

Immune Deviation Following Dupilumab Therapy: A Case of Psoriasiform Dermatitis

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Abstract: A 72-year-old male presented with generalized maculopapular rash and nodules accompanied by pruritus for over 3 years, which had worsened over the past 2 months. During the disease course, he developed bullous pemphigoid (BP) and prurigo nodularis. He was treated with dupilumab. One year later, erythema and hypertrophic white scales appeared on both lower limbs. A skin biopsy from the right upper arm revealed elongated and downward extension of rete ridges, and perivascular lymphocytic infiltration in the superficial dermis. These findings were consistent with psoriasiform dermatitis. A previous biopsy during the BP phase showed subepidermal bullae and eosinophilic infiltration in the superficial dermis (Th2 phenotype). The diagnosis was dupilumab-associated immune deviation (psoriasiform dermatitis). This case suggests that in the context of overlapping Th2 diseases, immune deviation toward Th1/Th17 phenotype may occur during dupilumab therapy. However, it is often overlooked due to phenotypic overlap. Biopsy remains crucial for definitive diagnosis.

1. Case Summary

1.1. Chief Complaint

A 72-year-old male presented on April 13, 2026, with a 3-year history of generalized erythema, bullae, and nodules accompanied by intense pruritus, and a 2-month worsening with scaling.

1.2. Present Illness

The patient had developed these skin lesions without obvious cause 3 years ago. He was diagnosed with “prurigo nodularis” at a local hospital and improved slightly after symptomatic treatment. However, the lesions gradually increased and extended over the whole body. A skin biopsy was performed at our dermatology clinic. The pathology report showed “subepidermal bullae, with infiltration of lymphocytes and eosinophils around vessels in the superficial dermis and

within the bullae, and edema of dermal papillae” (Figure 1). The diagnosis of bullous pemphigoid (BP) was confirmed. He was treated with dupilumab (initial dose 600 mg, then 300 mg every 2 weeks) in combination with methylprednisolone and mycophenolate mofetil. The methylprednisolone and mycophenolate mofetil were gradually tapered and discontinued. After one year of treatment, erythema, papules, and scaling appeared on the whole body, predominantly on the extremities. Two months ago, these lesions worsened further. He was admitted to the hospital with the diagnoses of bullous pemphigoid, prurigo nodularis, and suspected psoriasis.

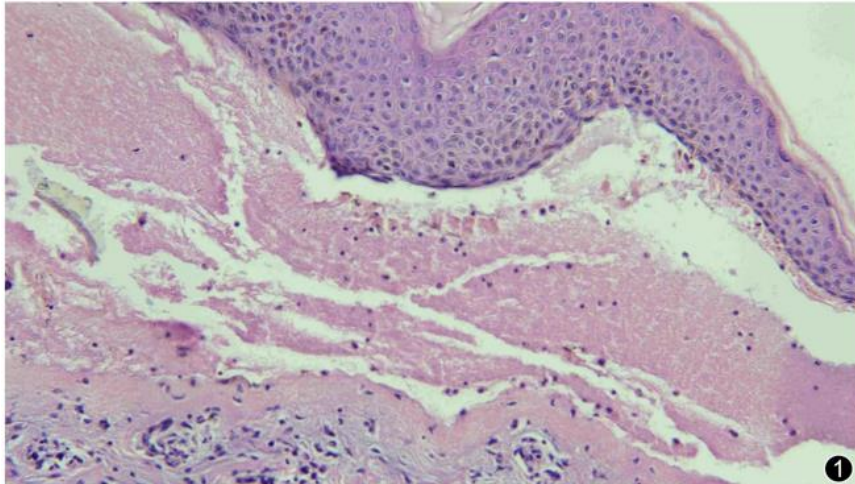


Figure 1. Bullous pemphigoid.

1.3. Past History

The patient had a 30-year history of hypertension and coronary heart disease. He had a 10-year history of diabetes mellitus. He also had a several-year history of chronic renal insufficiency. He denied any personal or family history of psoriasis.

