A Case Report of Pirfenidone-Induced Lichenoid Drug Eruption in a Patient with Idiopathic Pulmonary Fibrosis

Seung Ah Yoo, Hyo Eun Park, Miri Kim, Hyun Jeong Park

Department of Dermatology, Yeouido St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea

Received April 13, 2020
Revised June 30, 2020
Accepted July 9, 2020

INTRODUCTION

IPF is a chronic, progressive, and lethal lung disease with a five-year survival rate of approximately 20%\(^1\). It is accompanied by progressive dyspnea and irreversibly fibrotic change and loss of function in lungs\(^2\). Pirfenidone (5-methyl-1-phenyl-2-[1H]-pyridone) is a novel anti-fibrotic and anti-inflammatory drug, which reduces deterioration in the lung function and prolongs progression-free survival in patients with IPF. Known adverse effects include gastrointestinal symptoms, hepatic dysfunction or skin photosensitivity, and rash\(^3\).

CASE REPORT

An age 70 male presented with asymptomatic, multiple, variable-sized, erythematous to brownish scaly plaques on the face, neck, and both arms and hands, which were the sun-exposed area, for two months (Fig. 1A–F). He had a history of idiopathic pulmonary fibrosis (IPF) diagnosed three years ago, and started taking pirfenidone five months ago with gradual dose increasing from 600 mg/day to 1,800 mg/day. No adverse effect was reported for the first three months. Punch biopsy specimens from the face and right hand revealed hyperkeratosis and lichenoid infiltration in dermoepidermal junction (Fig. 2). Based on clinical and histopathological aspects, he was finally diagnosed with lichenoid drug eruption (LDE) on photo-distribution due to pirfenidone which was directly discontinued. For treatment, topical diflucortolone 0.3% ointment, tacrolimus 0.3% ointment, and prednicarbate 0.25% solution were prescribed, a month after which the lesions improved, leaving postinflammatory hyperpigmentation. After a total of two months of treatment, the lesions improved and no new lesion developed. Pirfenidone treatment was resumed with dosage starting at 600 mg/day gradually being increased up to 1,200 mg/day, which was lower than previous dose. As a result of the combination of strict ultraviolet (UV) protection, no evidence of recurrence has been observed during 6 months of follow-up.

Keywords: Drug eruptions, Idiopathic pulmonary fibrosis, Lichenoid eruptions, Pirfenidone


**DISCUSSION**

LDE refers to lichen planus (LP)-like drug eruption usually presenting symmetric eczematous plaques with a purple hue on large areas of the trunk. The lesions of LDE often indistinguishable clinically and histopathologically from LP. In LDE, however, mucous membranes and nails are not involved and Wickham’s striae on skin lesions are rare. Histologically, focal parakeratosis, focal interruption of the granular layer, cytoid bodies in the cornified and granular layers, the presence of eosinophils and plasma cells in the inflammatory infiltrate, and an infiltrate around the deep vessels favor a diagnosis of LDE\(^4\).

In our case, skin lesions of the patient at first were suspicious of LP or LDE. The biopsied specimen showed hyperkeratosis and lichenoid infiltration, which can be observed in LP and LDE. Clinically, mucosal involvement and Wickham’s striae were absent, and lesions showed photodistributed presentation on the face, neck, and both arms and hands. West et al.\(^5\) found that typical histological features of LDE often are observed in nonphotodistributed LDE, and seldom present in photodistributed eruptions. Thus, a biopsy specimen that shows less likely the classic features of LDE should not be used.

![Fig. 1.](A~F) Multiple erythematous to brownish scaly patches and plaques on the face, neck, and both arms and hands (arrows). (G, H) Higher magnification view showing the absence of Wickham’s striae.

![Fig. 2.](A) Histopathologic examination revealed hyperkeratosis, focal parakeratosis and necrotic keratinocytes in the epidermis with lichenoid infiltration in dermoepidermal junction (H&E, ×40). (B) Infiltrated cells dominantly consisting of lymphohistiocytes and melanin incontinence (H&E, ×200).
as evidence against a drug eruption, especially if the lesions are photodistributed\textsuperscript{5,6}.

The pathomechanism of photo-distributed LDE is unknown, but it is assumed to be due to drug’s ability to absorb UVA and UVB. UV light absorbed from skin tissue can generate reactive oxygen species and lipid peroxidation, causing skin lesions\textsuperscript{7}.

