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CASE REPORT

Influenza Vaccine as a Potential Trigger for Urticarial Phase Bullous Pemphigoid: A Case Report

Abdulaziz Madani[1], Bushra Alraddadi[2], Ahmed Alajlan[1], Renad Alkanaan[1]

[1]Department of Dermatology, College of Medicine, King Saud University, Riyadh, Saudi Arabia; [2]Department of Dermatology, Ohud Hospital, Ministry of Health, Medina, Saudi Arabia

Correspondence: Ahmed Alajlan, Email ahmed1alajlan@gmail.com

Introduction: Bullous pemphigoid (BP) is a chronic autoimmune blistering disorder that primarily affects older adults. While typically associated with tense bullae, its urticarial phase presents diagnostic challenges due to its nonspecific features, often mimicking other pruritic dermatoses.

Case Presentation: This report presents a unique case of urticarial phase BP triggered by influenza vaccination in a 58-year-old male, with a clinical course marked by widespread intensely pruritic annular erythematous plaques. Notably, no vesicles, bullae, or erosions were observed during the early phase. Histopathological analysis revealed subepidermal eosinophilic infiltration and characteristic direct immunofluorescence findings, confirming the diagnosis. Treatment with systemic corticosteroids and topical therapies resulted in clinical remission.

Conclusion: This case contributes to the growing evidence of vaccine-triggered autoimmune diseases, highlighting potential mechanisms such as molecular mimicry and immune dysregulation. By comparing this case with previous reports, we underscore the importance of recognizing vaccination as a potential BP trigger. Clinicians should maintain vigilance in diagnosing and managing this rare but significant complication. Further research is needed to elucidate the immunopathogenesis and establish guidelines for vaccination in high-risk individuals.

Keywords: bullous pemphigoid, urticarial phase, influenza vaccine, autoimmune blistering disorder, eosinophilic infiltrate, vaccine-induced bullous pemphigoid

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Introduction

Bullous pemphigoid (BP) is a chronic autoimmune subepidermal blistering condition with a strong predisposition for older adults.[1] Autoantibodies to hemidesmosome proteins BP180 (type XVII collagen) and BP230, major constituents of the dermal–epidermal junction, mediate this condition.[2] These antibodies (predominantly IgG) initiate the inflammatory cascade and complement activation, resulting in tense bullae and erythematous plaques.[1] Widespread tense blisters on normal or erythematous skin are the typical clinical presentation. In some cases, a prodromal phase of urticarial plaques and pruritus occurs, often under-recognized and delaying diagnosis.[3] BP has multiple triggers, including medication (diuretics and antibiotics), infection, physical trauma, and vaccination.[4,5]

Urticarial phase BP requires histopathological analysis, including immunofluorescence, to distinguish it from pruritic dermatoses.[6] Vaccinations have been recognized to play a role in autoimmune disease pathogenesis, including BP, and both influenza and COVID 19 vaccines are potential triggers.[7,8] Although rare, post-vaccination BP cases indicate a complex interplay between immune activation and autoimmunity. Garcia Doval et al[9] show an association between higher influenza vaccination rates and BP incidence, and systematic reviews likewise have reported BP after COVID 19 vaccination.[10,11] This report presents a case of urticarial phase BP after influenza vaccination to discuss diagnosis and treatment and highlight the association between vaccination and autoimmune susceptibility.

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Case Presentation

A 58-year-old male patient presented with a two-month history of widespread pruritic, erythematous plaques. His medical history included well-controlled hypertension and diabetes mellitus managed with oral hypoglycemic agents (dipeptidyl peptidase-4 inhibitors). Additional comorbidities included dyslipidemia, bronchial asthma, and gastroesophageal reflux disease. He reported no recent changes in diet or exposure to new environmental allergens.

Symptoms began approximately two weeks following influenza vaccination, initially localized to the abdomen and back as intensely pruritic plaques. Over the following weeks, these lesions spread to the upper and lower extremities. The patient described the itching as debilitating, significantly disrupting his sleep and daily activities. Notably, no vesicles, bullae, mucosal, or erosions were observed during the early phase, contributing to diagnostic difficulty. Upon clinical examination, multiple well-defined annular plaques with erythematous borders and post-inflammatory hyperpigmentation were observed on the trunk, arms, and legs (Figure 1). Crucially, there was no indication of vesiculation, bullae development, mucosal involvement, or actual erosions such crusting, exudation, or epidermal denudation. Furthermore, there was no evidence of systemic involvement or secondary infection was detected.

