OPEN ACCESS

**Saudi Journal of Medicine**
Abbreviated Key Title: Saudi J Med
ISSN 2518-3389 (Print) | ISSN 2518-3397 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

**Case Report**

# Vesiculo-Bullous Eruption Following COVID Vaccination

Raghda Saeed Al Maashari[1*], Al Mahmood Noaf S[2], Saleem Tausif[3]

[1]LRCPSI, MB, BCh, BAO (NUI), ABHS, Dermatology Consultant, Dermatology Department - Sheikh Khalifa Medical City, Abu Dhabi, U. A. E
[2]LRCPSI, MB, BCh, BAO (NUI), ABHS, Dermatology Specialist, Dermatology Department – Al Bahia Healthcare Center, Abu Dhabi, U. A. E
[3]MB, ChB, FRC Path, Consultant Dermatopathologist, Pathology and Laboratory Medicine Department - Sheikh Khalifa Medical City, Abu Dhabi, U. A. E

**DOI:** 10.36348/sjm.2022.v07i09.007 | **Received:** 12.08.2022 | **Accepted:** 05.09.2022 | **Published:** 23.09.2022

***Corresponding Author:** Raghda Saeed Al Maashari
LRCPSI, MB, BCh, BAO (NUI), ABHS, Dermatology Consultant, Dermatology Department - Sheikh Khalifa Medical City, Abu Dhabi, U. A. E

## Abstract

Bullous pemphigoid (BP) is an autoimmune sub-epidermal bullous disorder with a complex etiopathogenesis, predominately affecting the elderly. We report a case of COVID vaccination- induced BP, in a 30-year-old previously healthy Indian male who presented with a 1month history of itchy generalized vesiculo-bullous eruption that developed 3 days after receiving the first dose of the COVID vaccination. Histological examination and direct immunofluorescence study showed a sub-epidermal blister with a dermal inflammatory infiltrate and linear epidermal staining of IgG and C3 along the basement membrane zone in an n-serrated pattern. Treatment with oral prednisolone and oral doxycycline resulted in significant improvement in his condition. To our knowledge, there are limited case reports to date particularly in the Middle-East, which describe BP triggered by COVID vaccination.

**Keywords:** Autoimmune, bullous pemphigoid, COVID, sub-epidermal, vaccination.



## INTRODUCTION

As the international COVID vaccination campaigns ensue, several cutaneous adverse reactions have been commonly reported with various COVID vaccinations. However, there are limited case reports to date, which describe new-onset bullous pemphigoid (BP) triggered by COVID vaccination. BP is an autoimmune sub-epidermal bullous disorder with a complex etiopathogenesis; were drugs, immunization and viral infections have been implicated to be possible triggering factors. The immunological mechanism underlying BP post COVID vaccination is still unclear. In this article, we report a case of BP triggered by COVID vaccination.

## CASE PRESENTATION

30-year-old previously healthy Indian male who presented with a 1month history of moderately itchy generalized vesiculo-bullous eruption with associated oral mucosal involvement that developed 3 days after receiving the first dose of the Sinopharm COVID vaccination. Prior to developing these lesions, he had no symptoms of any infections and wasn't on any systemic medications.

There was no relevant family history for autoimmune or blistering disorders.

On examination, the patient had multiple generalized discrete tense clear blisters on an erythematous base. Few lesions were grouped in a herpetiform annular manner and others in a linear array (Figure 1-3) with associated oral mucosal and palmo-plantar involvement. There was no conjunctival injection.

Bacterial and viral analysis of the fluid within the blisters was negative. The patient's covid-19 PCR test result was negative. Histological examination and direct immunofluorescence study showed a sub-epidermal blister (Figure 4), which contained numerous neutrophils and eosinophils (Figure 5) and linear epidermal staining of IgG and C3 along the basement membrane zone in an n-serrated pattern (Figure 6); while IgA and IgM were negative. Indirect

immunofluorescence and detection of circulating autoantibodies against BP antigens were not performed. Based upon the clinical and histological findings, a diagnosis of COVID vaccination-induced bullous pemphigoid was made.