Since anti-fibrotic treatment is directly linked to the mortality in IPF patients, in the event of such an adverse effect, it would be reasonable to continue pirfenidone by combining preventive measures rather than discontinuing the drug. Gaikwad and Mukherjee\textsuperscript{6} presented the standard approach for preventing these adverse effects, which includes avoiding direct sun exposure, use of broad spectrum sunscreens, physical protection, and avoiding other phototoxic drugs. The management of the skin lesions includes reducing the drug dose, or discontinuation of the drug if rash lasts longer than 15 days. Once the symptoms have resolved, the gradual re-introduction of the drug can be attempted\textsuperscript{8}. In our case, despite resuming pirfenidone, no evidence of recurrence has been observed during 6 months of follow-up, as a result of the combination of avoiding sun exposure as possible and use of broad spectrum sunscreens.

To date, numerous cases of LDE due to various drugs and pirfenidone-associated photosensitivity have been reported\textsuperscript{1,3,6,9,10}. However, to our knowledge, only a case of pirfenidone-induced LDE has been reported\textsuperscript{11}. Herein, we report a case of pirfenidone-induced LDE so that clinicians can be aware of the possibility of LDE when using pirfenidone. We received the patient’s consent form about publishing all photographic materials.

**CONFLICTS OF INTEREST**

The authors have nothing to disclose.

**FUNDING SOURCE**

None.

**ORCID**

Seung Ah Yoo, https://orcid.org/0000-0002-5794-6046

Hyo Eun Park, https://orcid.org/0000-0003-1879-0269

Miri Kim, https://orcid.org/0000-0001-5167-3449

Hyun Jeong Park, https://orcid.org/0000-0002-0138-9885

**REFERENCES**

1. Ferrer Guillén B, Giacaman MM, Valenzuela Oñate C, Magdaleno Tapial J, Hernández Bel P, Pérez Ferríols A. Pirfenidone-induced photosensitivity confirmed by pathological phototest. Photodiagnostics Photodyn Ther 2019;25:103-105.
2. Noble PW, Albera C, Bradford WZ, Costabel U, Glassberg MK, Kardatzke D, et al. Pirfenidone in patients with idiopathic pulmonary fibrosis (CAPACITY): two randomised trials. Lancet 2011;377:1760-1769.
3. Papakonstantinou E, Prasse A, Schacht V, Kapp A, Raap U. Pirfenidone-induced severe phototoxic reaction in a patient with idiopathic lung fibrosis. J Eur Acad Dermatol Venereol 2016;30:1354-1356.
4. Lage D, Juliano PB, Metze K, de Souza EM, Cintra ML. Lichen planus and lichenoid drug-induced eruption: a histological and immunohistochemical study. Int J Dermatol 2012;51:1199-1205.
5. West AJ, Berger TG, LeBoit PE. A comparative histopathologic study of photodistributed and nonphotodistributed lichenoid drug eruptions. J Am Acad Dermatol 1990;23(4 Pt 1):689-693.
6. Gaikwad RP, Mukherjee SS. Pirfenidone induced phototoxic reaction in an elderly man. Indian J Dermatol Venereol Leprol 2016;82:101-103.
7. Seto Y, Inoue R, Kato M, Yamada S, Onoue S. Photosafety assessments on pirfenidone: photochemical, photobiological, and pharmacokinetic characterization. J Photochem Photobiol B 2013;120:44-51.
8. Costabel U, Bendstrup E, Cottin V, Dewint P, Egan JJ, Ferguson J, et al. Pirfenidone in idiopathic pulmonary fibrosis: expert panel discussion on the management of drug-related adverse events. Adv Ther 2014;31:375-391. Erratum in: Adv Ther 2014;31:575-576.
9. Woo YJ, Sohn KM, Kang H, Kim JE. Pirfenidone-induced phototoxic reaction in a patient with idiopathic pulmonary fibrosis. Eur J Dermatol 2017;27:545-546.
10. Droitcourt C, Adamski H, Polat A, Polard E, Kerjouan M, Arnouat B, et al. Pirfenidone photosensitization in patients with idiopathic pulmonary fibrosis: a case series. Br J Dermatol 2018;178:e222-e223.
11. Jeong II, Lee HJ, Yoon MS, Kim DH. Pirfenidone-induced lichenoid drug eruption in a patient with idiopathic lung fibrosis. Ann Dermatol 2019;31:103-105.