A punch biopsy from the abdomen was performed two weeks after the presentation. The biopsy findings were consistent with the urticarial phase of BP, demonstrating a spongiotic epidermis and dense eosinophilic infiltration predominantly localized to the upper dermis. Direct immunofluorescence (DIF) revealed characteristic linear IgG and C3 deposition along the basement membrane zone, a hallmark of BP (Figure 2). These findings confirmed the autoimmune nature of the condition.

The patient was initially prescribed oral prednisolone at 30 mg daily, which provided partial symptomatic relief. However, upon tapering the dose over five days, symptoms recurred, necessitating an increase to 40 mg daily with a slower tapering regimen. Topical corticosteroids, including clobetasol and mometasone, were applied to affected areas twice daily. Antihistamines (loratadine 10 mg daily) were added to control pruritus. Over six weeks, the patient showed marked improvement, with resolution of active lesions and reduced pruritus. Post-inflammatory hyperpigmentation persisted but was managed conservatively. Follow-up at three months revealed sustained remission with a maintenance dose of prednisolone at 5 mg daily and continued use of topical corticosteroids.

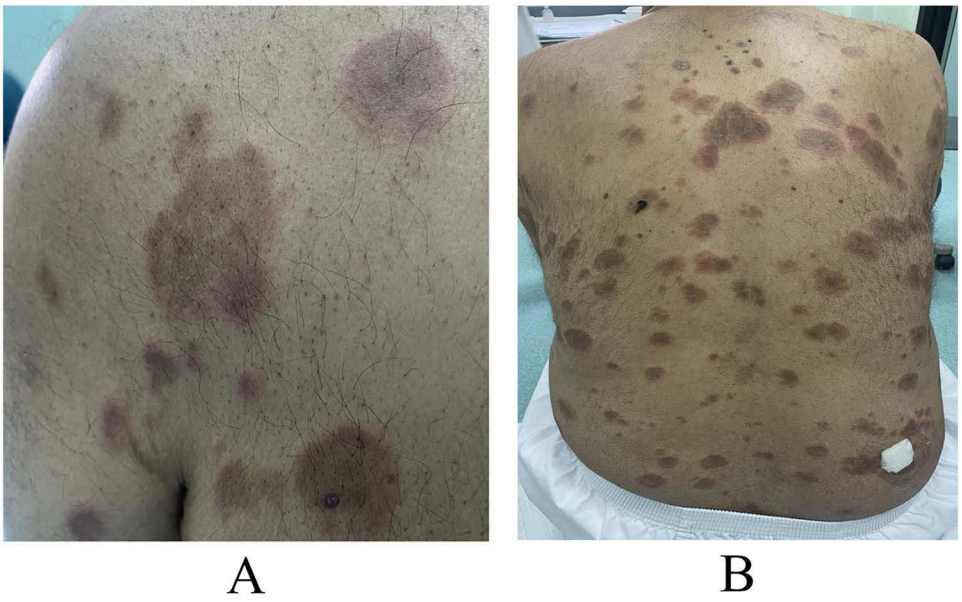

Figure 1 (**A** and **B**) Multiple well-defined annular erythematous plaques over the trunk and post-inflammatory hyperpigmented patches.

