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A Unique Triad of Bullous Pemphigoid: Coexistence of Classic, Vegetans, and Drug-Induced Phenotypes

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Abstract

Bullous pemphigoid (BP) is an autoimmune blistering disease that mainly affects the older population. The clinical presentation typically involves tense blisters, but some atypical variants may occur, including pemphigoid vegetans. The disease can also be triggered by certain medications. Here, we report the case of a 74-year-old male who exhibited a complex clinical journey encompassing three clinical phenotypes of BP: classic, vegetans, and suspected lisinopril-induced BP. He initially presented with tense bullae on both upper and lower limbs, as well as on the trunk. Histological examination of a biopsied lesion, along with direct and indirect immunofluorescence, confirmed the diagnosis of BP. The patient demonstrated resistance to 30 mg prednisolone and dupilumab therapy for over a year, requiring intravenous immunoglobulin rescue. Subsequent emergence of vegetative and suspected drug-induced lesions further complicated the case; however, he showed marked clinical and serological improvement following the withdrawal of lisinopril and the addition of mycophenolate mofetil to prednisolone and dupilumab. At three months of follow-up, there were no new vegetative or bullous lesions. This case highlights an uncommon combination of three different forms of BP. Increased awareness of the atypical forms of BP is necessary for early diagnosis and correct treatment.

Categories: Dermatology
Keywords: autoimmune blistering skin disease, bullous pemphigoid (bp), drug-induced bullous pemphigoid, mycophenolate mofetil (mmf), pemphigoid vegetans

Introduction

Bullous pemphigoid (BP) is a chronic, relapsing-remitting autoimmune blistering disease that primarily affects older adults. It is mediated by autoantibodies directed against two structural components of the hemidesmosome: BP180 and BP230 [1]. The typical clinical presentation involves generalized, intense pruritus, with or without urticarial and/or papular lesions, followed by the eruption of tense blisters on normal or erythematous skin. However, the cutaneous manifestations of BP can be extremely polymorphic, with atypical variants including the erythrodermic, nodular, and vegetans forms [2].

Pemphigoid vegetans is an exceptionally rare variant characterized by vegetating, verrucous plaques, usually in intertriginous and acral regions. Clinically, it resembles pemphigus vegetans, but shows histological and immunopathological features of BP [3].

In addition, some medications are known to be suspected triggers for inducing or exacerbating BP, including lisinopril, and the exact mechanism is not completely understood [4].

Here, we report the complicated journey of a patient who portrayed three clinical patterns of BP: classic, vegetans, and drug-induced.

Case Presentation

A 74-year-old male with type 2 diabetes mellitus, hypertension, recurrent cerebrovascular accident (CVA), protein S deficiency, right carotid artery stenosis, and hydrocephalus. He was a non-smoker, did not consume alcohol, and had been chair-bound and disoriented since his last CVA in 2021. His medications on presentation included dapagliflozin, metformin, sitagliptin, clopidogrel, amlodipine, and atorvastatin.

In March 2025, he was diagnosed with BP and had a generalized baseline of intensely pruritic eczematous and urticated lesions on his trunk, upper, and lower limbs, along with tense blisters on the dorsum of both hands and feet. Scattered blisters were also noted on the arms and trunk (Figure *1*).

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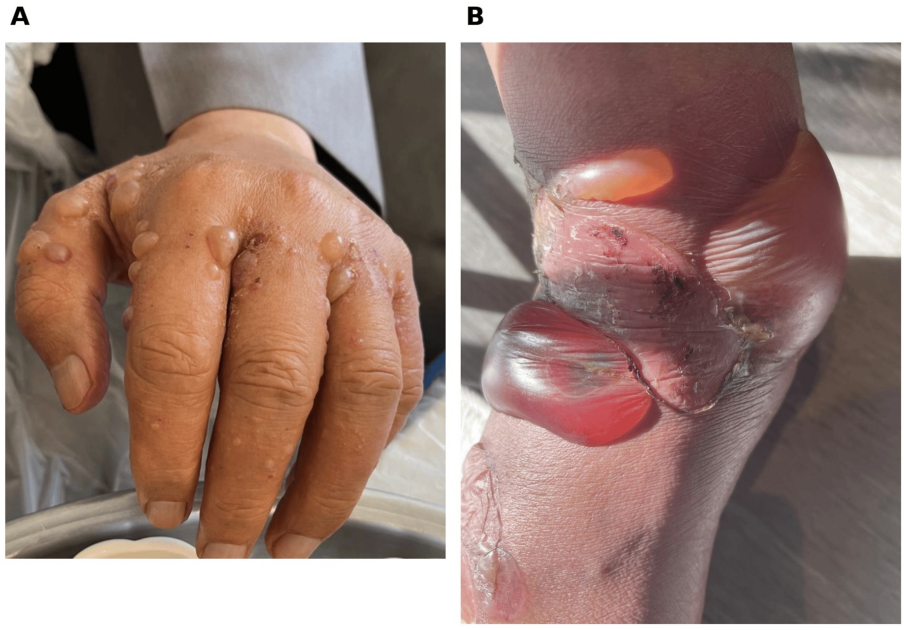


