Photoleukomelanoderma Possibly Caused by Etretinate in a Patient with Psoriasis

Mariko Seishima[1]*, Yoshinao Shibuya[2], Genichi Kato[2] and Kana Watanabe[2]
Department of Dermatology, [1]Gifu University Graduate School of Medicine, 1-1 Yanagido Gifu, and [2]Ogaki Municipal Hospital, Ogaki, Japan.
E-mail: marikoseishima@yahoo.co.jp
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Sir,

It is well known that etretinate, an aromatic retinoid, sometimes causes skin-related side-effects such as cheilitis, desquamation, dry mouth, thinning of the skin, and itching (1). Photosensitivity due to etretinate has rarely been reported (2–5). We report here a patient with psoriasis vulgaris who developed erythema and swelling on the face and dorsum of the hands after a 2-month history of etretinate administration. Although etretinate administration was discontinued, photoleukomelanoderma developed 1.5 months after the appearance of erythema and swelling. This is the first report of typical photoleukomelanoderma possibly induced by etretinate.

CASE REPORT

A 62-year-old man, who worked as a farmer, was referred to our hospital complaining of erythema and swelling of the face (Fig. 1a) and dorsum of the hands, which persisted for 2 weeks. Laboratory examinations including blood cell counts, liver and renal blood tests, and serum IgG, IgA, IgM, and IgE concentrations showed all parameters within normal limits. Serological tests for antinuclear, anti-SS-A/Ro, and anti-SS-B/La antibodies were negative. Histological findings showed the infiltration of lymphocytes and swelling in the upper to middle dermis.

He had been administered etretinate (20 mg/day) for the previous 2 months because of psoriasis vulgaris on the trunk and forehead. After this time the etretinate was discontinued and he was recommended to shield the skin from light. However, pigmentation and depigmentation were observed on the face, dorsum of the hands, and neck 1.5 months after discontinuation of etretinate (Fig. 1b). Laboratory examinations showed no abnormal data including blood cell counts and renal and liver function tests. Histological findings of the skin biopsy specimen from the pigmented cheek skin showed the degeneration of basal cells, lymphocyte infiltration in the basal layer and upper dermis, and melanin deposits in the upper dermis. A drug-induced lymphocyte stimulation test and closed patch test for 48 h using etretinate were negative. The minimal erythema dose (MED) of ultraviolet (UV) A and MED of UVB, 10 J/cm^2 and 90 mJ/cm^2, respectively, were within normal range. A photo-patch test for etretinate was positive after irradiation with a 1/2 MED of UVA, but not 1/2 MED of UVB. One and a half months after the discontinuation of etretinate treatment, the patient took this agent for 2 days as a provocation test, which reduced MED by UVA from 10 to 6 J/cm^2, but did not change UVB sensitivity. A diagnosis of photoleukomelanoderma due to etretinate was made based on these findings. As depigmentation expanded to the neck (Fig. 1c), 20 mg/day of prednisolone was administered, resulting in no additional enlargement of photoleukomelanoderma. The dose of prednisolone was gradually reduced, and the patient continued to use sunscreen. However, pigmentation and depigmentation remained on the face, dorsum of the hands, and neck 1.5 years after the cessation of etretinate.

DISCUSSION

Although new biological therapies have been introduced in recent years, retinoids remain one of the effective

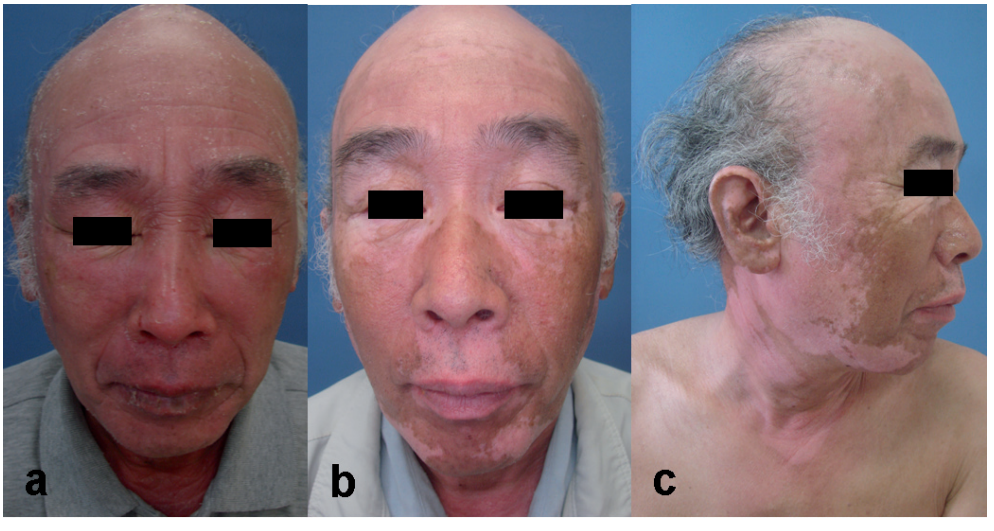

Fig. 1. (a) Clinical findings of the face after 2 months administration of etretinate. The entire face except for the eyelids shows erythema with slight swelling. (b) Clinical findings of the face 1.5 months after cessation of etretinate. Pigmentation and depigmentation with erythema are observed. (c) Clinical findings of the face and neck 2.5 months after discontinuation of etretinate. The areas of depigmentation have extended to the neck.

therapies for psoriasis (7–9). Etretinate sometimes causes skin-related side-effects, such as cheilitis, desquamation, dry mouth, granulomatous nodule (10), thinning of the skin, and itching (1, 8, 9). There have been some reports of photosensitivity caused by etretinate. Photosensitivity levels were tested in 14 psoriasis patients treated with 75–100 mg/day of etretinate for 3 weeks, resulting in an increased photosensitivity to UVA in 2 patients (2). In another report, etretinate administration for 27 days induced photosensitivity, involving a burning sensation followed by erythema, oedema, and pruritis on the face, neck, and dorsal aspects of the arms and hands in erythodermic psoriasis (3). In addition, there is a report of a patient who after taking 50 mg/day of etretinate for 3 months developed clinical photosensitivity, consisting of burning erythema on sunlight exposure (4). Etretinate causes sunburn reactions in 7–9% of patients (1), and also has a phototoxic potential (5). Pseudoporphyria, with blisters on the dorsa of the hands, has been reported after 1 mg/kg/day of etretinate therapy for 3 weeks (6). However, such photosensitivity and pseudoporphyria appear temporarily and disappear after drug discontinuation. Marked photoleukomelanoderma has not been described, although some cases showing erythema with a burning sensation as photosensitivity have been reported (3, 4).

In Europe and USA, etretinate has been replaced by acitretin, which is a pro-drug of etretinate that shows a lower possibility of foetal toxicity (7, 8). But etretinate is still used in Asia and is the only retinoid compound available for psoriasis in Japan. After cessation of the agent, etretinate disappears from the epidermis within one week, but remains in the subcutis for months and it is detectable in the plasma for up to 140 days after discontinuation because it is lipophilic and accumulates in the subcutis (11).

The present patient reported erythema after 2 months of etretinate therapy, photoleukomelanoderma developed after the cessation of etretinate regardless of shielding the skin from sunlight, and the areas of photoleukomelanoderma were extended for one more month. Although the expansion of photoleukomelanoderma stopped after the administration of a systemic steroid, it remained 1.5 years after onset. The patient had worked outside for more than 8 h almost every day in fine weather. Some of the factors related to the onset of photoleukomelanoderma (exposure dose and duration of sunlight, skin colour, and genetic background) were revealed by this case.

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