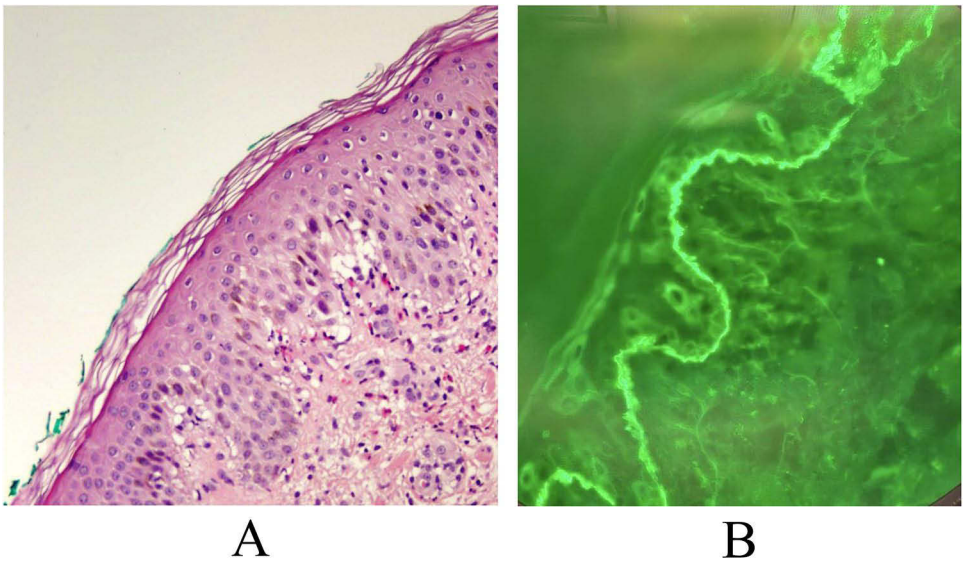

Figure 2 (**A**) Hematoxylin/eosin stain, Original Magnification 200X). (**B**) Direct Immunofluorescence, Original Magnification 400X. A Photomicrograph of a skin punch biopsy shows spongiosis and acanthosis, with an underlying eosinophilic infiltrate mainly around the basement membrane; direct immunofluorescence (DIF) study reveals linear positivity of IgG and C3.

Discussion

The urticarial phase of BP is a diagnostic entity of critical significance because it may present with a nonspecific appearance resembling chronic urticaria and/or eczema. This is an under-recognized phase that can delay diagnosis, unnecessarily prolong drug treatment, and worsen patient discomfort. Because this phase lacks blisters—the hallmark of BP—it requires a high clinical suspicion, especially in patients over 50 or with a personal or family history of autoimmune disease. Although DIF remains necessary for immunopathological confirmation of urticarial phase BP and to distinguish it from other dermatological conditions,[1] DIF may not be essential for all patients with tense blisters if the diagnosis can be made with a skin biopsy.

Vaccinations such as influenza and COVID-19 are now considered risk factors for BP.[12,13] Molecular mimicry, which gives rise to a vaccine antigen similar to a self-antigen and induces an autoimmune response, is likely involved in the pathogenesis. Secondly, adjuvants and intense antigenic stimulation may also cause immune dysregulation, which could thus exacerbate preexisting immune predispositions. In addition, eosinophil-rich hypersensitivity reactions are evidence of a vaccine-triggered mechanism.[14] When influenza vaccination and symptom onset occur in the same time frame, as in this case, this temporal relationship fits with what has been found in other studies.[9]

As shown in Table 1, there have been multiple documented cases where the vaccine acts as the trigger and have comparable clinical and histological characteristics. Baroero et al[4] described a pediatric case of BP as a vaccine side effect induced by hepatitis B vaccination and attributed pathogenesis to robust immune responses. Fournier et al[5] similarly described adult cases linked to influenza vaccines with similar histological findings. While the occurrence of BP post-COVID-19 vaccination has been recently reviewed,[10,11] a shared mechanism across vaccines has been elaborated (Table 1). According to Bar-Ilan et al, BP after immunization has also been observed in younger adults and newborns, despite the fact that the majority of reported instances involve elderly patients.[6]

Awareness of vaccine-triggered BP is essential for dermatologists and general practitioners. Early recognition, thorough evaluation, and appropriate diagnostics such as DIF can prevent disease progression and support effective management. Patients with new-onset urticarial plaques or pruritus should be asked about recent vaccinations, especially if they are at higher autoimmune risk. Although vaccines may rarely trigger BP, the danger posed by severe infections like influenza or COVID-19 remains far greater. Thus, maintaining vaccination programs while equipping healthcare providers to manage uncommon complications is crucial. Further research should clarify how vaccines contribute to BP,

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Table 1 Comparison of This Case with Previous Case Reports

