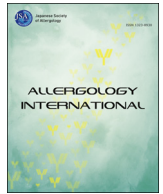




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Letter to the Editor

Drug eruption caused by esomeprazole: A case report and mini-review

Dear Editor,

Esomeprazole is a proton-pump inhibitor (PPI) that is used to treat peptic ulcers. Although many cases of drug eruptions after PPI treatment have been reported,^{1–3} there are only six reported cases of drug

eruption caused by esomeprazole in the English literature.^{4–8} Therefore, we report a very unusual case of drug eruption caused by esomeprazole and review the clinical features of the reported cases.

A 69-year-old woman was referred to our hospital for consultation regarding generalized pruritic papules and erythema (Fig. 1a, b). We

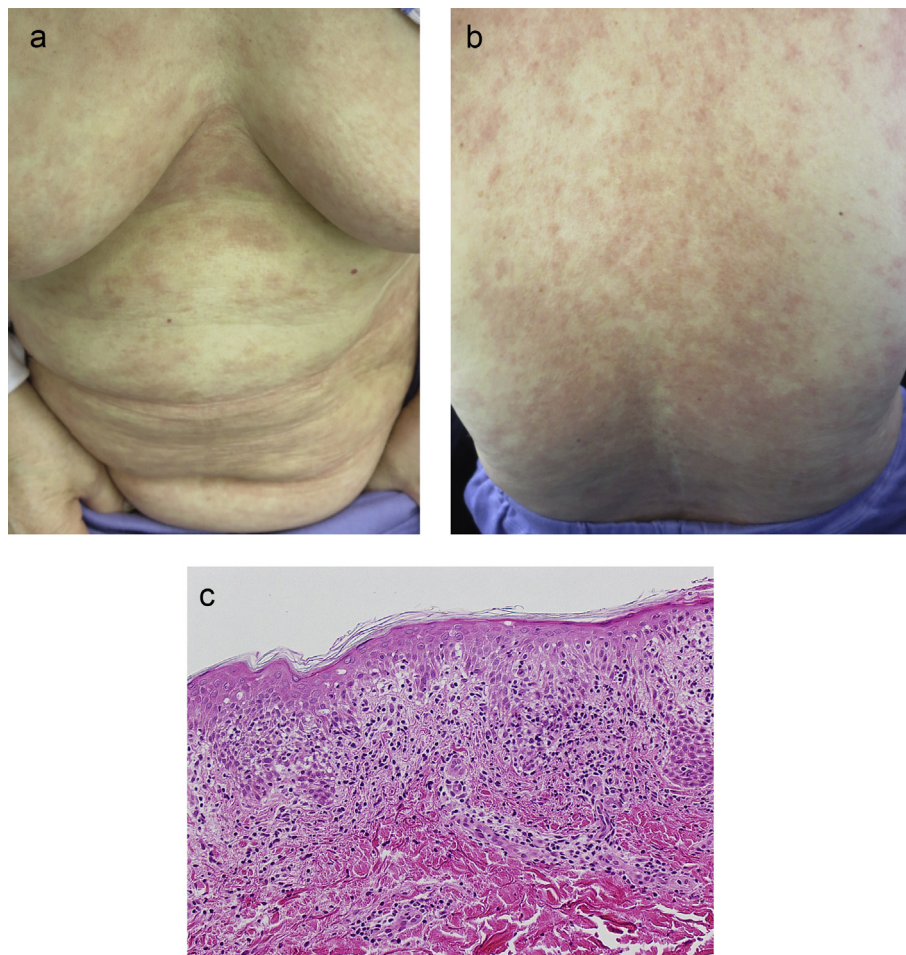


Fig. 1. (a, b) A clinical examination revealed pruritic papules and erythema on the patient's trunk. (c) Histopathological findings from the erythematous papules on the chest revealed superficial perivascular lymphocytic infiltration with vacuolar alteration (hematoxylin and eosin staining, original magnification: $\times 100$).

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Table 1
Cases of drug eruption caused by esomeprazole.

