Successful treatment of Brunsting-Perry pemphigoid with dupilumab

Franklin R. Blum, BS,[a] and Justin R. Sigmon, MD[b]
Chapel Hill and Asheville, North Carolina

Key words: Brunsting-Perry pemphigoid; cicatricial pemphigoid; dupilumab.

INTRODUCTION

Brunsting-Perry pemphigoid (BPP), a variant of cicatricial pemphigoid, is an autoimmune disease characterized by tense, pruritic bullae with subsequent atrophic scar formation. BPP, which most commonly affects older men, is characterized by preferential cutaneous involvement of the head, face, and neck, with rare mucosal involvement.[1,2]

The pathogenesis of BPP involves an autoantibody-mediated attack on the epidermal basement membrane. Specifically, autoantibodies targeting laminin 332, type VII collagen, and BP180 have been identified.[2,3] In BPP, autoreactive IgG targets these basement membrane proteins with subsequent deposition of C3 complement,[4] which is visualized by direct immunofluorescence. This autoimmune cascade continues with local recruitment of lymphocytes and other inflammatory mediators, resulting in a lymphocytic infiltrate with significant eosinophilia that is characteristic of BPP.[5] As seen on histologic examination, this inflammatory process results in obliteration of the epidermal attachment to the basement membrane, with subsequent formation of bullae in the newly created space between the basement membrane and the epidermis.

Treatment of BPP is often challenging because of the advanced age and comorbidities of the patients. As a variant of cicatricial pemphigoid, mild cases of BPP may be treated with potent topical corticosteroids, whereas moderate-to-severe disease typically requires systemic therapy with immunosuppressive drugs such as prednisone, azathioprine, mycophenolate mofetil, and cyclophosphamide.[6] These systemic therapies carry increased risks of adverse effects, including infection and malignancy.

Abbreviations used:

BPP:	Brunsting-Perry pemphigoid
FDA:	Food and Drug Administration
IL-4:	interleukin 4
IL-13:	interleukin 13

This case presents the use of dupilumab, a monoclonal antibody that blocks the actions of interleukin 4 (IL-4) and interleukin 13 (IL-13), to treat BPP. Dupilumab has been proven safe and efficacious for the treatment of atopic dermatitis, asthma, and chronic sinusitis with nasal polyposis.[7] It has shown immunologically that secretion of IL-4 and IL-13 by helper T cells results in immune activation, increasing IgE production by B cells and recruiting eosinophils to sites of inflammation. IL-4 and IL-13 have also been identified as potent mediators of tissue fibrosis.[8] In BPP, lymphocytosis with eosinophilia, elevated levels of basement membrane IgG, and tissue scarring with fibrosis are essential to disease pathogenesis, presenting a probable mechanism of the action of dupilumab therapy in BPP.

CASE REPORT

A 71-year-old man presented to our dermatology clinic with a bullous, scarring, and pruritic rash on the lateral aspect of the left side of the neck that had been ongoing for many years. On physical examination, he was noted to have erythematous plaques consisting of bullae and erosions on a background of fibrosis and scarring (Fig 1). No oral mucosa or ocular involvement was identified on examination. In previous years, punch biopsies had been performed on lesional and perilesional skin on his neck for

From the University of North Carolina Chapel Hill School of Medicine[a] and Forest Dermatology, Asheville.[b]
Funding sources: None.
IRB approval status: Not applicable.
Correspondence to: Justin R. Sigmon, MD, 1119 Hendersonville Rd #200, Asheville, NC 28803. E-mail: jrsigmon@gmail.com.
JAAD Case Reports 2021;10:107-9.
2352-5126

https://doi.org/10.1016/j.jdcr.2021.02.010

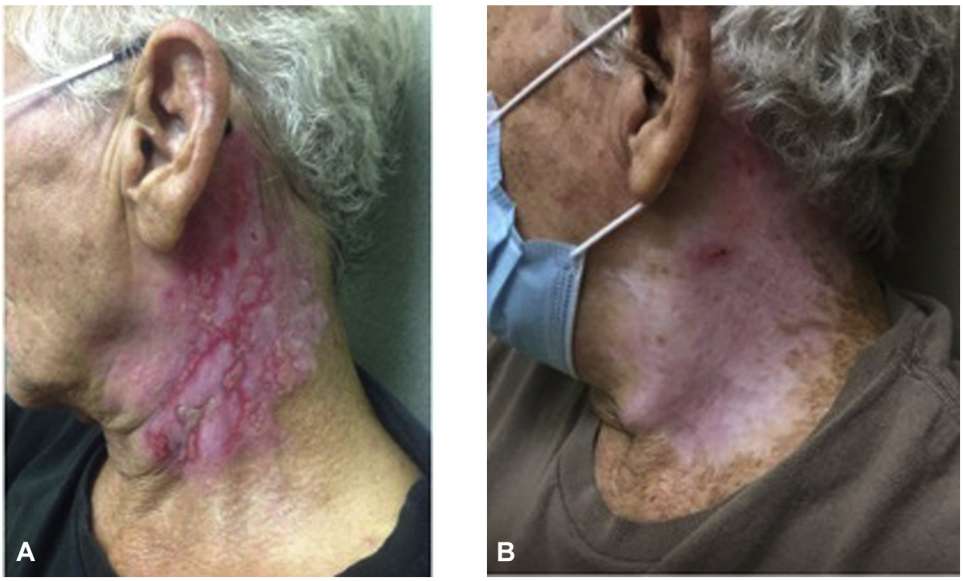

Fig 1. Brunsting-Perry pemphigoid before (left) and after (right) dupilumab therapy. Before dupilumab therapy, the rash showed erythematous plaques with bullae, erosions, and surrounding scarring on the lateral aspect of the left side of the neck. Postinflammatory hypopigmentation and scarring remained after 6 months of dupilumab therapy.

