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CASE REPORT

Dupilumab-Induced Generalized Lichen Planus: A Case Report

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Background: Lichen planus (LP) is a chronic inflammatory skin disease of unknown cause. Common subtypes include generalized LP, linear LP, annular LP, and hypertrophic LP. Current clinical evidence suggests that lichen planus is a T-cell-mediated autoimmune disorder. Therefore, an increasing number of clinicians are opting for biologics or immunomodulators to manage lichen planus, but the reported evidence on their efficacy and safety remains limited.

Case Summary: This case report describes a 32-year-old female with pre-existing localized lichen planus (LP) who developed generalized LP after IL-4Rα inhibitor dupilumab therapy. Following three dupilumab injections, progressive dissemination of pruritic pink-to-flesh-coloured or light-brown papules to the trunk and limbs was observed. The lesions regressed upon dupilumab discontinuation and pharmacological intervention. Diagnosis was confirmed by dermoscopy and histopathology.

Conclusion: A temporal correlation and Naranjo adverse drug reaction score of 8 indicated dupilumab as the trigger, likely via Th1/Th2 immune deviation. This first-documented paradoxical reaction underscores dupilumab's potential to trigger generalized LP through immune deviation.

Plain Language Summary:

What's already known about this topic?

- Dupilumab is a well-established IL-4Rα inhibitor that safely improves multiple type-2 inflammatory diseases, and existing small series have documented its use either to treat lichen planus or to cause de-novo lichen planus when prescribed for other indications.
- Paradoxical worsening of lichen planus after dupilumab has not previously been reported.

What does this study add?

- This report details the first documented case in which dupilumab, given to treat pre-existing localized lichen planus, precipitated generalized lichen planus after only three injections.
- It provides a high-certainty causality assessment (Naranjo score 8) and emphasizes the need for close monitoring for paradoxical immune deviation when dupilumab is used in patients with lichen planus.

Keywords: lichen planus, IL-4Rα inhibitor, dupilumab, immune deviation, adverse drug reaction

Introduction

Lichen planus (LP) is a chronic inflammatory skin disease of unknown cause. Erasmus Wilson first described it in 1869.[1] It typically affects tissues originating from the ectoderm, including the skin, mucous membranes, hair follicles, and nails.[2,3] Cutaneous lichen planus (CLP) affects approximately 0.22–1% of the population.[4] The global prevalence of oral lichen planus (OLP) is considerably higher than that of CLP, estimated at 0.22–5%. Failure to achieve timely diagnosis or

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treatment carries a risk of malignant transformation. Current research indicates that whether the misdirected immune response targets the skin or mucosal surfaces, pathogenesis primarily involves apoptosis within the stratum basale.[5,6] CLP displays significant clinical and morphological diversity. Common subtypes include generalized LP, linear LP, annular LP, and hypertrophic LP.[7] Typical skin lesions can be summarized by the "6 P's": Pruritic, Purple-colored, Polygonal-shaped, Planar, Papules, and Plaques.[8] These lesions most frequently appear on the flexural surfaces of the wrists, around the ankles, on the front of the lower legs, and over the sacral region. They are usually symmetrically distributed.[7] The intensity of itching varies significantly from person to person.[9]

The etiology and pathogenesis of this disease remain unclear; however, an increasing body of research and clinical evidence indicates that lichen planus is a T-cell-mediated autoimmune disorder. It is driven by an autoimmune response elicited when exogenous or self-antigens are presented by antigen-presenting cells (APCs), such as dendritic cells (DCs) or keratinocytes (KCs).

Diagnosis is based primarily on clinical features and is usually confirmed with dermoscopy and histopathologic examination of lesional skin. Dermoscopy typically reveals linear or dotted vessels arranged radially, together with white reticular streaks (Wickham striae).[10,11] Histopathologic hallmarks include hyperkeratosis, a wedge-shaped thickening of the granular cell layer, liquefactive degeneration of basal cells, and a band-like lymphocytic infiltrate in the upper dermis.[11–13]

In recent years, biologics and immunosuppressive agents have become increasingly common in clinical practice. Compared with immunosuppressants-which may heighten the risk of infection-biologics are regarded as safer, and both physicians and patients show greater willingness to adopt them. Dupilumab is a fully human monoclonal antibody, which is now routinely used for atopic dermatitis, alopecia areata, bullous pemphigoid, and several other skin disorders, all with favorable outcomes.[14]

Here we report a case in which generalized lichen planus was precipitated after dupilumab therapy, to raise awareness among clinicians and pharmacists. Even when using safer biologics, it's essential to record treatment progress and any drug reactions during clinical use. This documentation helps expand approved uses and identify side effects for future reference. The study was approved by the Ethics Committee of Dongzhimen Hospital Affiliated to Beijing University of Chinese Medicine, and written informed consent was obtained from the patient.

