

LETTER TO THE EDITOR

**Allergic contact dermatitis due to epsilon-aminocaproic acid:
A case report and mini-review of the published work**

Dear Editor,

Epsilon-aminocaproic acid (EAA) is a fibrinolytic that has been used to control various hemorrhagic disorders worldwide.¹ In Japan, EAA is also contained in household products and drugs on the market, including eye drops, soap and toothpaste.¹ Here, we report a case of allergic contact dermatitis (ACD) due to EAA and describe the characteristics of this condition based on a review of published cases.

A 78-year-old Japanese woman visited our department for diagnosis of pruritic erythema and mild lichenification on the periorbital areas (Fig. 1a). She reported that she had used sodium hyaluronate 0.1% eye drops (Hyalein; Santen Pharmaceutical, Osaka, Japan), sodium chloride 0.4% eye drops (Soft-santear; Santen Pharmaceutical) and fluorometholone 0.1% eye drops (Flumetholone; Santen Pharmaceutical) for treatment of allergic keratoconjunctivitis for 4 years. A month before her first visit to our department, she noticed the eruption. On the basis of her history, ACD due to these three eye drops was suspected. The eye drops were stopped and the eruption disappeared in 5 days with p.o. administration of fexofenadine hydrochloride 120 mg/day and topical application of hydrocortisone butyrate. Patch and scratch-patch tests were performed using pure samples of the three eye drops according to the International Contact Dermatitis Research Group guidelines.² All patch tests were negative. However, positive scratch-patch test reactions (1+) to sodium hyaluronate 0.1% eye drops were found on days 2 and 3. The sodium hyaluronate 0.1% eye drop is a viscous solution consisting of sodium hyaluronate, EAA, edetate sodium and benzalkonium chloride. Patch and scratch-patch tests were performed individually for the four components (0.1% sodium hyaluronate, 0.2% EAA, 0.01% edetate sodium, 0.003% benzalkonium chloride). Distilled water was used as a vehicle. Positive patch test reactions (1+) to EAA on days 2 and 3 and a positive scratch-patch test reaction (1+) to EAA on day 3 were obtained (Fig. 1b). The erythemas faded but they still remained on day 7. The patch and scratch-patch test reactions to the other three components were negative. Therefore, we diagnosed this case as ACD due to EAA.

Including our case, there have been 16 reports of ACD due to EAA in the English-language published work (Table 1).^{1,3–7} These patients (two male and 14 females) were aged 43–79 years old. Eye drops were the most common cause ($n = 13$, 81.3%).^{1,3,6} Therefore, the skin around the eyes and

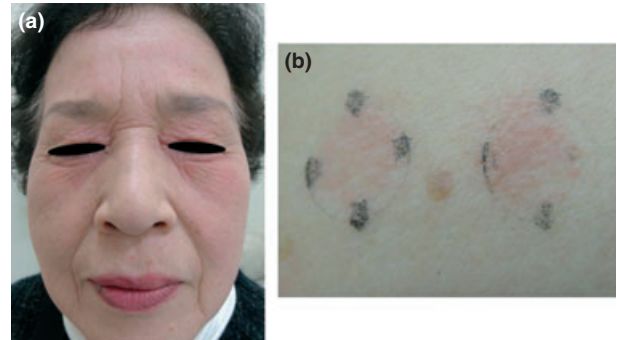


Figure 1. (a) A clinical photograph showing erythema and mild lichenification on the periorbital areas. (b) In skin tests, positive patch and scratch-patch test reactions to epsilon-aminocaproic acid on day 3 were seen. Left, patch test; right, scratch-patch test.

cheek was the most frequently affected site. In all seven evaluable cases, the eruptions were erythematous types with or without scales, edema or lichenification. In four out of five evaluable cases, eruption onset occurred between 7 months and 14 years after the start of exposure to EAA, suggesting that sensitization occurred after long-term exposure to EAA. In all six evaluable cases, topical corticosteroids were effective for treatment of the eruption. In all seven evaluable cases, positive patch test results were seen at concentrations of 0.1–30.0% in petrolatum or aqua, suggesting that a positive reaction to EAA may occur even at a relatively low concentration and 1% of EAA in aqua may be recommended for patch testing. From these results, we suggest that long-term use of drugs and household products that contain EAA may cause ACD, even if the concentration of EAA is low. Thus, inquiries into medical and life history and skin tests are crucial for identification of ACD due to EAA. The present case illustrates the importance of medical practitioners paying attention to products containing EAA.