The patient was started on 0.75 mg/kg/day of oral prednisolone, which was tapered gradually; along with 200 mg daily doxycycline with significant improvement in his condition within the first week.

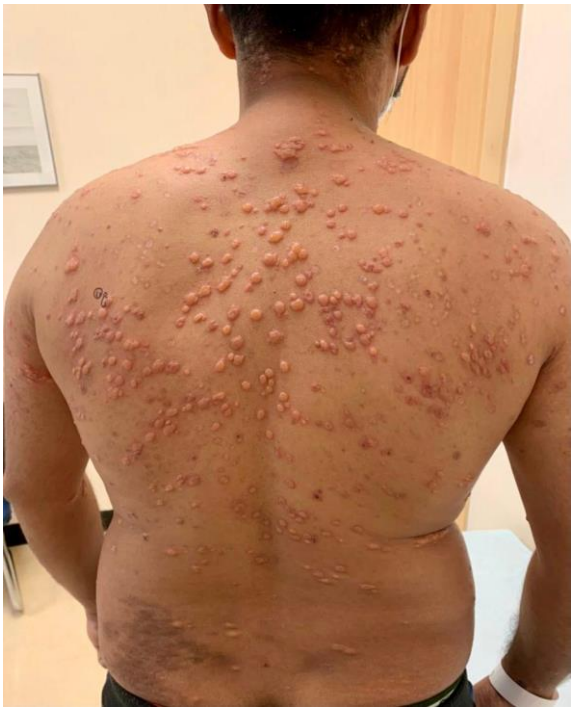

**Figure 1: Generalized blisters on the patients' body with some blisters arranged in a linear array and others in a herpetiform pattern**