1.4. Dermatological Examination

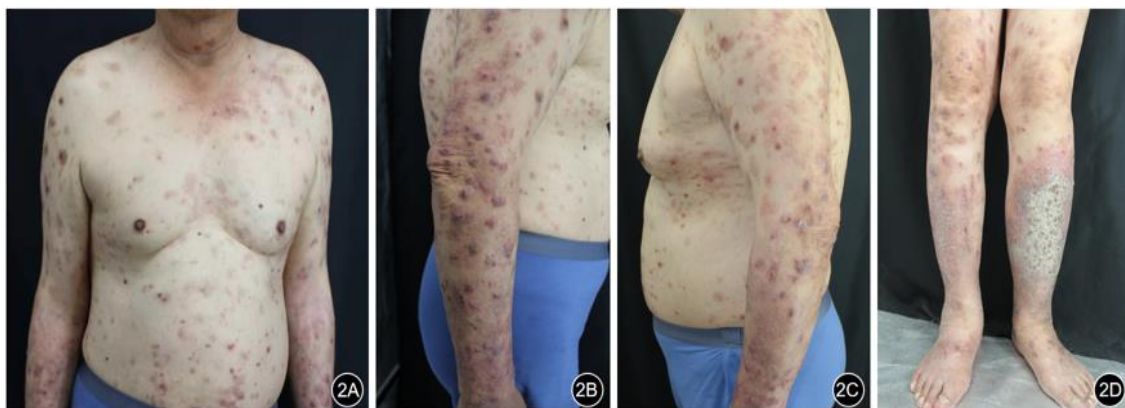


Figure 2. Skin lesion manifestations on the patient's trunk, upper limbs, and lower limbs. Trunk (2A), upper limbs (2B, 2C); lower limbs (2D).

Generalized erythematous macules and dark brown hyperpigmentation were observed on multiple sites. On the trunk and upper limbs, multiple papules and nodules ranging in size from soybean to broad bean were present, with firm consistency, accompanied by excoriations and ulcerations. On both lower limbs, patchy erythema with thick white scales were observed,

predominantly on the extensor surfaces, accompanied by excoriations and hemorrhagic crusts. Obvious edema was noted on both lower limbs, more severe on the left side. No bullae, pustules, erosions, or mucosal lesions were observed (Figure 2). The body surface area (BSA) involvement was 41%.

1.5. Auxiliary Examinations

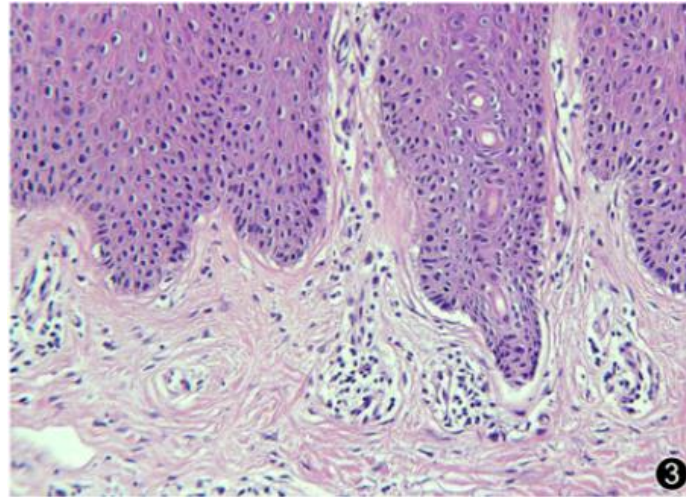


Figure 3. Histopathological findings of the skin lesion on the right upper arm.

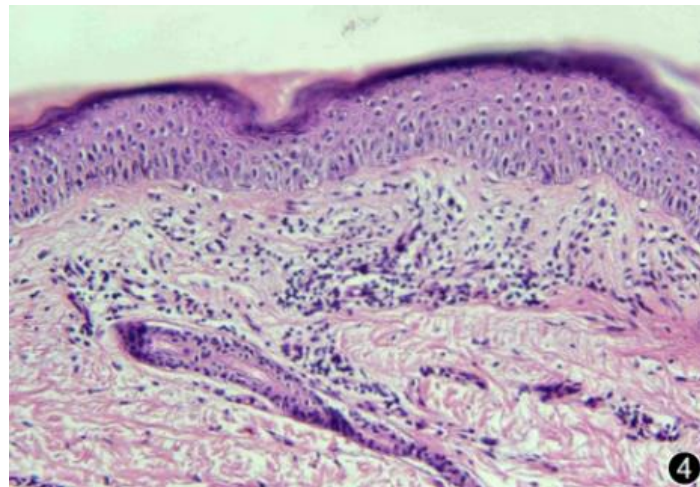


Figure 4. Histopathological findings of the skin lesion on the left thigh.