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Table 1. Summary of cases of allergic contact dermatitis due to epsilon-aminocaproic acid

Authors	Case no.	Year	Age, years	Sex	Original illness	Cause	Eruption sites	Eruption types	Sensitization period	Treatment	Patch test
Sugai ⁶	1	1986	59	F	nw	Eye drops	nw	nw	nw	nw	nw
Shono ¹	2	1986	60	F	nw	Eye drops	nw	nw	nw	nw	nw
	3	1989	60	F	Eye	Eye drops	Periorbital regions	Edematous Erythema	7 mo	TC	+
Washizaki <i>et al.</i> ⁶	4	1992	70	F	Irritation	Eye drops	nw	nw	nw	nw	(0.1%, 1%, 10% aq)
Tanaka <i>et al.</i> ³	5	1993	53	F	nw	Eye drops	Cheeks, periorbital regions	Erythema	nw	TC	+
Tanaka <i>et al.</i> ⁴	6	1993	43	F	nw	Nylon body-stockings	Trunk	Scaly Erythema	2 y	TC	+
	7	1994	54	F	nw	Eye drops	nw	nw	nw	nw	(3%, 6% pet)
Kiyokawa <i>et al.</i> ⁶	8	1995	62	M	nw	Occupation	Almost whole body	Scaly Erythema	14 y	nw	+
Aguirre <i>et al.</i> ⁵	9	1996	72	F	nw	Eye drops	nw	nw	nw	nw	(5% aq)
Kawada <i>et al.</i> ⁶	10	1996	78	F	nw	Eye drops	nw	nw	nw	nw	nw
Tsunoda <i>et al.</i> ⁶	11	1996	72	M	nw	Eye drops	nw	nw	nw	nw	nw
Tsunoda <i>et al.</i> ⁶	12	1997	78	F	nw	Eye drops	nw	nw	nw	nw	nw
Miyamoto and Okajima ⁶	13	1997	79	F	nw	Eye drops	nw	nw	nw	nw	nw
	14	2000	63	F	nw	Eye drops	Cheeks, periorbital regions	Erythema	nw	AH inj TC	+
Cunha <i>et al.</i> ⁷	15	2009	47	F	Vaginal Bleeding	AA Treatment	Axilla, mamma, Inguen, Lateral trunk	Erythema	1 w	AH TC emollients	+
Our case	16	2012	78	F	AK	Eye drops	Periorbital regions	Erythema, Lichenification	4 y	AH TC	+

AA, aminocaproic acid; AH, antihistamine; AK, allergic keratoconjunctivitis; aq, aqua; F, female; inj, injection; M, male; mo, months; nw, not written; pet, petrolatum; TC, topical corticosteroids; w, week; y, years; +, positive.

REFERENCES

- 1 Shono M. Allergic contact dermatitis from epsilon-aminocaproic acid. *Contact Dermatitis* 1989; **21**: 106–107.
- 2 Rietschel RL, Fowler JF Jr. Practical aspects of patch testing. In: Rietschel RL, Fowler JF Jr, eds. *Fishers Contact Dermatitis*, 6th edn. Hamilton, Ontario: BC Decker Inc., 2008; 26–27.
- 3 Tanaka M, Niizeki H, Miyakawa S. Contact dermatitis from epsilon-aminocaproic acid. *Contact Dermatitis* 1993; **28**: 124.
- 4 Tanaka M, Kobayashi S, Miyakawa S. Contact dermatitis from nylon 6 in Japan. *Contact Dermatitis* 1993; **28**: 250.
- 5 Aguirre A, Gonzalez Perez R, Zubizarreta J, Landa N, Sanz de Galdano C, Diaz Perez JL. Allergic contact dermatitis from epsilon-caprolactam. *Contact Dermatitis* 1995; **32**: 174–175.
- 6 Miyamoto H, Okajima M. Allergic contact dermatitis from epsilon-aminocaproic acid. *Contact Dermatitis* 2000; **42**: 50.
- 7 Cunha D, Carvalho R, Santos R, Cardoso J. Systemic allergic dermatitis to epsilon-aminocaproic acid. *Contact Dermatitis* 2009; **61**: 303–304.