FIGURE 1: Clinical photographs of the first presentation of bullous pemphigoid

(A) Tense blisters over the dorsum of his left hand. (B) Multiple blisters over the left foot.

A biopsy was taken for direct immunofluorescence; it showed positive linear deposition of IgG and C3 at the dermal-epidermal junction. Indirect immunofluorescence also confirmed the diagnosis of BP with linear deposition on monkey esophagus and human split skin substrates. Anti-BP180 titer was 70.28 and anti-BP230 titer was 96.038 (Table *1*). Histopathological examination demonstrated eosinophilic spongiosis and mild perivascular lymphocytic infiltrate (Figure *2*).

Diagnostic test	Finding / result	Reference range
Direct immunofluorescence (DIF)	Positive linear deposition of IgG and C3 at the dermal-epidermal junction	Negative
Indirect immunofluorescence (IIF)	-	-
• Monkey esophagus (MO)	Positive linear deposition	Negative
• Human split skin (SS)	Positive linear deposition to the epidermal side (titer up to 1:100)	Negative
ELISA autoantibody testing	-	-
• Anti-BP180	70.28 U/mL	≥9 U/mL (positive)
• Anti-BP230	96.038 U/mL	≥9 U/mL (positive)

TABLE 1: Baseline immunological workup

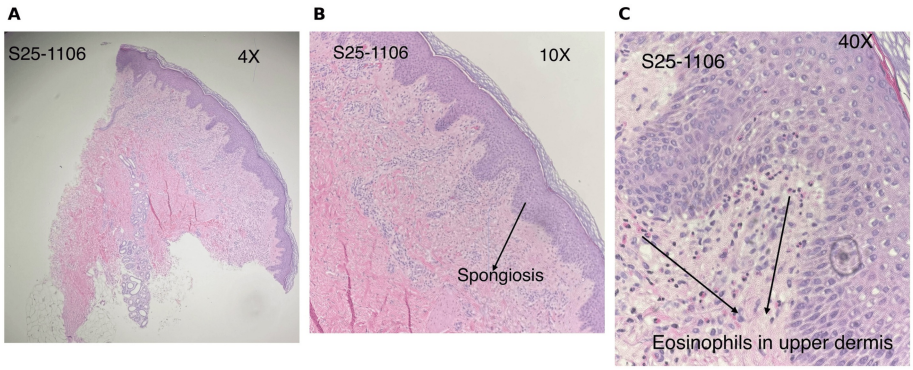


FIGURE 2: Histopathological examination of the first presentation of bullous pemphigoid (BP)

(A) Hematoxylin and eosin (H&E) stain, 4x, demonstrating mild spongiosis, edema in papillary dermis, and interstitial eosinophils with mild perivascular lymphocytic cell infiltrate. (B) and (C) Higher-power H&E views 10x and 40x, showing mild spongiosis and eosinophils in the upper dermis.

He was started on prednisolone 30 mg OD and clobetasol ointment to be applied to active bullae BD. There were no new lesions at follow-up three weeks later, so prednisolone was tapered down. After a few months of the disease being under control with prednisolone 5 mg OD, the patient started erupting new tense blisters, especially on the arms, groin, and the dorsum of his left hand. He was started on dupilumab 600 mg loading dose and then 300 mg every two weeks while continuing on prednisolone 5 mg OD.

Upon follow-up two weeks later, the patient was still experiencing a severe flare of BP with multiple blisters on the arms, legs, and trunk. Therefore, his prednisolone dose was increased to 30 mg OD. He then developed a rapidly progressive course of BP despite being on prednisolone (0.5 mg/kg), so he was admitted to receive a five-day course of IVIG (400 mg/kg/day). Following IVIG rescue therapy, the disease stabilized; old lesions healed, and no new blisters formed, so a cautious prednisolone taper was re-initiated while also being on dupilumab.