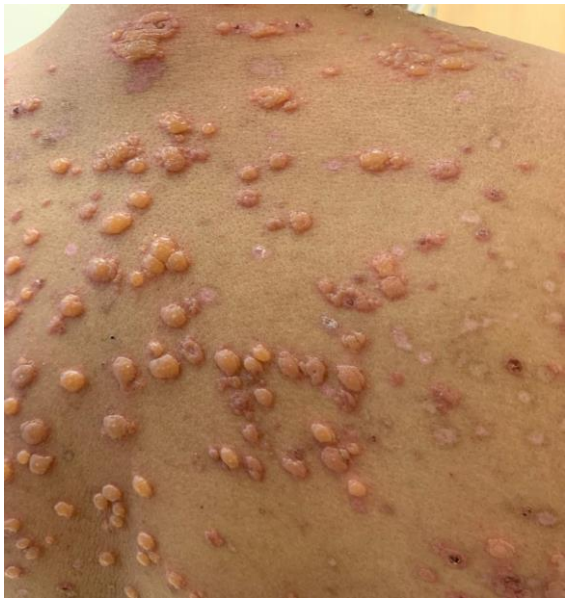

**Figure 2: Close up of the tense clear blisters on the patients back**

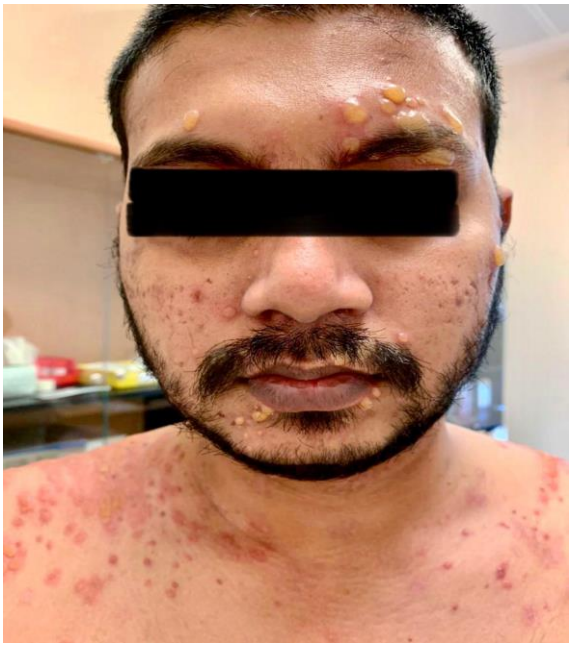

**Figure 3: Facial discrete blisters on an erythematous base**

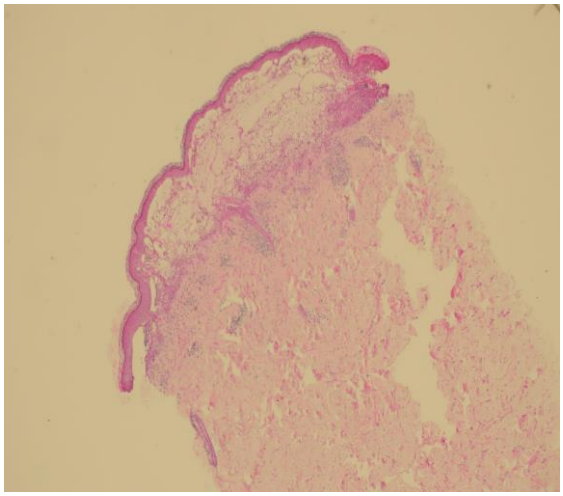

**Figure 4: Histological examination (low power): Sub-epidermal blister**

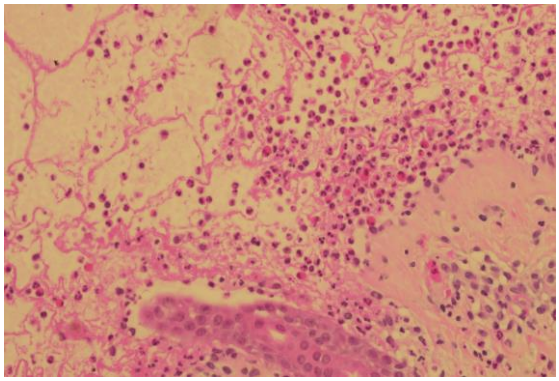

**Figure 5: Histological examination (high power): Sub-epidermal blister with numerous eosinophils and neutrophils**

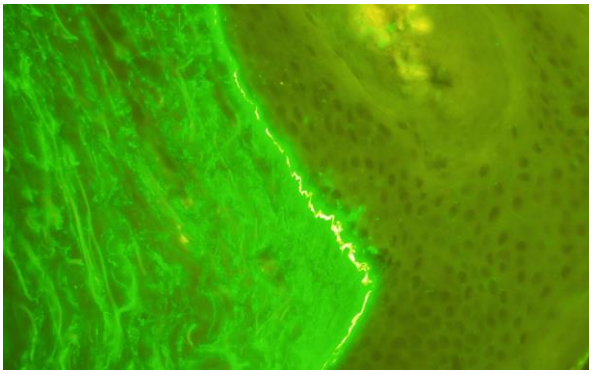

**Figure 6: Direct immunofluorescence: linear epidermal staining of IgG and C3 along the basement membrane zone in an n-serrated pattern**

## DISCUSSION

BP is an autoimmune sub-epidermal bullous disorder, presenting with intensely pruritic tense blisters predominantly affecting elderly people [1].

The etiopathogenesis of BP is complex [2] and is associated with presence of tissue-bound and circulating IgG autoantibodies directed against hemi-desmosomal proteins BP antigen 180 and 230 [2]. Several triggering factors have been reported in literature [3] including trauma, ultraviolet radiation, burns, vaccines and drugs such as DPP-4 inhibitors [4], PD-1/PD-L1 inhibitors and penicillamine. Vaccines reported to trigger BP [3] include diphtheria, pertussis, tetanus toxoid (DPT), polio, haemophilus influenza B, pneumococcus, swine flu and rabies. The time interval between vaccine administration and the development of BP ranged from 1 day to 1 month [3].

