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CASE REPORT

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Lichenoid drug eruption due to pirfenidone in a patient with idiopathic pulmonary fibrosis

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Abstract

Idiopathic pulmonary fibrosis (IPF) is a chronic progressive disease of unknown cause characterized by relentless scarring in the lung parenchyma, leading to decreased quality of life and early mortality. Pirfenidone and nintedanib have been approved for the treatment of IPF based on their ability to slow functional decline and disease progression. Lichenoid drug eruption (LDE) refers to a drug-induced eruption resembling lichen planus, typically presenting as purple, symmetrical, eczematous plaques. While skin reactions due to pirfenidone have been reported in numerous cases, pirfenidone-induced LDE is rarely observed. In this case, we present a rare instance of pirfenidone-induced LDE.

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Introduction

Idiopathic pulmonary fibrosis (IPF) is a chronic progressive age-related interstitial lung disease of unknown origin, with an average life expectancy of 3-5 years after diagnosis if left untreated (1). Pirfenidone is one of the two approved treatments for idiopathic pulmonary fibrosis (IPF). Randomized controlled clinical trials and subsequent analyses have shown that pirfenidone reduces the decline in lung function, decreases mortality, and improves progression-free survival (2). Known adverse effects include gastrointestinal symptoms, liver function impairment, or photosensitivity and skin rashes (3).

Case description

A 74-year-old male patient presented to our clinic with relatively well-defined erythematous plaques with dense scales on his hands, neck, face, and nape, and erythematous macular lesions on his trunk and legs, which began approximately three weeks ago (**Figure 1**). The patient had no mucosal involvement, and Wickham striae were not observed on dermoscopy. The patient had been diagnosed with IPF approximately two years ago and had been started on pirfenidone tablets. The pirfenidone dose was initiated at 600 mg/day and gradually increased to 2400 mg/day. With a preliminary diagnosis of LDE and photodermatitis, a punch biopsy was taken, and