Study	Patient Demographics	Type of Vaccine	Clinical Presentation & Onset Timeline	Histological/Immunological Findings	Treatment & Outcomes
Baroero et al[4]	3 patients: 6 months, 18 months, 2 years, Male	Hepatitis B	Widespread tense bullae appeared 1-week post-vaccination	Subepidermal blistering with eosinophil infiltration. DIF: linear IgG and C3 deposition at BMZ.	Systemic corticosteroids and topical corticosteroids led to complete remission in all cases within a few weeks.
Garcia-Doval et al[9]	12 adults, mean age 65, both sexes	Influenza	Erythematous plaques and vesicles, onset 3–4 weeks post-vaccination	Subepidermal blisters with eosinophilic infiltrate. DIF: strong linear IgG and C3 positivity at BMZ.	Systemic corticosteroids and antihistamines were effective. Symptoms resolved within 8–12 weeks.
Ghanaatpisheh et al[10]	17 cases, 45–82 years, both sexes	COVID-19	Tense blisters or pruritic plaques within 2 weeks post-vaccination.	Subepidermal split, eosinophilic infiltrate. DIF: linear IgG and C3 deposition.	Systemic corticosteroids (prednisolone 30–60 mg/day) combined with antihistamines. Partial to complete remission in 12–16 weeks.
De la Fuente et al[15]	3 infants: 4–6 months, both sexes	Diphtheria-Tetanus -Pertussis (DTP)	Vesicles and tense blisters on the trunk within 1–2 weeks post-vaccination.	Subepidermal blisters, eosinophilic infiltrate. DIF: IgG and C3 deposition at BMZ.	Topical corticosteroids and systemic corticosteroids (oral prednisone, 1 mg/kg/day) achieved remission in all cases within 4 weeks.
Lear et al[12]	1 adult: 62 years, Male	Influenza	Itchy plaques progressing to tense bullae 3 weeks post-vaccination.	Subepidermal blistering, eosinophilic infiltrate. DIF: IgG and C3 positivity at BMZ.	Prednisolone (40 mg/day), tapered over 8 weeks, resolved symptoms with residual post-inflammatory hyperpigmentation.
Walmsley and Hampton[16]	81-year-old man	Pandemrix, GlaxoSmithKline	2-week erythematous rash with small, localized blisters post-vaccination.	Subepidermal blistering with eosinophil-rich infiltrate. DIF positive for linear IgG and C3 at the basement membrane zone; indirect immunofluorescence showed IgG binding to the blister roof.	On day 18, topical dermovate and oral prednisolone 40 mg daily resulted in blister-free discharge.
Hassanin et al[17]	4-month-old male infant	Haemophilus influenzae type b	4-day erythematous and oedematous macular rash with blister.	Subepidermal blistering with eosinophil-predominant infiltrate. DIF showed linear IgG and C3 deposition at the BMZ; ELISA positive for anti-BP180 antibodies	Prehospital therapy included systemic and topical corticosteroids, mycophenolate mofetil, IVIG, and antibiotics for 7 days
Alberta-Wszolek et al[18]	54-year-old woman	Influenza	2-week of a severely pruritic, vesiculobullous eruption post intramuscular vaccination	Subepidermal blistering with neutrophilic infiltrate. DIF showed linear IgA deposition at the BMZ (IgG, IgM, C3, and fibrinogen negative), consistent with linear IgA bullous dermatosis.	After two prednisone rounds and a mid-potency topical corticosteroid, the eruption subsided.
Corrà et al[19]	1-year-old infant	Amoxicillin-clavulanic-acid	1 week tense bullous lesions of about 3–10 mm in diameter, most in 'string-of-pearls'	Subepidermal blister with neutrophils. DIF: linear IgA and C3 at BMZ. IIF negative.	Resolution after drug withdrawal; recurrence on rechallenge. Naranjo score 5 (probable).
Corrà et al[19]	14-year-old girl	Human papillomavirus (HPV) vaccine injection (Gardasil)	1 week eruption with vesicles and small blisters on normal to slightly erythematous skin	Grouped 'string-of-pearls' vesicles consistent with LABD, with focal honey-colored crusting. DIF of perilesional skin showed linear IgA deposition at the BMZ, confirming the diagnosis.	Systemic steroids and topical retapamulin achieved complete resolution in 3 weeks.

Abbreviations: DIF, Direct Immunofluorescence; IgG, Immunoglobulin G; C3, Complement component; BMZ, Basement Membrane Zone.

identify genetic or immunologic susceptibilities, and evaluate vaccine safety in predisposed individuals. Exploring alternative formulations or adjuvants may also reduce rare adverse events.

Conclusion

This case highlights the importance of recognizing BP as a potential post-vaccination manifestation. The patient's presentation, supported by histopathology and immunofluorescence, underscores the need for awareness of this under-reported form of BP, particularly in individuals predisposed to autoimmune disease who develop new pruritic plaques. The report emphasizes vaccination as a possible trigger and calls for further research into the immunopathogenesis of vaccine-associated BP, including mechanisms such as molecular mimicry or immune dysregulation. Improved understanding will enhance diagnosis, management, and vaccine safety for at-risk populations.

Ethical Approval

Ethical approval is not required for this study in accordance with our institution, local, or national guidelines.

Consent for Publication

Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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