Ref.	Case no	Year	Age (years)	Sex	Clinical manifestations	Time interval [†]	Treatment	Patch test	DLST	Oral provocation test	Time to improvement [‡]
4	1	2007	41	F	DRESS syn	20 d	Discontinuation, Systemic prednisolone	+	na	na	4 m
5	2	2010	56	F	Fixed drug eruption	2 w	Discontinuation, Prednisolone	+	na	+	Rapid resolution
6	3	2011	82	M	Severe exfoliative dermatitis	2 w	Discontinuation, Systemic methylprednisolone and prednisolone	na	na	na	na
7	4	2013	60	M	DRESS syn	na	na	+	na	na	na
7	5	2013	28	F	SJS/TEN	na	na	+	na	na	na
8	6	2015	84	F	DRESS syn	8 d	Discontinuation, Systemic methylprednisolone	na	na	na	Died of MOF
Our case	7	2016	69	F	maculopapular	2 m	Discontinuation, Topical steroid	–	+	nd	1 m

Ref, reference; DLST, drug lymphocyte stimulation test; M, male; F, female; DRESS syn, drug rash with eosinophilia and systemic symptoms syndrome; d, day; w, week; m, month; na, not available; nd, not done; MOF, multiple organ failure.

[†] Time from the start of esomeprazole treatment to symptom onset.

[‡] Time from the initial treatment to resolution of the eruption.

did not observe any other general symptoms, such as fever, lymph node swelling, liver dysfunction, or kidney dysfunction. She had a history of rheumatoid arthritis, hypertension, and gastric ulcer, and have received a 2-month treatment using iguratimod, salazosulfapyridine, nifedipine, and esomeprazole. Because we suspected drug eruption, all drugs were discontinued and the eruption subsequently disappeared within 1 month. We restarted treatment using esomeprazole and celecoxib, although the skin eruption recurred soon after restarting treatment. Thus, we suspected drug eruption caused by esomeprazole, and performed a skin biopsy, patch test (using esomeprazole, omeprazole, and lansoprazole), and a drug lymphocyte stimulation test (DLST) using esomeprazole. Histological examination of a punch biopsy specimen from the right chest revealed superficial perivascular lymphocytic infiltrates with severe vacuolar alteration, which was consistent with drug eruption (Fig. 1c). A DLST using esomeprazole revealed positive results with a stimulation index of 11.0. Although the patch test was negative for all three PPIs, we diagnosed the patient with drug eruption caused by esomeprazole based on the clinical course and the DLST results. We did not perform additional DLSTs for other PPIs or the oral provocation test for esomeprazole, as the patient refused to undergo further evaluations. We discontinued the esomeprazole treatment again, and the eruption completely disappeared with no recurrence during our follow-up.

Including the present case, there are only seven reported cases of drug eruption caused by esomeprazole in the English literature (Table 1).^{4–8} These cases involved 2 men and 5 women, and the median age at onset was 69 years. The types of eruptions included Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN),⁸ drug rash with eosinophilia and systemic symptoms (DRESS) syndrome,^{4,7,8} fixed drug eruption,⁵ severe exfoliative dermatitis,⁶ and maculopapular eruption (our patient). The interval between the start of esomeprazole treatment and symptom onset ranged from 8 days to 2 months.

Drug eruptions caused by PPIs are frequent and usually mild in intensity,³ and commonly involve maculopapular eruptions, pruritus, and urticaria. Esomeprazole was developed as the S-isomer of omeprazole to improve its pharmacokinetic properties, and esomeprazole-induced eruptions are extremely rare. Interestingly, no cross-reactivity between esomeprazole and omeprazole was observed in case 1,⁴ despite these molecules' structural similarities. Thus, slight structural differences may affect the antigenicity of PPIs. It is also interesting to note that esomeprazole-induced eruptions are relatively severe, with two cases of DRESS syndrome (patient 6 subsequently died), one case of SJS/TEN, and one case of severe exfoliative dermatitis. Compared to the previously reported cases, the present case had mild progression and a prolonged

interval to the disease onset. As the patient had received iguratimod and salazosulfapyridine with the esomeprazole, it is possible that these immunosuppressants might inhibit the onset and progression of the drug eruption, which prolonged the time to development. Although drug eruption caused by esomeprazole is rare, general physicians and dermatologists should be aware that drug eruptions caused by esomeprazole may be relatively severe.

Conflict of interest

The authors have no conflict of interest to declare.

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