associated with acute ocular involvement in Stevens-Johnson syndrome and toxic epidermal necrolysis. *Am J Ophthalmol* 2015; **160**: 228–237.
- 3 Matsudate M, Murao K, Kubo Y. Contact dermatitis caused by Hya-lein-mini[®] and Mydrin-P[®]. *Practical Dermatol (in Japanese)* 2015; **37**: 475–478.
- 4 Villarreal O. Reliability of diagnostic tests for contact allergy to mydri-atic eyedrops. *Contact Dermatitis* 1998; **38**: 150–154.
- 5 BenEzra D. Membranes and pseudomembranes. In: BenEzra D, ed. *Blepharitis and conjunctivitis*, 1st edn. Barcelona: Editorial Glosa SL, 2006; 35–36.