

# Allergic contact dermatitis caused by $\epsilon$ -aminocaproic acid in a purified sodium hyaluronate ophthalmic solution

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Epsilon ( $\epsilon$ )-Aminocaproic acid (EACA) (CAS no. 60-32-2) is an anti-fibrinolytic agent discovered in Japan in 1953. In addition, EACA acts as buffer and has an anti-inflammatory effect. Therefore, EACA is included in various products in Japan, such as eye drops, eye rinses, detergents, toothpastes, soaps, creams, and cosmetics. Allergic contact dermatitis caused by EACA is supposedly rare (1). We report a case of allergic contact dermatitis of the eyelids caused by EACA in a purified sodium hyaluronate ophthalmic solution.

## Case Report

A-78-year-old woman presented with bilateral periocular pruritic erythema and oedema. She had used purified sodium hyaluronate ophthalmic solution 0.1% (Hyalein<sup>®</sup> Mini ophthalmic solution 0.1%; Santen Pharmaceutical, Osaka, Japan), levofloxacin hydrate ophthalmic solution 1.5% (Cravit<sup>®</sup> ophthalmic solution 1.5%; Santen Pharmaceutical) and ofloxacin ophthalmic ointment 0.3% (Tarivid<sup>®</sup> ophthalmic ointment 0.3%; Santen Pharmaceutical) for the treatment of 'dry eye' and keratoconjunctivitis sicca for 2 years before her first visit to our department. We suspected allergic contact dermatitis caused by these three ophthalmic preparations.

Patch tests were performed with the above-mentioned ophthalmic preparations, applied 'as is' with a Torii<sup>®</sup>

patch tester (Torii Pharmaceutical, Tokyo, Japan), and left under occlusion for 2 days. We found a positive reaction only to purified sodium hyaluronate ophthalmic solution 0.1% 'as is' [day (D) 2; -, D3, + (Fig. 1a); D7, +] according to the ICDRG/ESCD criteria (2). Subsequent patch tests were performed with the single constituents, with appropriate concentrations and vehicles as recommended in the literature (1–5). We found positive reactions to EACA 1% aq. [D2, -; D3, + (Fig. 1b); D7, +] and EACA 2% aq. [D2, +; D3, + (Fig. 1c); D7, +]. The patient was therefore diagnosed with allergic contact dermatitis caused by EACA in a purified sodium hyaluronate ophthalmic solution. After the patient stopped using the eye drops, and following treatment with topical corticosteroids, the periorbital contact dermatitis disappeared, and it has not recurred since.

## Discussion

Hyalein<sup>®</sup> Mini ophthalmic solution is a sodium hyaluronate ophthalmic solution frequently used for the treatment of 'dry eye'. The product is marketed as disposable eye drops with unit dose packaging in East and Southeast Asian countries. As such, it is preservative-free, but still contains other additives, such as EACA used as a buffer (4). According to publications in the English-language literature on allergic contact dermatitis caused by EACA, by 2013, 13 of 16 cases of allergic contact dermatitis occurred in Japan after the use of eye drops (5). According to above results, allergic contact dermatitis caused by EACA should be borne in mind when eye drops containing EACA are used for the long-term treatment of chronic ophthalmopathy.

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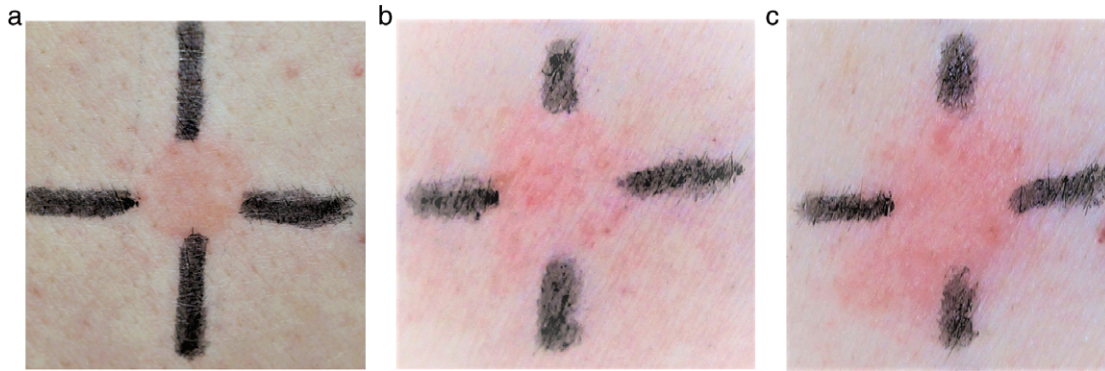


**Fig. 1.** Positive patch test reaction on day (D) 3 to (a) purified sodium hyaluronate ophthalmic solution 0.1% 'as is' on the upper back. (b) Positive patch test reaction on D3 to  $\epsilon$ -aminocaproic acid 1% aq. on the upper back. (c) Positive patch test reaction on D3 to  $\epsilon$ -aminocaproic acid 2% aq. on the upper back.

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