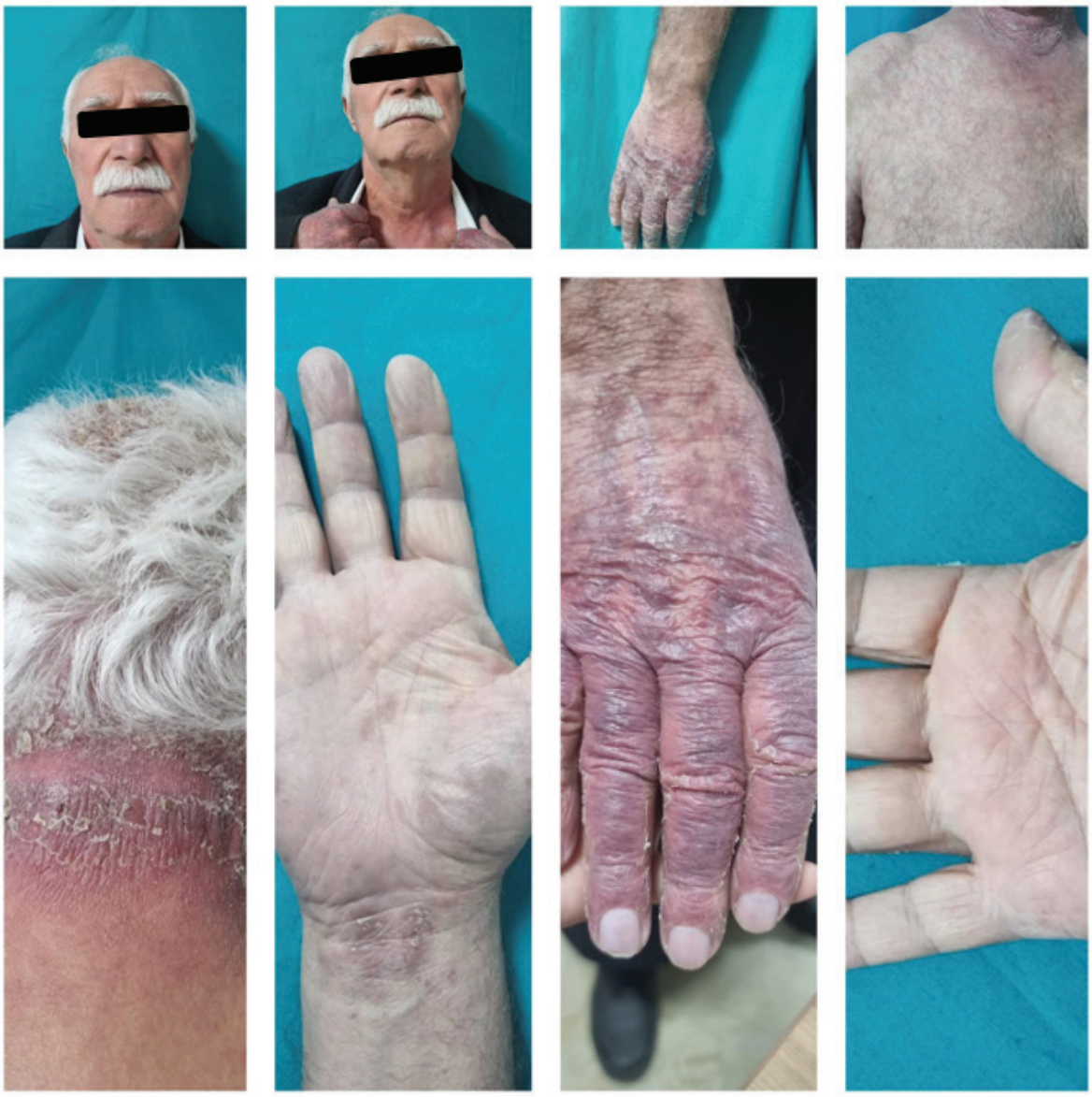

Figure 1: On the hands, neck, face, and nape, relatively well-defined erythematous plaques with dense scales, and on the trunk, erythematous macular lesions blanching with pressure.

