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LETTER TO THE EDITOR

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A case of photoallergic dermatitis caused by pirfenidone

Dear Editor,

Pirfenidone is a medicine for idiopathic pulmonary fibrosis (IPF) released in 2008. The drug exhibits both anti-inflammatory and antifibrotic effects, and thereby extends the progression-free survival time of patients with IPF.[1] The most important side effect of pirfenidone is photosensitivity, whose incidence of which was as high as 51.7% in clinical trials. The drug's photosensitivity is caused by the phototoxic effect because of the clinical characteristics that patients exhibit—such as sunburn-like painful blisters or non-itchy erythema occurring immediately after UV exposure.[1] Here, we report a case of photosensitive drug eruption due to a photoallergic reaction, which was proven through a photopatch test and drug-induced lymphocyte stimulation test (DLST).

A 58-year-old woman had started pirfenidone due to interstitial pneumonia associated with anti-ARS antibody syndrome. Six months later, in May, she noticed rashes on the exposed areas of her face and hands. She was treated with topical steroids, but the rashes worsened.

When she visited our department in August, well-bordered, itching, severely edematous erythemas were seen on her face, anterior cervix, and hands (Figure 1A, left). A skin biopsy from the erythema of her left forearm showed thickened stratum corneum, acanthosis of the epidermis, liquefaction degeneration of the basal layer, and perivascular inflammatory infiltrates with some eosinophils (Figure 1A, right).

As the minimum reaction dose (MRD) and the minimum erythema dose were in normal range, a photopatch test was performed using pirfenidone 10% and 1% pet. (Figure 1B). A duplicate set of those was applied on the patient's upper back, and, on Day 1 (D1), one set was removed and 4.86 J/cm^2 UVA, half dose of the MRD, was irradiated. The reactions were read on D2 and D3 according to ICDRG patch test guidelines.[2] In the UVA-irradiated side, the reaction to pirfenidone 1% pet. was D2, −; D3, +?; D7, +, and that to pirfenidone 10% pet. was stronger, D2, +; D3, +; D7, +. However, all were negative in the non-irradiated side. From those results, a photosensitive drug eruption caused by pirfenidone was diagnosed. Furthermore, in a DLST, the stimulation index for pirfenidone showed 208%, which was more than the 180% defined as positive, suggesting an ordinary sensitivity to pirfenidone. It was difficult to stop pirfenidone for the treatment of IPF, but a sunscreen with SPF 50, PA +++, and a topical steroid (clobetasol propionate) improved the erythemas in eight weeks.

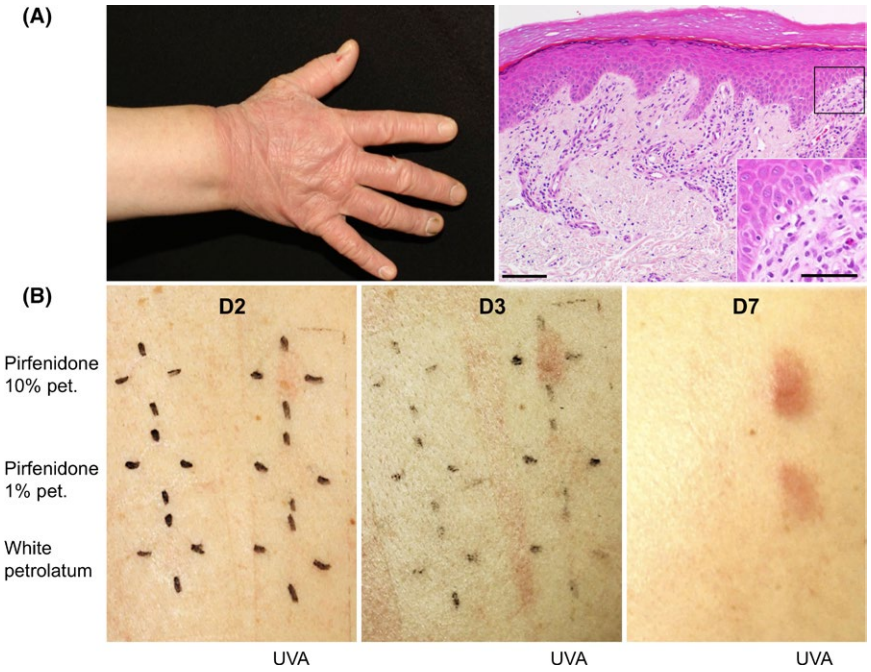

FIGURE 1 Clinical appearance, histology, and photopatch test of the case. A (left), Well-bordered edematous erythema on the sun-exposed dorsum of the right hand. A (right), H&E staining of the skin from the left forearm. Bar, 100 μm. (Inset). Liquefaction degeneration of the basal layer and eosinophil infiltration. Bar, 50 μm. B (left), Photopatch test for pirfenidone on Day 2 (D2). B (center), Day 3 (D3). B (right), Day 7 (D7). Patches on the right side were UVA-irradiated on Day 1

The reported cases with serious photosensitizing drug eruptions caused by pirfenidone are due to its phototoxic effect,[3,4] the clinical features of which resemble sunburn. On the other hand, reports on pirfenidone-induced photoallergic drug eruptions seem rare,[5] and cutaneous symptoms are various, but resemble eczematous dermatitis. However, it is sometimes difficult to clearly discriminate photoallergic and phototoxic effects, because both mechanisms might coexist in clinical settings.[6] Pirfenidone-induced photoallergic dermatitis was diagnosed based on clinical images and a photopatch test.[7] In the present case, positive DLST is suggestive of an allergic mechanism in addition to the clinical features and positive photopatch test for pirfenidone.

DECLARATION

Approval of the research protocol: N/A.
Informed Consent (especially for Case): Written informed consent was obtained from the patients.
Registry and the Registration No. of the study/trial: N/A.
Animal Studies: N/A.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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