Complete blood count, urinalysis, immunoglobulin and complement levels, and liver and kidney function tests were generally within normal limits. Total IgE level, C-reactive protein level, and erythrocyte sedimentation rate were all within normal ranges. Antinuclear antibody panel was negative. Hepatitis B surface antigen, hepatitis C antibody, syphilis antibody, and HIV antigen/antibody were all negative. A skin biopsy from the right upper arm (current) showed surface hyperkeratosis, elongation and downward extension of rete ridges, and perivascular lymphocytic infiltration in the superficial dermis. The morphology was consistent with psoriasiform dermatitis (Figure 3). A skin biopsy from the left thigh (current) showed superficial perivascular inflammatory dermatitis. Chronic superficial dermatitis could not be excluded (Figure 4). A previous skin biopsy during the BP phase (before treatment) showed subepidermal bullae, with infiltration of lymphocytes and eosinophils around vessels in the superficial dermis and within the bullae, and

edema of dermal papillae (Figure 1).

1.6. Diagnosis

The patient was comprehensively diagnosed with three concurrent skin disorders: psoriasiform dermatitis, bullous pemphigoid, and prurigo nodularis. The psoriasiform lesions were confirmed to be a paradoxical immune deviation triggered by long-term dupilumab administration, supported by distinct pre- and post-treatment histopathological contrasts. No personal or family history of psoriasis ruled out spontaneous primary psoriasis.

1.7. Treatment and Outcome

During hospitalization, the patient received intravenous infusion of vitamin C and calcium gluconate, and topical application of compound flumetasone ointment and mometasone furoate cream on the skin lesions. After 2 weeks of treatment, the patient's pruritus partially relieved, and the scales on both lower limbs became thinner. However, the papules and nodules on the trunk and upper limbs showed no significant regression. Given that the psoriasiform lesions were considered to be associated with dupilumab, and that re-administration might carry a risk of exacerbation of immune deviation or other paradoxical reactions, the patient did not resume dupilumab after discharge. He was instructed to continue topical therapy for maintenance and to attend regular outpatient follow-up. At follow-up, the erythema and scales on both lower limbs further decreased compared with that at discharge. The prurigo nodularis lesions on the trunk and upper limbs remained in a chronic state. No new bullae were observed. The bullous pemphigoid was in clinical remission, and the patient's general condition was stable.

2. Discussion

Dupilumab inhibits the IL-4/IL-13 pathway and blocks Th2 inflammation. However, this may lead to compensatory activation of the unopposed Th1/Th17 axis. Clinically, this manifests as psoriasiform skin lesions, also known as “immune deviation” or “paradoxical reactions.”^[1] During dupilumab therapy for bullous pemphigoid and after discontinuation, the patient had persistent erythematous scaly lesions on both lower limbs. Biopsy after discontinuation confirmed psoriasiform dermatitis. The pre-treatment BP-phase pathology showed typical Th2 infiltration (predominantly eosinophils), while the post-treatment psoriasiform pathology showed a Th1/Th17 phenotype (lymphocytic infiltration and elongation of rete ridges)^[2]. This longitudinal comparison provided direct histological evidence for immune deviation.

The particularity of this case lies in the extremely strong baseline Th2 background. The patient had two overlapping Th2 diseases, bullous pemphigoid and prurigo nodularis, in succession. This demonstrates a potent Th2 immune response potential.

3. Conclusions

This case illustrates dupilumab-induced immune deviation from Th2 to Th1/Th17 inflammation in a patient with concurrent bullous pemphigoid and prurigo nodularis, confirmed by paired histopathology. Clinical implications of this case are as follows. For patients with multiple Th2 disease backgrounds, even after dupilumab discontinuation, vigilance should be maintained for delayed psoriasiform lesions. Regarding treatment strategy, if psoriasiform lesions overlap with bullous pemphigoid, switching to agents that inhibit multiple pathways, such as JAK inhibitors^[3], or switching to other biologics may be considered. Limitations of this case include that it is a single

case report, the lack of long-term follow-up data, and the lack of dynamic monitoring of serological biomarkers (e.g., BP180 antibodies). The exact mechanism of immune deviation still requires further investigation.

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