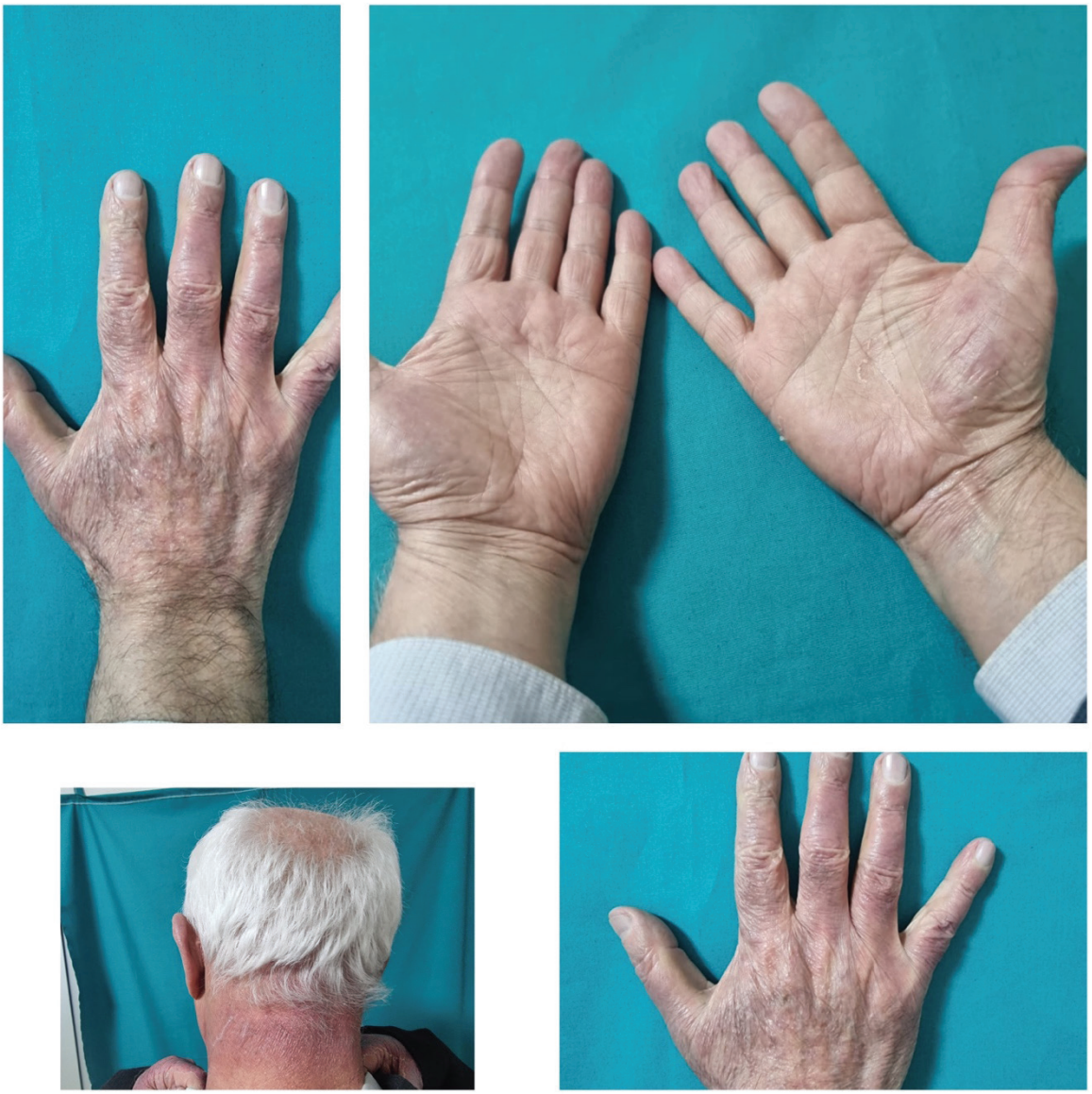

Figure 2: The complete regression of the lesions one month after the discontinuation of pirfenidone therapy.

the patient was consulted with chest diseases for discontinuation of pirfenidone therapy. The patient was started on methylprednisolone 32 mg/day, and topical corticosteroid therapy was added. One week later, the patient's rash had decreased, and systemic methylprednisolone therapy was gradually stopped. Approximately one month later, the patient's rash had completely regressed (**Figure 2**). The biopsy results showed orthoparakeratotic hyperkeratosis in the epidermis, microabscess formation in the keratinous layer due to excoriation with neutrophils and nuclear debris, mild spongiosis, irregular acanthosis, lymphocyte exocytosis in the epidermis, vacuolar degeneration in the basal layer, and scattered dyskeratotic keratinocytes in the epidermis, consistent with lichenoid interface dermatitis (**Figure 3**).

Discussion

Lichenoid drug eruption is a cutaneous drug reaction that mimics lichen planus. The lesions are typically purple, flat, and polygonal, resembling classical lichen planus. However, LDE is characterized by a pronounced polymorphism, including lichenoid, psoriasiform, and eczematiform lesions without Wickham striae. They tend to spread more symmetrically on the trunk and limbs and are more commonly found in photodistributed areas, rarely involving mucosa. Some histological findings such as scattered dyskeratotic

keratinocytes in the epidermis, vacuolar degeneration in the basal layer, absence of Wickham striae, and spontaneous resolution after discontinuation of the offending drug support the diagnosis of LDE (4).

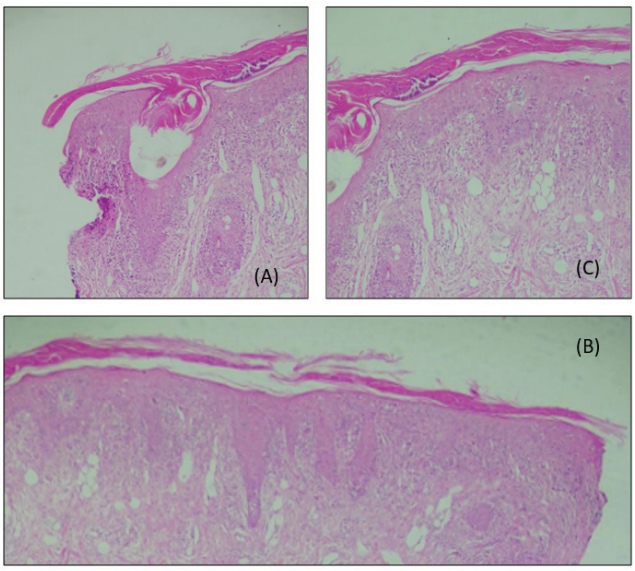

Figure 3: (A) Orthoparakeratotic hyperkeratosis on the surface and microabscess formation in the second keratinous layer due to excoriation with neutrophils and nuclear debris (H&E X200). (B) Spongiosis and irregular acanthosis with lymphocyte exocytosis in the epidermis (H&E X200). (C) Vacuolar degeneration in the basal layer and scattered dyskeratotic keratinocytes in the epidermis (H&E X200).