Case Presentation

A 32-year-old woman first attended our outpatient clinic on 12 December 2024. She reported that red, flat-topped maculopapules had appeared on her lower legs and dorsal feet in June 2024, accompanied by pruritus. She had applied calamine lotion for symptomatic relief, without further treatment. The lesions on the ankles persisted, gradually darkened, and became hypertrophic. In September 2024 an outside hospital performed a skin biopsy (Figure 1) that revealed hyperkeratosis, acanthosis, thickening of the granular layer, basal-cell liquefaction, occasional sub-epidermal micro-vesiculation, and a band-like lymphocytic infiltrate in the superficial dermis—findings consistent with lichen planus.

Dupilumab therapy was initiated on 11 October 2024: 600 mg at first time, followed by 300 mg every 2 weeks. After three injections the patient noted that each dose was followed by crops of new lesions on the limbs. With successive injections the eruption became more extensive and spread to the trunk. She therefore discontinued dupilumab. No further lesions appeared after cessation, and some pre-existing lesions began to fade, but the number of rashes has not decreased.

After the referring hospital raised the possibility of "flat warts", topical tretinoin was prescribed. The patient subsequently presented to our centre requesting CO_2 laser ablation. On dermatological examination she had numerous discrete, flat-topped, pink-to-flesh-coloured or light-brown papules scattered over the trunk and limbs; the ankles showed brown, hypertrophic, smooth-surfaced plaques. No lesions were present on the head, face, or neck.

To clarify the diagnosis, dermoscopy was performed first (Figure 2). She was started on an individualised Chinese herbal decoction and continued on topical tretinoin.

The patient returned for follow-up two weeks later. She reported that after taking the Chinese herbal decoction and topical tretinoin, the lesions had begun to desquamate and were slightly pruritic. On examination, several papules had flattened and were now level with the surrounding skin; the hypertrophic plaques on the ankles had likewise become less

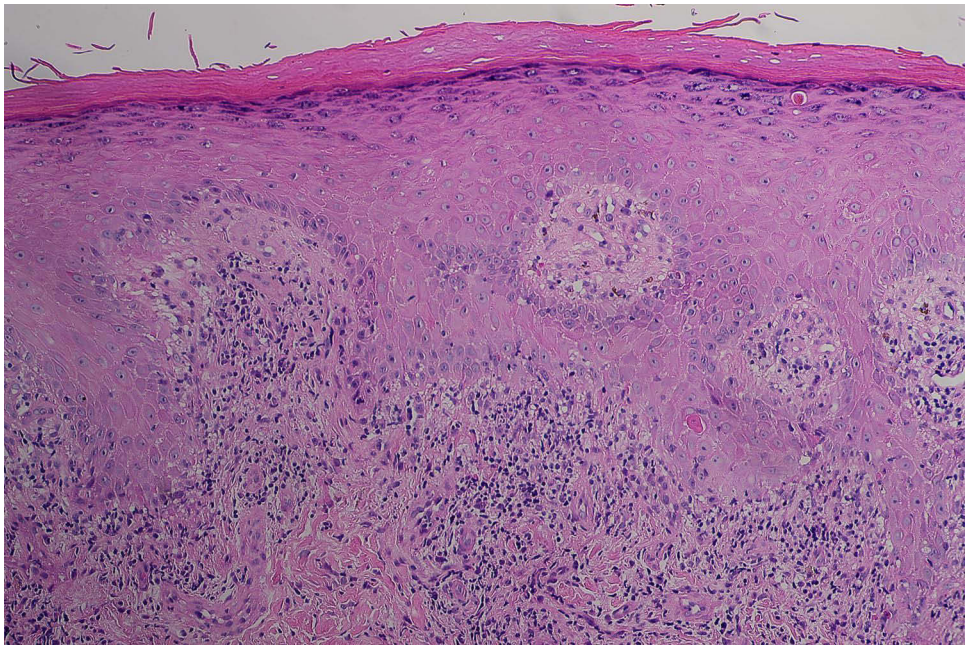

Figure 1 First skin biopsy (H&E staining).

