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# Successful Use of Dupilumab in Bullous Pemphigoid: A Series of 3 Cases in Mexico

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**ABSTRACT**

This review explores three recent case reports detailing the successful treatment of bullous pemphigoid (BP) with Dupilumab, a monoclonal antibody targeting interleukin-4 receptor alpha subunit (IL-4Rα). Each case highlights unique clinical presentations, treatment approaches, and outcomes, underscoring Dupilumab's potential as a therapeutic option in BP management.

**KEYWORDS:** Bullous pemphigoid, Dupilumab, Autoimmune blistering disease, IL-4 receptor alpha antagonist, Case series, Dermatology, Refractory bullous pemphigoid, Targeted therapy.

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## I. INTRODUCTION

Bullous pemphigoid (BP) is the most common autoimmune blistering disease, predominantly affecting the elderly, with an estimated prevalence of 12 to 13 cases per 100,000 persons per year (1). BP is characterized by subepidermal blistering and the presence of autoantibodies against hemidesmosomal proteins BP180 and BP230 (2). Standard treatments primarily involve systemic corticosteroids and immunosuppressive agents, which often lead to significant side effects, especially in the elderly population (3).

Despite conventional treatment, approximately 20-30% of BP patients are refractory to standard therapies, resulting in persistent disease activity and increased morbidity (4). Long-term use of corticosteroids and immunosuppressive agents is associated with adverse effects such as infections, diabetes, hypertension, and osteoporosis, complicating the management of BP (5). For instance, a recent study highlighted that around 25% of BP patients experience severe side effects from prolonged corticosteroid use (6).

Advances in understanding the immunopathogenesis of BP have underscored the roles of interleukin-4 (IL-4) and interleukin-13 (IL-13) in disease progression (7). Dupilumab, a monoclonal antibody targeting the IL-4 receptor alpha, inhibiting both IL-4 and IL-13 signaling, has shown efficacy in treating atopic dermatitis and other inflammatory diseases (8). Recent case studies and trials have suggested that Dupilumab may be effective in managing refractory BP, offering a targeted therapeutic approach with a potentially favorable safety profile (9).

This article presents three cases of BP successfully managed with Dupilumab, providing evidence for its potential use as a targeted therapy in patients who are refractory to conventional treatments.

### *A. Assessment:*

Complete remission is defined as an absence of new or established lesions or pruritic symptoms while the patient with minimal therapy or off therapy for at least 3 months.

Partial improvement is defined as the presence of transient new lesions that healed within 1 week, healing of at least 50 % of lesions.

## II. CASE PRESENTATION

### *A. Case 1:*

A 72-year-old male with a history of squamous cell carcinoma in the oral cavity. A skin biopsy reported BP. He was treated with oral corticosteroid with partial response. Later He was treated with Dupilumab 300mg monthly. He showed partial improvement within 4 weeks of treatment. and showed complete remission within 12 weeks of initiating Dupilumab therapy. Clinical assessment revealed reduced blister formation and pruritus, with no adverse events reported during follow-up.

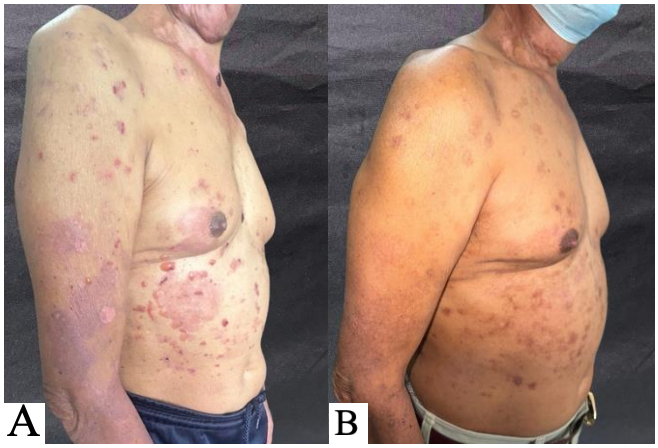


**Figure 1. Clinical presentation before and after dupilumab therapy in patient A) Exudative and hemorrhagic crusts over the trunk and upper limbs. B) Follow up showing complete remission of bullae with treatment after 12 weeks.**

***B. Case 2:***

A 72-year-old male with a history of squamous cell carcinoma in the oral cavity. A skin biopsy reported BP. He was treated with oral corticosteroid with partial response. Later He was treated with Dupilumab 300mg monthly. He showed partial improvement within 4 weeks of treatment. and showed complete remission within 12 weeks of initiating Dupilumab therapy. Clinical assessment revealed reduced blister formation and pruritus, with no adverse events reported during follow-up.