Unfortunately, while tapering the steroid one year after the diagnosis, he developed vegetative pemphigoid lesions (pemphigoid vegetans) on his arms and legs (Figure *3*). Upon biopsy, there was dermal edema and superficial perivascular lymphocytic infiltrate with interstitial eosinophils (Figure *4*). Repeat indirect immunofluorescence reflected this altered state, showing persistently high titers of anti-BP230 and only mild improvement in anti-BP180 levels compared to baseline pre-treatment values (Table *2*). Thus, prednisolone was increased again to 35 mg OD, and he was put on mycophenolate mofetil 500 mg OD with a goal of incrementing the dose to 2 g/day, while still receiving dupilumab once every two weeks.

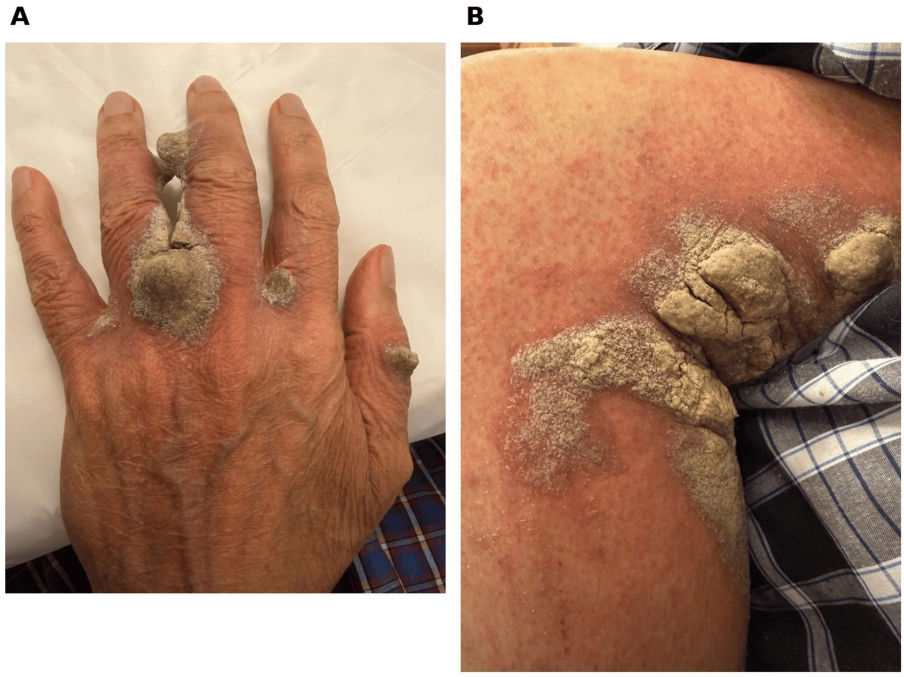


FIGURE 3: Clinical photographs of pemphigoid vegetans

(A) and (B) vegetative lesions on the dorsum of his left hand and right lower limb, resepctively.

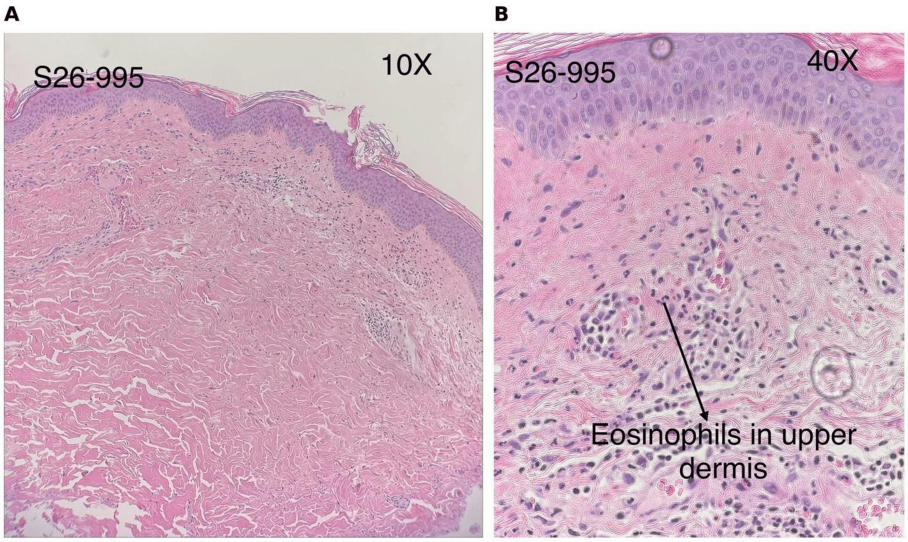


FIGURE 4: Histopathological examination of a vegetative lesion

(A) Hematoxylin and eosin (H&E) stain, 10x, demonstrating dermal edema and superficial perivascular lymphocytic infiltrate with interstitial eosinophils. (B) Higher-power H&E view, 40x, highlighting neutrophils in the upper dermis.