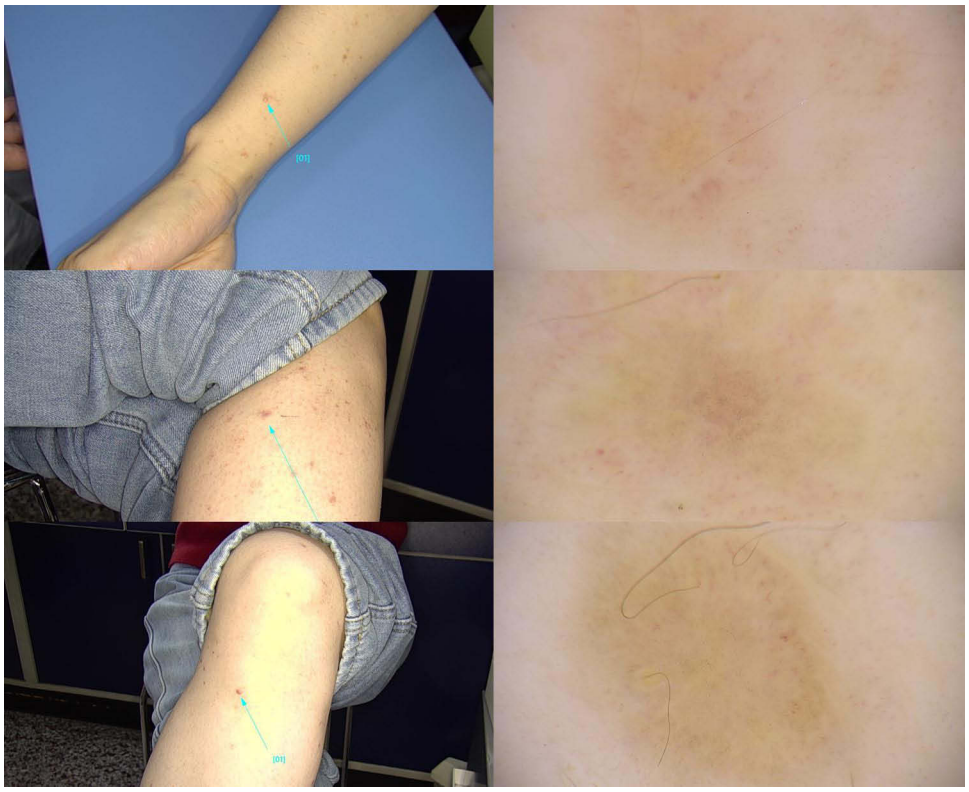

Figure 2 Dermoscopic findings of the generalized eruption.

raised and lighter in colour. No new lesions were observed. Dermoscopy (Figure 2) revealed: (1) white reticular structures and polygonal lesions, favouring lichen planus; (2) light-brown macules with a pseudonetwork and scattered dotted vessels, not excluding flat warts; (3) a large brown macule with a few atypical vascular structures at its periphery.

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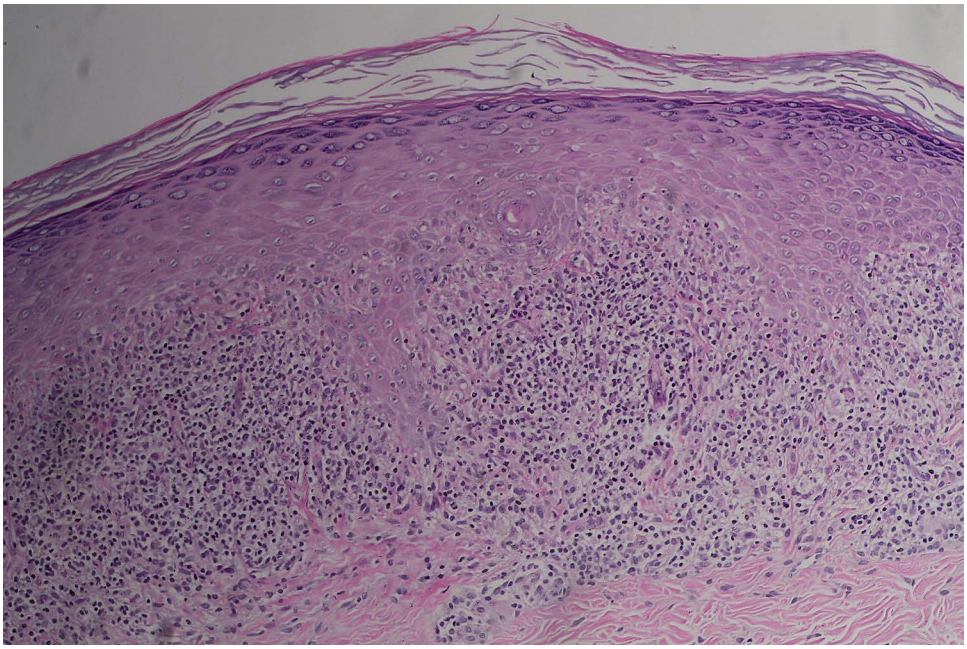

Figure 3 Second skin biopsy (H&E staining).

Histopathology (Figure 3) showed mild epidermal hyperplasia and a lichenoid lymphocytic infiltrate in the upper dermis, accompanied by rare eosinophils—findings consistent with lichen planus. The current regimen was continued.

Two weeks later the patient returned, reporting no new lesions and markedly reduced pruritus. On examination several lesions had resolved completely. The previous regimen was maintained.

