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CASE REPORT

A Case Report of Tislelizumab-Induced Lichen Planus Pemphigoides

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Abstract: Lichen planus pemphigoides (LPP) is a rare autoimmune subepidermal bullous disorder characterized by lichenoid lesions resembling lichen planus (LP) and bullous pemphigoid(BP). LPP may be triggered by medications, malignancies, or viral infections. Herein, we present a 67-year-old male patient with brain-metastatic non-small cell lung cancer (NSCLC) who developed pruritic violaceous plaques, tense bullae, and verrucous hyperplasia on the trunk and extremities following tislelizumab therapy. Histopathological examination confirmed LPP. The condition significantly improved with methylprednisolone combined with dupilumab treatment, and there was no recurrence during a 10-month follow-up.

Keywords: lichen planus pemphigoides, dupilumab, PD-1 inhibitors, tislelizumab, immune-related cutaneous adverse event

Introduction

Programmed cell death-1 (PD-1) inhibitors, such as tislelizumab, are widely used in advanced NSCLC due to their efficacy in enhancing antitumor immunity. However, immune-related adverse events (irAEs), particularly cutaneous toxicities, occur in 20–40% of patients.[1] These include rash/pruritus, vitiligo, granulomatous disease, psoriasis, BP, and LPP. LPP is a rare autoimmune blistering disease characterized by lichenoid interface dermatitis and subepidermal bullae, mediated by autoantibodies targeting type XVII collagen (COL17). Diagnosis requires histopathological confirmation, direct immunofluorescence (DIF) showing linear IgG/C3 deposition, and serological detection of anti-BP180/BP230 antibodies.[2] While corticosteroids remain first-line therapy, refractory cases necessitate alternative immunomodulatory agents. We report a case of tislelizumab-induced LPP successfully managed with systemic steroids and dupilumab, an interleukin-4 receptor alpha antagonist, underscoring its potential role in recalcitrant irAEs.

Case Presentation

A 67-year-old man was referred to the dermatology department for a 6-month history of severely pruritic, purplish-red papules, plaques, blisters, and verrucous hyperplasia involving the trunk and extremities. One year prior, the patient was diagnosed with lung adenocarcinoma with brain metastasis at an external hospital and subsequently received tislelizumab, which achieved disease control. Approximately 6 months ago, he developed violaceous papules, blisters, and plaques on both upper limbs, which gradually spread to the trunk and lower limbs, accompanied by intense pruritus and mild pain. Antihistamines and topical halometasone ointment were administered without significant improvement. Dermatological Examination revealed scattered erythema, papules, and nodules on the trunk and extremities, some papules exhibiting a glistening waxy film on the surface. Multiple erosions with verrucous hyperplasia were noted on the right foot, the largest measuring 3×3 cm. Most blisters had dried and formed crusts. Mucosal surfaces and nails remained unaffected (Figure 1A–C). Blood tests revealed an increased numbers of eosinophils (0.73 × 10^9/L; range 0.02–0.52). Ancillary Tests demonstrated elevated serum total IgE (1533.0 IU/mL, range 1.0–190.4),with low levels of anti- BP180

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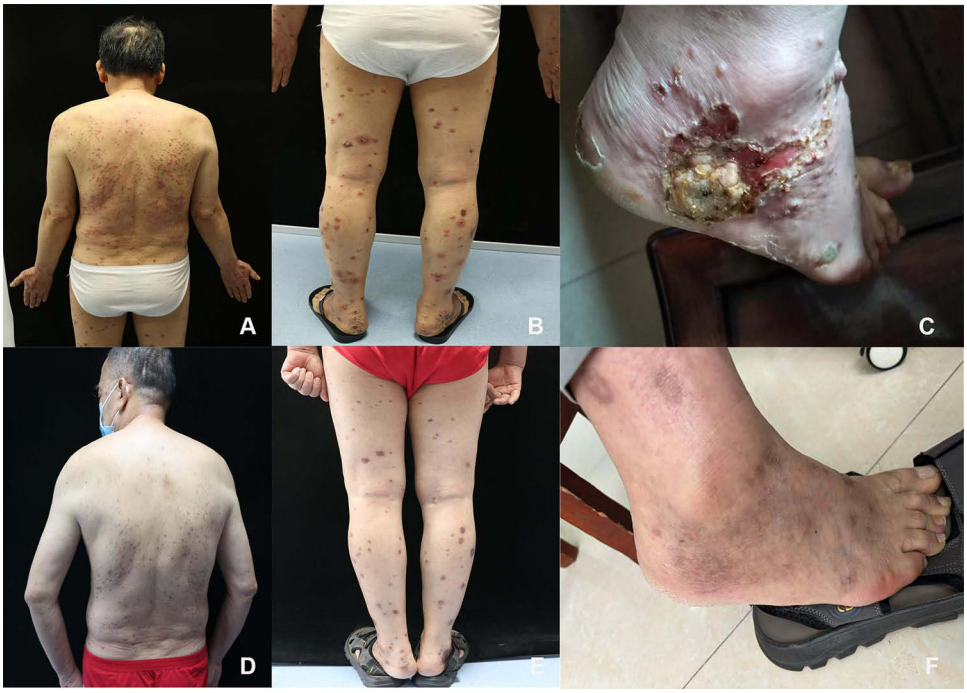

Figure 1 Clinical manifestations before and after treatment on the back, lower limbs and insteps. (**A**–**C**) Pretreatment findings: erythematous to violaceous flat papules, papulovesicles, macules, and ulcerations. (**D**–**F**) Post-treatment: resolution of papules, papulovesicles, and ulcerations, with residual post-inflammatory hyperpigmentation.