histopathologic examination. Hematoxylin and eosin staining of lesional skin showed subepidermal bullae with an associated superficial and mid-dermal perivascular infiltrate consisting of lymphocytes, histiocytes, plasma cells, and eosinophils. Direct immunofluorescence of perilesional skin demonstrated a thick, meshy, linear IgG with weaker C3 deposition along both the dermal and the epidermal sides of the salt-split epidermal basement membrane, consistent with cicatricial pemphigoid. Indirect immunofluorescence was not performed. Given his clinical presentation and characteristic histologic findings, a diagnosis of BPP was made. He was given trials of potent topical steroids and mycophenolate mofetil in various combinations with prednisone, which he used for years with minimal to no improvement. He then went for several years without follow-up until eventually returning back to our clinic for re-evaluation. At his return, he was using only petroleum jelly for symptomatic improvement.

At his follow-up visit, dupilumab injections were initiated using the loading dose of 600 mg that is Food and Drug Administration (FDA) approved for atopic dermatitis, followed by 300-mg doses every other week for 6 weeks. Rapid improvement and clearance were noted after the first 3 doses of dupilumab (Fig 1). He has maintained these results for 6 months with monthly 300-mg injections of dupilumab. He still reports an occasional bulla and mild pruritus, but overall, his disease is much more manageable and his quality of life has significantly improved.

DISCUSSION

BPP can be a difficult condition to treat, especially when patients are older, have many comorbidities, and do not respond well to topical steroids or traditional treatment regimens. In this case, mycophenolate mofetil, prednisone, and topical steroids were implemented with minimal to no improvement. Subsequently, treatment with dupilumab improved the patient's BPP, and he remains clear after 6 months of follow-up. Although dupilumab is often used to treat diseases such as atopic dermatitis, asthma, and chronic sinusitis with nasal polyposis, its function as an anti-IL-4 and anti-IL-13 monoclonal antibody points to a probable application in the treatment of BPP, as both interleukins are integral to recruiting eosinophils and other inflammatory mediators involved in the pathogenesis of BPP.

This patient achieved significant remission of his BPP after initiation of dupilumab, with no side effects. Currently, there are no FDA-approved therapies for BPP, and many patients must use off-label immunosuppressive medications such as prednisone. In elderly patients, this greatly increases the risk of adverse events such as bone fracture, infections, and malignancy. The safety profile of dupilumab appears to be far superior to that of prednisone and the other currently used systemic therapies, including oral antibiotics, mycophenolate mofetil, and cyclophosphamide. Currently, dupilumab is FDA approved only for atopic dermatitis, asthma, and rhinosinusitis with nasal polyposis.[8]

Although reports of the use of dupilumab for treatment of other bullous diseases (eg, bullous pemphigoid) have been published, a PubMed search using the terms "dupilumab" and "Brunsting-Perry pemphigoid" found no reports of BPP successfully treated with dupilumab. However, one case report identified the potential use of dupilumab in the treatment of cicatricial pemphigoid.[9] Successfully treating this patient's BPP with dupilumab illustrates the need for more studies to further elucidate the potential benefit of dupilumab in patients with BPP.

Conflicts of interest

None disclosed.

REFERENCES

1. Brunsting LA, Perry HO. Benign pemphigoid?: a report of seven cases with chronic, scarring, herpetiform plaques about the head and neck. *AMA Arch Derm*. 1957;75(4):489-501.
2. Jedlickova H, Niedermeier A, Zgažarová S, Hertl M. Brunsting-Perry pemphigoid of the scalp with antibodies against laminin 332. *Dermatology*. 2011;222(3):193-195.
3. Asfour L, Chong H, Mee J, Groves R, Singh M. Epidermolysis bullosa acquisita (Brunsting-Perry pemphigoid variant) localized to the face and diagnosed with antigen identification using skin deficient in type VII collagen. *Am J Dermatopathol*. 2017;39(7):e90-e96.
4. Joly P, Ruto F, Thomine E, et al. Brunsting-Perry cicatricial bullous pemphigoid: a clinical variant of localized acquired epidermolysis bullosa? *J Am Acad Dermatol*. 1993;28(1):89-92.
5. Fukuda S, Tsuruta D, Uchiyama M, et al. Brunsting—Perry type pemphigoid with IgG autoantibodies to laminin-332, BP230 and desmoplakins I/II. *Br J Dermatol*. 2011;165(2):433-435.
6. Kourosh AS, Yancey KB. Therapeutic approaches to patients with mucous membrane pemphigoid. *Dermatol Clin*. 2011;29(4):637-641.
7. Simpson EL, Bieber T, Guttman-Yassky E, et al. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. *N Engl J Med*. 2016;375(24):2335-2348.
8. Food and Drug Administration. Dupixent. Accessed September 24, 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761055s007lbl.pdf
9. Kaye A, Gordon SC, Deverapalli SC, Her MJ, Rosmarin D. Dupilumab for the treatment of recalcitrant bullous pemphigoid. *JAMA Dermatol*. 2018;154(10):1225-1226.