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LETTER TO THE EDITOR

WILEY

Effectiveness and safety of Dupilumab for the treatment at 104 weeks of recalcitrant bullous pemphigoid

Bullous pemphigoid (BP) is an autoimmune disease characterized by the occurrence of subepidermal blistering classically caused by immunoglobulines (Ig) G1/G4 directed against the structural proteins BP-180 and BP-230.[1] Less frequently, the autoantibodies belong to the IgE subgroup.[2] The 1st line treatment is represented by oral corticosteroids, while 2nd line therapy includes immunosuppressants, plasmapheresis and antibiotics which still present limitations in terms of efficacy and adverse events.[3]

A caucasian 74-year-old male presented at our clinic in August 2020 with a 6-months history of new-onset bullous lesions disseminated all over the trunk and limbs. The medical history was positive for pancreatic adenocarcinoma and urothelial bladder cancer. A biopsy of the lesional and perilesional skin revealed subepidermal bullae with linear IgG and C3 deposit at the dermal-epidermal junction; moreover, it was registered the presence of circulating autoantibodies anti-BP180 (112.3 U/mL; cutoff <9). A diagnosis of BP was made and

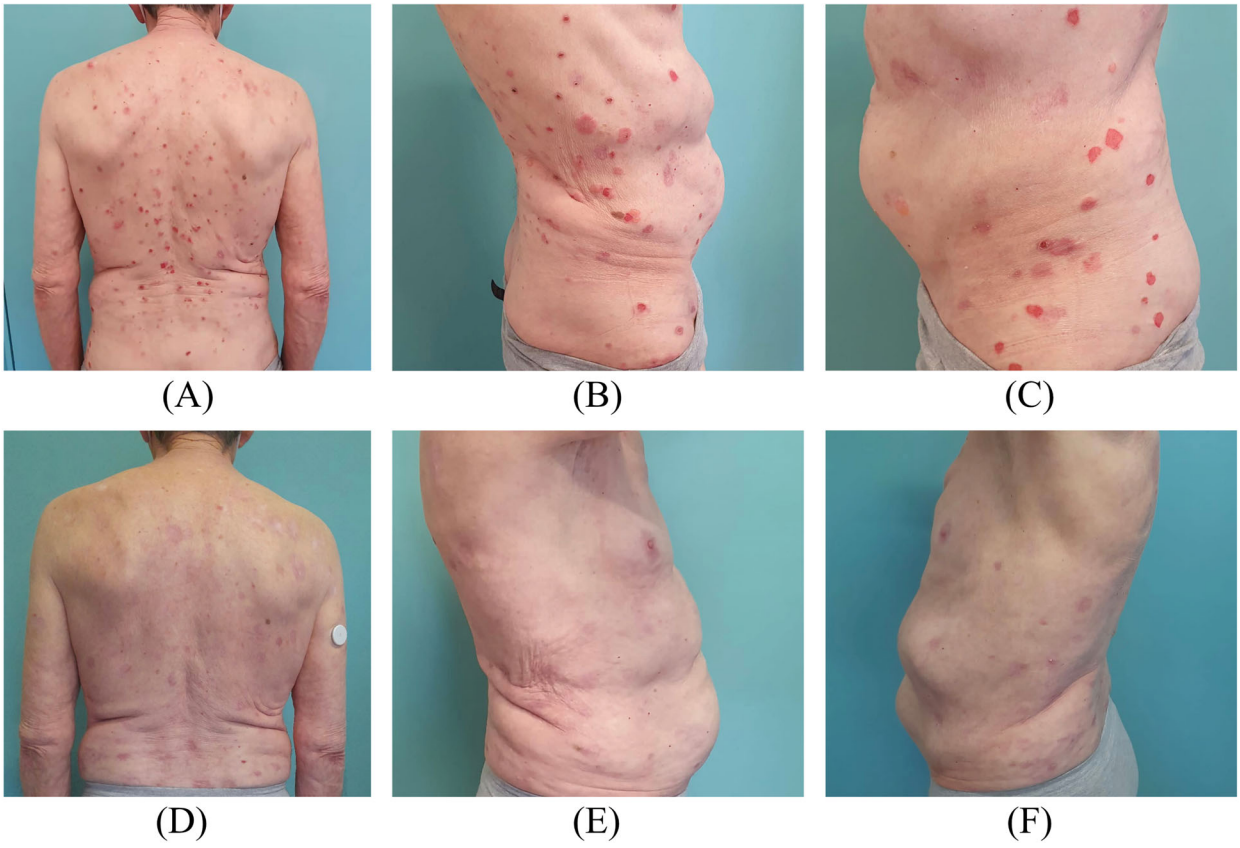

FIGURE 1 Case of the patient with recalcitrant bullous pemphigoid treated with Dupilumab. (A–C) Clinical Images taken at week 0 (Bullous Pemphigoid Disease Area Index: 36). (D–F) Clinical images taken at week 104 (Bullous Pemphigoid Disease Area Index: 0).

Abbreviations: BP, Bullous pemphigoid; Ig, Immunoglobuline; Th, T-helper.

TABLE 1 Trend of clinical disease scores and blood tests.

	Week 0 (May 2021)	Week 16 (September 2021)	Week 32 (February 2022)	Week 52 (May 2022)	Week 104 (May 2023)
BPDAI pruritus score	18/30	1/30	0/30	0/30	0/30
BPDAI	36/120	5/120	1/120	0/120	0/120
IgE	596 U/mL	341 U/mL	259 U/mL	206 U/mL	134 U/mL
Anti-BP180	125.1 U/mL	115.9 U/mL	102 U/mL	93.5 U/mL	24 U/mL

Abbreviations: BP, bullous pemphigoid; BPDAI, bullous pemphigoid disease area index; IgE, immunoglobulin E.

the patient started to be treated with Prednisone 25 mg/day, Nicotinamide 250 mg/day, Doxycycline 200 mg/day and topical Clobetasol. In October 2020 Dapsone 100 mg/day was added to the initial therapy, with subsequent complete resolution in January 2021. Once the Dapsone was tapered off, a flare of bullous lesions occurred in May 2021. Given the lack of BP control, it was decided to stop Dapsone and, since clinical history contraindicated the use of traditional immunosuppressants, subcutaneous injections of Dupilumab (600 mg, followed by 300 mg every 2 