After continuing the original regimen for another 6 weeks (during which no new lesions appeared and the eruption had faded to post-inflammatory hyperpigmentation), both the oral Chinese medicine and topical tretinoin were discontinued. A follow-up visit 12 weeks after stopping all therapy confirmed complete clearance of the lesions and further improvement of the residual hyperpigmentation.

Discussion

Based on the patient's clinical course and post-discontinuation outcome, we conclude that dupilumab-induced immune deviation precipitated generalized lichen planus. Using her detailed timeline and medication history, we completed the Naranjo Adverse Drug Reaction Probability Scale.[15] The key observations are: (1) Prior to dupilumab, she had stable, hypertrophic, localized lichen planus confined to the ankles, with no new lesions. (2) She received three dupilumab injections: the initial 600-mg dose was followed by two 300-mg doses. After every injection—especially the first—numerous new lesions erupted, so the total lesion count rose with each cycle. (3) She explicitly noted that, once she self-discontinued dupilumab, no further lesions appeared. (4) Both dermoscopy and histopathology corroborated the transformation from localized to generalized lichen planus, consistent with an immune-deviation phenomenon. Supported by objective evidence, the Naranjo adverse drug reaction score is 8, indicating that dupilumab is "probable" as the cause of the generalized lichen planus. The attending physician promptly reported the case to our clinical pharmacists, who then entered it into the Chinese National Adverse Drug Reaction Monitoring System.

Dupilumab is a fully human monoclonal antibody that binds to the interleukin-4 receptor α (IL-4Rα) and thereby blocks signaling of both IL-4 and IL-13. It has proven highly effective in disorders driven by type 2 inflammation. Regulatory approvals already cover atopic dermatitis (AD), prurigo nodularis (PN), asthma, chronic rhinosinusitis with nasal polyps (CRSwNP), and eosinophilic esophagitis (EoE).[16–21] Clinical trials have also demonstrated efficacy in chronic spontaneous urticaria (CSU),[22] chronic obstructive pulmonary disease (COPD),[23] bullous pemphigoid,[24] and

alopecia areata.[25] Beyond these indications, numerous case reports describe successful off-label use, underscoring the drug's expanding therapeutic reach.

Although biologics are generally regarded as safe and effective, their immunomodulatory effect essentially seeks a dynamic equilibrium within the immune system; when this balance is perturbed, off-target adverse reactions-now often termed "immune deviation"[26]-may emerge. Starting from the present case, we conducted a targeted literature review and found clinical studies supporting dupilumab as a therapeutic option for lichen planus,[27–33] as well as case reports in which dupilumab prescribed for other indications was followed by the new onset of lichen planus.[34–37] However, no publications describe dupilumab being used to treat lichen planus and subsequently triggering generalized lichen planus. Although the pathogenesis of lichen planus remains incompletely understood, current evidence links the disease to Th1-driven immunity; elevated serum IL-6 can induce IL-4 expression, thereby activating a Th2 response. Dupilumab may thus exert bidirectional control over lichen planus by readjusting the Th1/Th2 balance.[38,39]

While reviewing this case and similar adverse reaction reports, our hypothesis regarding immune shift as the cause still has limitations. If we encounter similar patients in the future, we will test key inflammation markers (including IL-4, IL-6, IFN-γ, and TNF-α) before and after dupilumab treatment. This will help measure Th1/Th2 activity and provide solid evidence for such clinical outcomes.

Conclusion

This case report presents a novel and paradoxical adverse reaction demonstrates that dupilumab may paradoxically trigger generalized lichen planus through immune deviation. Clinicians should consider this contradictory effect when managing patients on biologic therapy.

Abbreviations

LP, lichen planus; IL-4Rα, interleukin-4 receptor α; AD, atopic dermatitis; PN, prurigo nodularis; CRSwNP, chronic rhinosinusitis with nasal polyps; EoE, eosinophilic esophagitis; CSU, chronic spontaneous urticaria; COPD, chronic obstructive pulmonary disease.

Data Sharing Statement

Due to patient confidentiality, some data cannot be shared publicly. Further inquires can be directed to the corresponding author.

Statement of Ethics

Written informed consent was obtained from the patient for the publication of any potentially identifiable images or data included in this article. The Ethics Committee of Dongzhimen Hospital Affiliated to Beijing University of Chinese Medicine approved the study (No. 2025DZMEC-442-01).

Author Contributions

Hui-shang Feng, Chuang Zhang, Yang Guo, Tai Zhang, Bao-chen Zhu, Guo-dong Hua contributed to the conceptualization of the study. Yuan-ning Jia, Ye Zhai, Xiao-ran Zheng, Wan-tong Zhang contributed to investigation. Bao-chen Zhu and Hui-shang Feng prepared the original draft. All authors took part in revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have no financial or ethical conflict of interest regarding the content of the paper.

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