(11 u/mL; cutoff<20) and anti-BP230 (4 u/mL; cutoff<20). Histopathology of right thigh revealed hyperkeratosis, irregular acanthosis, marked spongiosis, eosinophil and lymphocyte exocytosis into the epidermis, focal basal cell liquefaction degeneration, superficial dermal edema, and subepidermal cleft formation. The superficial dermis demonstrated moderate band-like lymphocytic and eosinophilic infiltration, consistent with BP. Direct immunofluorescence (DIF) showed Ig G were deposited linearly in the epidermal basal membrane zone, with negative results for IgA, IgM, and C3 (Figure 2). Based on clinical presentation, histopathology, and DIF findings, the case was diagnosed as anti-PD-1 antibody-induced LPP.

The patient received intravenous methylprednisolone (50 mg/day), oral doxycycline (0.2 g/day), nicotinamide (600 mg/day), and topical clobetasol propionate and mupirocin ointments. Initial improvement was noted, and steroids were tapered. Upon reducing methylprednisolone to 30 mg/day, new erythematous papules emerged with severe pruritus and elevated IgE. Subcutaneous dupilumab (600 mg) was added, resulting in significant symptom relief and cessation of new blister formation. One week later, the patient's pruritus significantly subsided, with no new erythema or blisters, and

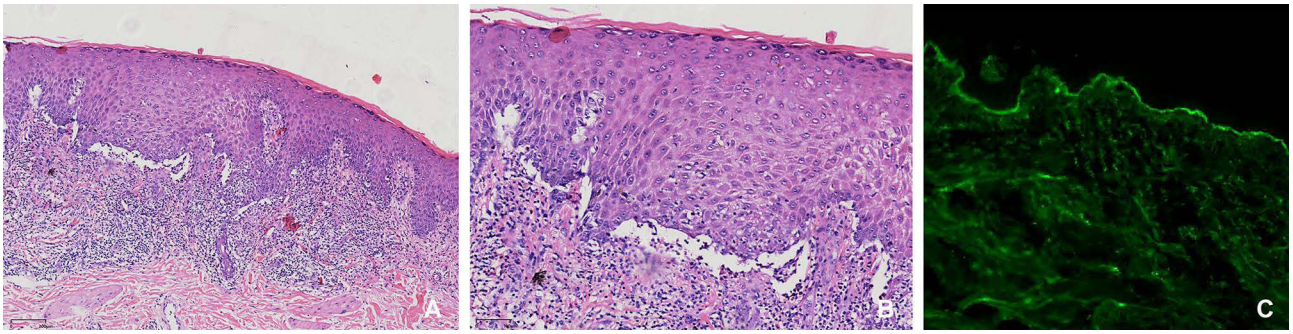

Figure 2 Histopathological features of skin biopsy (H&E staining). (**A**) Epidermal hyperkeratosis, acanthosis with edema, basal cell liquefaction degeneration, and band-like lymphocytic and eosinophilic infiltrates in the superficial dermis (H&E, ×20). (**B**) Higher magnification (H&E, ×100) demonstrating detailed inflammatory infiltrates and basal layer disruption. (**C**) Direct immunofluorescence (DIF) showed Ig G were deposited linearly in the epidermal basal membrane zone.

the original skin lesions gradually resolved. At a two-week outpatient follow-up, the patient refused to continue dupilumab injections due to financial reasons and was prescribed oral prednisone 15 mg once daily. The ulcers healed, the erythema decreased, and no new erythema or blisters appeared. The corticosteroid dose was gradually tapered. At a 12-month follow-up, prednisone was reduced to 5 mg every other day, and the patient experienced no pruritus or new erythema (Figure 1D–F).