Diagnostic test	Pre-treatment (at the time of diagnosis of pemphigoid vegetans)	Post-treatment (after the addition of mycophenolate mofetil)	Reference range
Indirect immunofluorescence (IIF)	-	-	-
• Human split skin (SS)	Positive linear deposition to the epidermal side up to 1:100	Positive linear deposition to the epidermal side up to (1:100)	Negative
ELISA autoantibody testing	-	-	-
• Anti-BP180	33.661 U/mL	14.199 U/mL	≥ 9 U/mL (Positive)
• Anti-BP230	109.937 U/mL	18.263 U/mL	≥ 9 U/mL (Positive)

TABLE 2: Pre- and post-treatment immunological workup (pemphigoid vegetans)

Concurrently, a dull, violet plaque bordered by a thin, active inflammatory margin was seen on his lower limbs, denoting the possibility of drug-induced BP, as this occurred when amlodipine was switched to lisinopril. The rest of his medications remained unchanged.

The patient throughout follow-ups was monitored for treatment-induced myelosuppression, hepatotoxicity, and opportunistic infections.

Following the addition of mycophenolate mofetil to the treatment regimen and the withdrawal of lisinopril, our patient experienced significant clinical improvement at the three-month follow-up, marked by the resolution of vegetative and drug-induced skin lesions. This clinical response was paralleled by a notable decrease in anti-BP 180 and anti-BP 230 antibody titers (Table *2*).

Discussion

This case illustrates an unusual degree of clinical heterogeneity within a single patient. The evolution from classic BP to pemphigoid vegetans represents a rare presentation of tissue remodelling and localized proliferation. Pemphigoid vegetans was first described in 1979 by Winkelmann and Su. It is similar to pemphigus vulgaris in that it manifests as pustular and vegetative lesions in the inguinal, axillary, hand, thigh, eyelid, and perioral regions. However, it is histologically consistent with BP, with subepidermal bullae with superficial papillary dermal edema and prominent eosinophilic inflammatory infiltrate [3,5] and linear IgG deposits at the basement membrane [6-8]. These findings mirror the histopathological findings observed in our patient's biopsy.

The pathogenesis of pemphigoid vegetans is still unknown, but the persistently high titers of anti-BP230, which our patient's serology highlighted, may play a role in the vegetative lesions. Some cases in the literature revealed that the anti-BP230 titers decreased after improvement of the lesions, which supports the involvement of these antibodies in the pathogenesis of pemphigoid vegetans. Other speculated causes include bacterial infection of the primary lesions and an eosinophilic infiltration [3,7].

Only a few cases have been reported in the literature (around seven cases), and most of them have been successfully treated with topical and/or oral antibiotics or steroids. Other treatment modalities mentioned in the literature include minocycline, tacrolimus ointment, ketoconazole cream, and dapsone, but unfortunately, our patient has been steroid-resistant and had recurrent relapses of the vegetative lesions [5,6]. In a case reported by Mathieu et al., mycophenolate mofetil was used with favourable outcomes for the vegetative lesions. Mycophenolate mofetil is a modulator of the adaptive immune system and an established corticosteroid-sparing agent in BP. Assuming a similar pathogenesis, there is a strong rationale for its use in pemphigoid vegetans [6]. Aligning with their findings, our patient’s vegetative lesions improved with mycophenolate mofetil, with a reduction in anti-BP 180 and anti-BP 230 autoantibody levels.

Drug-associated BP (DABP) is one of the many forms of BP that our patient demonstrated after starting lisinopril. It is a subset of BP that is caused by the ingestion or application of certain medications; up to 80 medications have been associated with DABP up to this point. The clinical manifestation of this subset varies widely, as the findings may be similar to BP or may resemble a drug reaction or even a dermatitis [9]. The overall clinical progression of DABP remains unclear, but it generally follows one of two patterns: either acute, self-limited, and resolves upon cessation of the responsible drug, or chronic form that is

indistinguishable from idiopathic BP, which may require prolonged management [10]. Our patient mostly developed the second, chronic form, following initiation of lisinopril, an ACE inhibitor, which was reported to induce bullous pemphigoid [4]. The mechanism by which ACE inhibitors induce BP is not well known, but one hypothesis suggests that they may possess hapten-like properties or an ability to potentiate the kinin pathway and lead to a proinflammatory state [9,11]. Nonetheless, their hapten-like properties remain more accredited [10]. Early clinical recognition of DABP allows for earlier management and improved patient quality of life [12].