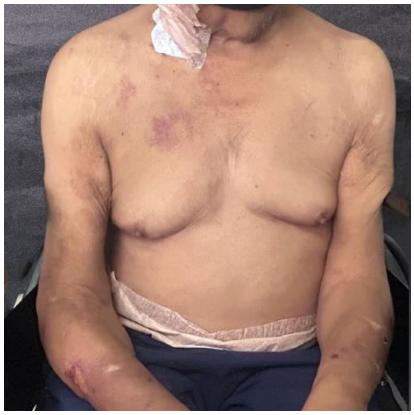

**Figure 2. Clinical remission after 4 weeks of treatment**.

***C. Case 3:***

A 72-year-old male with a history of squamous cell carcinoma in the oral cavity. A skin biopsy reported BP. He was treated with oral corticosteroid with partial response. Later He was treated with Dupilumab 300mg monthly. He showed partial improvement within 4 weeks of treatment. and showed complete remission within 12 weeks of initiating Dupilumab therapy. Clinical assessment revealed reduced blister formation and pruritus, with no adverse events reported during follow-up.

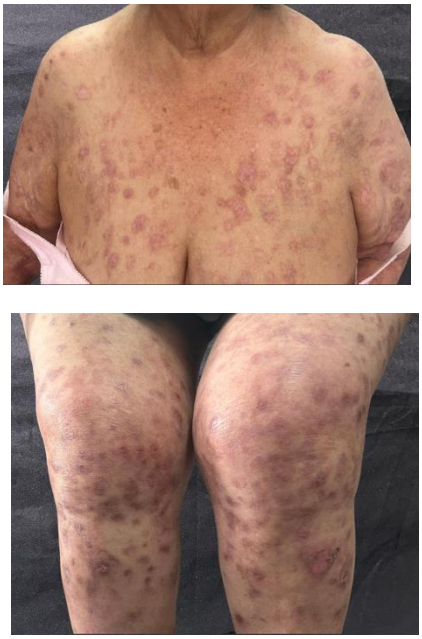

**Figure 3. Clinical remission, lesions resolved with post-inflammatory hyperpigmentation after 8 weeks of treatment.**

**III.DISCUSSION**

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These case reports provide compelling evidence for the efficacy of Dupilumab in the treatment of bullous pemphigoid (BP), particularly in cases refractory to conventional therapies (9). The mechanisms underlying Dupilumab's therapeutic effects in BP are likely multifaceted (11). By inhibiting interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling pathways, Dupilumab modulates Th2-driven immune responses implicated in BP pathogenesis (11). These cytokines play pivotal roles in B cell activation, antibody production, and tissue inflammation, suggesting that their blockade could mitigate autoimmune processes leading to blister formation and skin damage (11).

Moreover, Dupilumab's immunomodulatory properties extend beyond Th2 cytokine inhibition (11). Studies have shown that IL-4 and IL-13 contribute to epithelial barrier dysfunction and eosinophil recruitment, which are hallmark features of BP pathology (12). By restoring barrier integrity and reducing eosinophilic infiltration, Dupilumab may exert a dual therapeutic effect in BP, addressing both the underlying immunological dysregulation and the resultant tissue damage (11).

Clinically, the rapid and sustained responses observed in some cases in the literature presents a promising alternative to traditional therapies, particularly for patients who are refractory to standard treatments. (10,12). The timely resolution of blistering, erosions, and pruritus without significant adverse events highlights its favorable safety

profile and tolerability in elderly patients, who are often more susceptible to adverse effects associated with systemic corticosteroids and immunosuppressants (10,12)

Liang et al. and Smith et al., administered an initial dose of 600 mg, followed by 300 mg every two weeks (10). This regimen mirrors the dosing schedule approved for atopic dermatitis, and it was found to be effective in reducing disease activity in BP patients within two weeks of initiation (10,12). Similar to the reported cases, Dupilumab was typically initiated at a induction dose of 600mg subcutaneously and continued with a maintenance dose of 300 mg every two weeks. Patients in our case series experienced substantial reduction in blister formation and pruritus within 2 to 4 weeks. Complete remission was observed within 4 to 12 weeks, which is relatively rapid compared to the prolonged courses often required with traditional medications (3).

The time to achieve significant clinical improvement with Dupilumab was notably shorter compared to conventional therapies (3). While standard treatments with corticosteroids and immunosuppressants can take several months to control BP symptoms (3). Further, one of the key advantages of Dupilumab is its favorable safety profile, especially for long-term use (7). Unlike corticosteroids, which are associated with severe adverse effects such as osteoporosis, diabetes, and infections, Dupilumab has been shown to have a lower risk of systemic side effects, making it a viable option for long-term management of BP (7).

Despite these promising findings, several questions remain regarding the long-term safety and durability of Dupilumab therapy in BP management (3). While the reported cases demonstrate short to medium-term efficacy, larger prospective studies are needed to evaluate its effectiveness in diverse patient populations and to assess potential risks such as infection susceptibility and immunogenicity (11)

Furthermore, elucidating patient-specific factors predictive of treatment response and optimizing treatment protocols will be crucial in maximizing Dupilumab's therapeutic benefits in BP (11). Future research should aim to clarify the optimal duration of therapy, potential for combination with other immunomodulators, and mechanisms underlying treatment resistance to refine clinical guidelines and improve outcomes for BP patients (7).

## CONCLUSIONS

In conclusion, successful outcomes reported in these case series support Dupilumab as a promising therapeutic option for bullous pemphigoid refractory to conventional treatments. Continued research efforts are warranted to further define its role in BP management and to address remaining uncertainties regarding long-term efficacy and safety.

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