Discussion

LPP is a rare autoimmune subepidermal bullous disorder characterized by overlapping features of LP and BP. Clinically, LPP typically begins with lichenoid papules or plaques, followed by the development of tense blisters on both normal-appearing skin and adjacent to LP lesions, predominantly on the extremities. Nails can also be involved, and oral mucosal involvement is less common. In terms of pathogenesis, lichenoid degeneration of the basal epidermis in LPP exposes antigens at the dermal-epidermal junction, triggering a breakdown in immune tolerance. This leads to the production of autoantibodies targeting type XVII collagen and other basement membrane zone components.[3] LP-like changes, such as hyperkeratosis, saw-toothed rete ridges, and band-like lymphocytic infiltrates, are observed in lichenoid papules. At blister sites, subepidermal clefts with intact basal keratinocytes overlying the blister cavity are noted, lacking typical LP histopathology. DIF of both lesional and perilesional skin reveals linear deposition of IgG and C3 along the basement membrane zone (BMZ). Approximately 50% of patients demonstrate circulating anti-BMZ antibodies on indirect immunofluorescence (IIF). Immunoblot studies identify reactivity to the 180-kDa (BPAG2) and 230-kDa (BPAG1) antigens, as well as a unique 200-kDa keratinocyte-derived antigen specific to LPP.[2] In our case, the patient's serum was negative for both BP180 and BP230. Therefore, further immunoblotting analysis is necessary to determine the specific type of linear deposit. However, due to limited available resources, additional experimental validation could not be performed. Based on the patient's clinical presentation, histopathological findings, and direct immunofluorescence results, a diagnosis of lichenoid pemphigus-like pemphigus erythematosus was made.[4] Clinicopathologic differentiation includes LP, BP, paraneoplastic pemphigus (PNP), erythema multiforme, atypical subacute cutaneous lupus erythematosus, and non-bullous pemphigoid.[1]

Programmed cell death receptor 1 (PD-1) inhibitors are increasingly utilized in the treatment of various malignancies. However, approximately 20–40% of patients treated with PD-1 inhibitors may develop cutaneous immune-related adverse events (irAEs). Tislelizumab, a novel PD-1 inhibitor, has been associated with diverse dermatologic toxicities, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), exfoliative dermatitis, psoriasis-like eruptions, vitiligo-like hypopigmented plaques, LPP, pemphigus herpetiformis-type drug reaction, and radiation memory dermatitis. Emerging evidence suggests that blockade of the PD-1 pathway may enhance the production of autoantibodies targeting BP180, thereby contributing to Lichen planus pemphigoides.[1]

Currently, there is no consensus on the optimal treatment regimen for LPP. Systemic and topical corticosteroids, combined with dapsone or acitretin, have demonstrated favorable clinical efficacy in managing this condition.[2] Treatment of LPP induced by immunotherapy included topical corticosteroids, systemic steroids, doxycycline, rituximab, and discontinuation of immunotherapy.[5] However, rituximab, a B-cell-depleting monoclonal antibody, carries a significant risk of infection due to its immunosuppressive effects.[6] The pathogenesis of LPP involves not only the classical interferon-γ (IFN-γ)-mediated T-helper 1 (Th1) response characteristic of LP but also a dysregulated Th2 immune response, which may contribute to bullae formation.[7] This dual mechanism highlights potential therapeutic targets for novel agents. The primary reasons for not administering rituximab, immunosuppressants, or JAK inhibitors to this patient are his underlying lung cancer with brain metastasis. The decision to omit omalizumab was based on the lack of significant urticaria-like symptoms. Instead, considering his elevated eosinophil count, high IgE levels, and pruritus, dupilumab was chosen as the most appropriate treatment. Dupilumab, a monoclonal antibody targeting the interleukin-4 receptor α (IL-4Rα) subunit, has shown success in treating BP, LP, non-bullous pemphigoid-like pemphigus, and Immune checkpoint inhibitors(ICIs)-induced eczematous eruptions, pruritus, and BP.[8,9] Unlike conventional immunosuppressants, dupilumab inhibits Th2-driven inflammation by blocking IL-4 and IL-13 signaling pathways, thereby reducing IgE production, eosinophil recruitment, and tissue destruction, while maintaining a favorable safety profile. Notably, IL-4Rα is highly expressed in solid tumors, and its activation may promote tumor proliferation, survival, and metastasis.[10] This

suggests that dupilumab may exert dual anti-inflammatory and potential antitumor effects. In our clinical experience, a patient with LPP exhibited persistent erythematous papules and pruritus despite systemic corticosteroid therapy. The addition of dupilumab resulted in lesion stabilization and marked symptom relief. Furthermore, dupilumab facilitated rapid disease clearance and allowed for accelerated corticosteroid tapering, underscoring its potential as a promising therapeutic option for LPP. Further studies are warranted to elucidate the precise cytokine networks in LPP pathogenesis and to optimize the safety, dosing, and duration of dupilumab in this context.

Conclusion

Checkpoint inhibitor therapy has become a cornerstone in cancer treatment; however, severe immune-related adverse events such as LPP may necessitate the interruption of antitumor therapy. Dermatologists increasing their awareness of LPP will help in the more accurate and timely diagnosis of LPP. Furthermore, the combination of systemic steroids and dupilumab emerges as a promising strategy for managing ICIs-induced LPP, leveraging dupilumab's favorable safety profile and targeted mechanism to potentially mitigate broad immunosuppression risks.

Abbreviations

LPP, Lichen planus pemphigoides; NSCLC, non-small cell lung cancer; BP, bullous pemphigoid; DIF, Direct immunofluorescence; LP, lichen planus; BMZ, basement membrane zone; PD-1,Programmed cell death receptor 1.

Ethics Statement

The patient provided written informed consent for publication of this report and accompanying images. The Ethics Committee of Guangzhou Dermatology Hospital, has approved the publication of the case details.

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Disclosure

The authors report no conflicts of interest in this work.

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