Conclusions

This case highlights the diagnostic and therapeutic difficulties of managing a patient who concurrently manifested three patterns of bullous pemphigoid: classic, suspected DABP, and the exceedingly rare vegetans variant. To our knowledge, this is the first case in the literature where one patient exhibited more than two variants of BP. The clinical pictures of these entities vary, but histopathology and immunofluorescence of the lesions support a diagnosis of bullous pemphigoid.

In this challenging, multimorbid scenario, dupilumab alone failed to provide adequate steroid-sparing control after a year of treatment, and escalation to IVIG and addition of mycophenolate mofetil were required to induce remission.

A high index of clinical suspicion is needed to identify the atypical variants of bullous pemphigoid in order to ensure correct diagnosis and management.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Fatma AlAmiri, Doaa AlAwadhi

Acquisition, analysis, or interpretation of data: Fatma AlAmiri, Doaa AlAwadhi

Drafting of the manuscript: Fatma AlAmiri, Doaa AlAwadhi

Critical review of the manuscript for important intellectual content: Doaa AlAwadhi

Supervision: Doaa AlAwadhi

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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References

1. Akbarialiabad H, Schmidt E, Patsatsi A, et al.: Bullous pemphigoid. Nat Rev Dis Primers. 2025, 11:12. 10.1038/s41572-025-00595-5
2. Bolognia JL, Jorizzo JL, Schaffer JV: Chapter Five: Vesiculobullous Disease. Dermatology. Elsevier Saunders, Philadelphia, PA; 2012. 3rd edition:477-8.
3. Doi C, Shiraishi K, Koga H, Ishii N, Sayama K: Case of pemphigoid vegetans with autoantibodies against the BP180 C-terminal domain and BP230 antigen. J Dermatol. 2021, 48:1286-90. 10.1111/1346-8138.15941
4. Ballout RA, Musharrafieh U, Khattar J: Lisinopril-associated bullous pemphigoid in an elderly woman: a case report of a rare adverse drug reaction. Br J Clin Pharmacol. 2018, 84:2678-82. 10.1111/bcp.13737
5. Kim J, Chavel S, Girardi M, McNiff JM: Pemphigoid vegetans: a case report and review of the literature . J Cutan Pathol. 2008, 35:1144-47. 10.1111/j.1600-0560.2008.01016.x
6. Mathieu A, Chababi-Atallah M, Allard-Chamard H, Fernandes CL: Management of pemphigoid vegetans

with mycophenolate mofetil: a case report. SAGE Open Med Case Rep. 2024, 12:2050313X241231535. 10.1177/2050313X241231535

7. Winkelmann RK, Su WP: Pemphigoid vegetans. Arch Dermatol. 1979, 115:446-8. 10.1001/archderm.1979.04010040024008
8. Kuokkanen K, Helin H: Pemphigoid vegetans. Report of a case . Arch Dermatol. 1981, 117:56-7. 10.1001/archderm.1981.01650010062028
9. Soura E, Gerochristou M, Douvali T, Chasapi V, Stratigos A: Drug associated bullous pemphigoid: what's new?. Ital J Dermatol Venerol. 2024, 159:626-37. 10.23736/S2784-8671.24.07907-6
10. Verheyden MJ, Bilgic A, Murrell DF: A systematic review of drug-induced pemphigoid . Acta Derm Venereol. 2020, 100:adv00224. 10.2340/00015555-3457
11. Lo Schiavo A, Ruocco E, Brancaccio G, Caccavale S, Ruocco V, Wolf R: Bullous pemphigoid: etiology, pathogenesis, and inducing factors: facts and controversies. Clin Dermatol. 2013, 31:391-9. 10.1016/j.clindermatol.2013.01.006
12. Swiderski M, Vinogradova Y, Knaggs RD, et al.: Association between drugs and vaccines commonly prescribed to older people and bullous pemphigoid: a case-control study. Br J Dermatol. 2025, 192:440-9. 10.1093/bjd/ljae416