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SHORT COMMUNICATION

Lichenoid Drug Eruption Caused by Limaprost Alfadex

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Limaprost alfadex is a prostaglandin E1 (PGE1) derivative, which is effective in the treatment of thromboangitis obliterans through its pharmacological effect of improving peripheral blood circulation (1). Although some PGE1 analogue-related adverse events have been reported, e.g. liver dysfunction, to our knowledge, there have been only 2 case reports of cutaneous drug eruption caused by PGE1 analogue published in English (2, 3). We report here a case of lichenoid drug eruption caused by limaprost alfadex, as an unusual skin manifestation.

CASE REPORT

An 88-year-old woman was referred to our department for the evaluation of an eruption on her trunk and extremities. She had developed generalized scaly erythematous plaques (Fig. 1A and B) after taking limaprost alfadex (Prorenal®, Sumitomo Dainippon Pharma Co., Ltd) for 2 months to improve her thromboangitis obliterans. A skin biopsy from a scaly erythematous plaque on her trunk revealed a dense, band-like cell infiltration composed predominantly of lymphocytes in the papillary dermis (Fig. 1C). There were necrotic keratinocytes in the epidermis (Fig. 1D), but no abnormality of the mucous membrane. Her family history was unremarkable. Laboratory examinations were negative for hepatitis C virus. Although there was a risk of exacerbation of skin inflammation during the cutaneous adverse event, we performed patch-testing at the first visit at the patient's request. Patch-testing with 20% limaprost alfadex using Vaseline® vehicle was negative.

A lymphocyte stimulation test (LST) with limaprost alfadex was performed as described previously (4–6). ^{3}H-thymidine incorporation was significantly increased by the addition of 4.1×10^{-12} M limaprost alfadex (corresponding to C_{max}) to the peripheral lymphocyte culture with a stimulation index of 1.96 (Fig. 1E). Although she had other medications, LST and patch test were all negative for each medicine. Based on the clinical course and laboratory examination, the eruption was diagnosed as limaprost alfadex-induced lichenoid drug eruption.

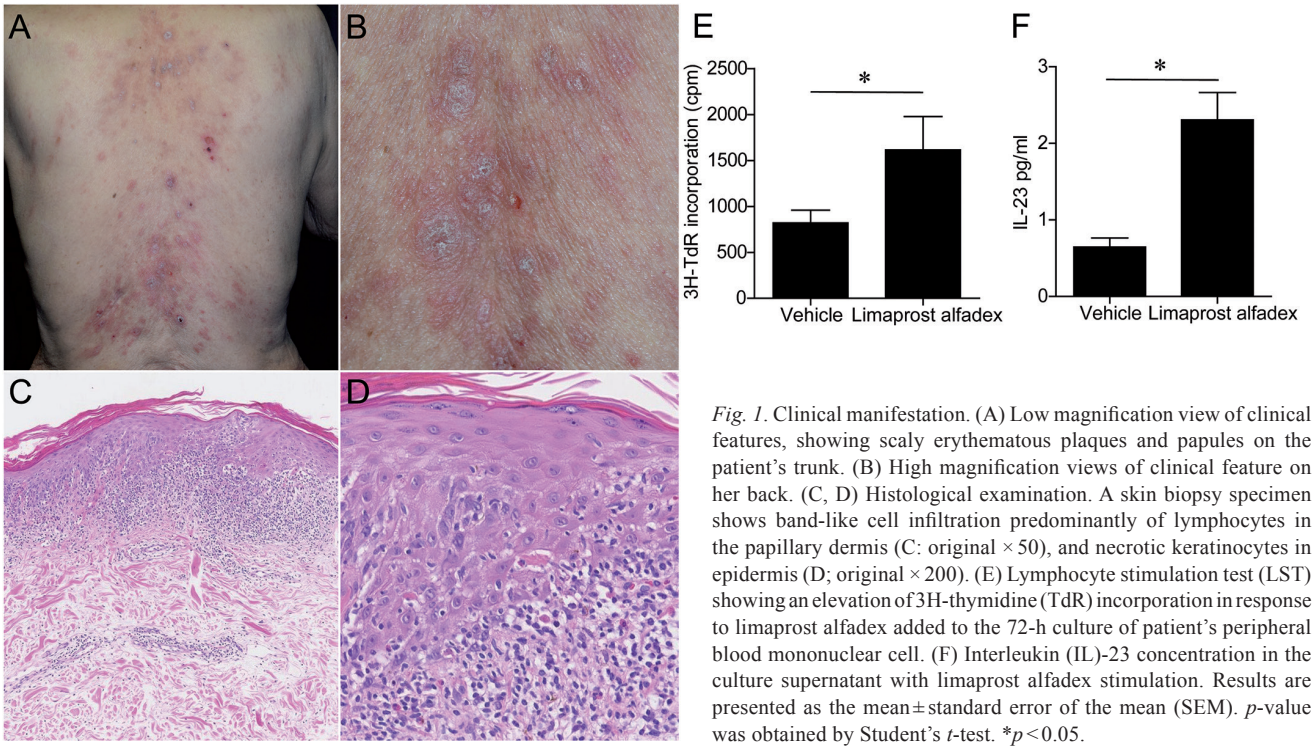

Fig. 1. Clinical manifestation. (A) Low magnification view of clinical features, showing scaly erythematous plaques and papules on the patient's trunk. (B) High magnification views of clinical feature on her back. (C, D) Histological examination. A skin biopsy specimen shows band-like cell infiltration predominantly of lymphocytes in the papillary dermis (C: original × 50), and necrotic keratinocytes in epidermis (D; original × 200). (E) Lymphocyte stimulation test (LST) showing an elevation of 3H-thymidine (TdR) incorporation in response to limaprost alfadex added to the 72-h culture of patient's peripheral blood mononuclear cell. (F) Interleukin (IL)-23 concentration in the culture supernatant with limaprost alfadex stimulation. Results are presented as the mean ± standard error of the mean (SEM). *p*-value was obtained by Student's *t*-test. **p* < 0.05.

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After treatment with oral methyl prednisolone, 5 mg per day, and topical betamethasone butyrate propionate ointment, the eruption improved gradually with residual pigmentation.

DISCUSSION

Lichenoid drug eruption has clinical similarity to lichen planus. Although the detailed mechanism of lichenoid drug eruption remains unclear, it is known that interleukin (IL)-17 production is elevated in the skin in patients with lichen planus (7). As IL-23 from dendritic cells activates IL-17 and IL-22 production from Th17 cells, DC might have some role in the pathogenesis of lichenoid drug eruption. This study revealed that IL-23 concentration in culture supernatant of LST was significantly increased with limaprost alfadex stimulation (Fig. 1F). Therefore, IL-23 might play an important role in the pathogenesis of lichenoid drug eruption. Further investigation is necessary to clarify this issue.

The authors declare no conflicts of interest.

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