In our case, the patient's lesions were first suspected to be LDE and photodermatitis due to their location in photodistributed areas, and a punch biopsy was taken. The punch biopsy results showing parakeratosis, eosinophils, plasma cells, and dermal vascular infiltrations supported the diagnosis of LDE. Additionally, the absence of mucosal involvement, the absence of Wickham striae, and the resolution of lesions after discontinuing the drug also supported the diagnosis of LDE.

The patient's pirfenidone therapy was discontinued in consultation with chest diseases, and sun protection and avoidance of phototoxic drugs were recommended. No recurrence was observed during follow-up.

Numerous photosensitivity reactions due to pirfenidone have been observed, but LDE cases are rarely reported. In one case, a 75-year-old female patient was diagnosed with IPF and had been using pirfenidone for five months when LDE was observed two months after the dose increase. The pirfenidone dose was reduced, and the lesions were controlled with topical steroids (5). In another case, a patient with IPF who had been on pirfenidone therapy for approximately five months developed LDE two months after a dose increase, and the lesions healed with topical treatments, leaving pigmentation (6).

The mechanism by which pirfenidone causes lichenoid drug eruptions is not clear. Drug eruptions are generally mediated by T cells. Pirfenidone inhibits the TNF pathway. Lichenoid drug eruptions have been reported in many cases with drugs that inhibit this pathway. However, since pirfenidone does not solely use this pathway, more extensive research is needed to determine the exact mechanism by which pirfenidone causes lichenoid drug eruptions.

Pirfenidone-induced LDE cases are rarely observed. Our case is one of these rare cases, and we present it to contribute to the literature on pirfenidone-induced LDE cases. We have obtained consent for the publication of all photographs and pathological images of the patient.

Conclusions

This case report highlights a lichenoid drug eruption that developed after pirfenidone treatment. Although numerous photoallergic events related to pirfenidone have occurred, lichenoid drug eruptions are rarely observed. Pathology, in addition to clinical presentation, plays a significant role in diagnosis. By publishing this case report, we aim to contribute to the literature.

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Ethical approval: This is a case report. No need for ethical approval. This study was performed in line with the principles of the Declaration of Helsinki. Written and verbal consent was obtained from the patient.

Informed consent: Written informed consent was obtained from all individual participants and/or their gaurdians.

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Contributions

Research concept and design: MSC, CC, NC, MSO

Data analysis and interpretation: MSC, CC, NC, MSO

Collection and/or assembly of data: MSC, CC, NC, MSO

Writing the article: MSC, CC, NC, MSO

Critical revision of the article: MSC, CC, NC, MSO

Final approval of the article: MSC, CC, NC, MSO

All authors read and approved the final version of the manuscript.

References

1. Spagnolo P, Kropski JA, Jones MG, Lee JS, Rossi G, Karampitsakos T, et al. Idiopathic pulmonary fibrosis: disease mechanisms and drug development. Pharmacol Ther. June 2021;222:107798.
2. Lancaster LH, de Andrade JA, Zibrak JD, Padilla ML, Albera C, Nathan SD, et al. Pirfenidone safety and adverse event management in idiopathic pulmonary fibrosis. Eur Respir Rev. December 6, 2017;26(146):170057.
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 JEADV. August 2016;30(8):1354-6.
4. Tziotzios C, Lee JYW, Brier T, Saito R, Hsu CK, Bhargava K, et al. Lichen planus and lichenoid dermatoses: Clinical overview and molecular basis. J Am Acad Dermatol. November 2018;79(5):789-804.
5. Jeong IJ, Lee HJ, Yoon MS, Kim DH. Pirfenidone-Induced Lichenoid Drug Eruption in a Patient with Idiopathic Lung Fibrosis. Ann Dermatol. February 2019;31(1):103-5.
6. Yoo SA, Park HE, Kim M, Park HJ. A Case Report of Pirfenidone-Induced Lichenoid Drug Eruption in a Patient with Idiopathic Pulmonary Fibrosis. Ann Dermatol. April 2022;34(2):136-8.