weeks) in combination with low dose of Prednisone 5 mg/day were started. At week0 anti-BP180 (125.1 U/mL; cutoff <9) and total serum IgE were both elevated (596 U/mL). At week 16 the bullae and pruritus had completely resolved. Given the therapeutic outcome, in October 2021 Prednisone was discontinued. At week 104, BP remained in complete resolution without itching (Figure 1) and with progressively decreasing levels of total IgE and anti-BP180 (134 and 24 U/mL, respectively). During the treatment, the patient did not experience any side effects.

BP is characterized by the overexpression of T-helper (Th) 2 cytokines that play a central role in the pathogenesis of blister formation and pruritus.[4] Patients with BP also show increased serum levels of total IgE and peripheral eosinophils that would contribute to blister formation and correlates with the severity of the disease.[5] Dupilumab is a fully human monoclonal antibody that targets the IL-4 receptor alpha (IL4Rα) resulting in the inhibition of IL-4/IL-13 signaling; moreover, it is able to reduce IgE serum levels.[5] The drug would therefore block a double pivotal Th-2 pathogenetic pathway of BP and literature data suggest that it could represent a valid therapeutic alternative for patients not responsive to standard therapies.[4,5] We reported a case of a patient with BP who was successfully treated with Dupilumab for 104 weeks (Figure 1) and that showed complete remission of the disease accompanied by a consistent reduction in total serum IgE with a mild, progressive, reduction of anti-BP180 (Table 1). This could be related to a shutdown of the pathogenetic mechanisms mediated by the proinflammatory Th-2 axis that sustain BP180 antibodies formation. On the other side, remission could be linked to the reduction of putative specific IgE anti-BP180 already shown in literature as possible pathogenic drivers of the condition[3], even if they were not dosed in our clinical case. Although IgE levels are not a predictor of Dupilumab response that is classically used even in non-IgE-mediated type of atopic dermatitis,[4] a future suggestion could concern the dosage of total serum IgE in patients with BP as a marker of type 2 inflammation to enhance the identification of the immunological profile of patients eligible for Dupilumab therapy.

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The patients in this manuscript have given written informed consent to publication of their case details.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available from the corresponding author on request.

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