The immunological mechanism underlying BP post COVID vaccination is still unclear. It has been hypothesized that in a subset of genetically predisposed patients, certain vaccines may act through antigenic mimicry of viral antigens to incite a stimulus generating an autoimmune reaction against the basement membrane zone and producing autoantibodies to BP antigens 180 & 230 [5]. Tomayka *et al.*, reported 12 cases of new onset sub-epidermal blistering eruptions including BP following COVID-19 vaccination [6], where they theorized that in some individuals, certain vaccines may unmask subclinical BP or alternately prime a new cutaneous immune response [6]. In a case series of patients with bullous disorders in remission who developed a flare-up upon receiving the first dose of COVID vaccination; no similar reaction was noted with the second dose [7]. Therefore, full vaccination should be encouraged and flare ups should be treated accordingly.

Other cutaneous adverse reactions reported with various COVID vaccinations include local injection site reactions, delayed large local reactions, urticarial eruptions, morbilliform eruptions, herpes simplex flares, herpes zoster, cosmetic filler reactions [8], and bullous fixed drug eruption [9]. Additionally, Goon *et al.*, reported a case of BP developing during concurrent Covid-19 disease [5].

Diagnosis of BP is made on basis of clinical, histologic and immunologic findings [1]. BP should be differentiated from other sub-epidermal disorders such as epidermolysis bullosa acquisita, linear IgA disease and mucous membrane pemphigoid [3], which could be distinguished using direct and indirect immunofluorescence and enzyme-linked immunosorbent assay testing.

In severe generalized cases, oral prednisolone at a dose of 0.5- 1 mg/kg/day is adequate to control disease. Other documented therapies with reported benefit include topical potent steroids, erythromycin and tetracycline as a monotherapy or with nicotinamide, mycophenolate mofetil, azathioprine, methotrexate, cyclosporin, chlorambucil, dapsone, cyclophosphamide, plasma exchange, intravenous immunoglobulin and rituximab in treatment-resistant cases [1].

## CONCLUSION

BP is a chronic auto- immune sub-epidermal blistering disorder associated with tissue-bound and circulating autoantibodies directed against BP antigen 180 and BP antigen 230. There are several case reports of vaccinations inducing BP, however; the mechanism of induction is still unclear. To our knowledge, there are limited case reports to date, particularly in the Middle-East, which describe BP triggered by COVID vaccination. As the corona virus pandemic continues and the international COVID vaccination campaigns ensue, further assessment of gathered data will help us quantify the true incidence and acknowledge the patho-mechanisms of this novel side effect.

**ACKNOWLEDGEMENT:** None.

**PRIOR PUBLICATION:** Nil.

**SUPPORT:** Nil.

**CONFLICTS OF INTEREST:** Nil.

## REFERENCES

1. Bernard, P., & Luca, B. (2012). Pemphigoid group. Bolognia, J. L., Jorizzo, J. L., & Schaffer, J. V. (Eds.) Dermatology, 3rd Edition, *Elsevier Saunders Company Amsterdam*, pp. 475-481.
2. Baroero, L., Coppo, P., Bertolino, L., Maccario, S., & Savino, F. (2017). Three case reports of post immunization and post viral Bullous Pemphigoid: looking for the right trigger. *BMC pediatrics*, *17*(1), 1-5. doi:10.1186/s12887-017-0813-0
3. Jindal, A., Nayak, S., Shenoi, S., Rao, R., & Monappa, V. (2020). Bullous pemphigoid triggered

by rabies vaccine. *Indian journal of dermatology, venereology and leprology*, *86*(1), 66-68.

4. Lambadiari, V., Kountouri, A., Kousathana, F., Korakas, E., Kokkalis, G., Theotokoglou, S., ... & Papadavid, E. (2021). The association of bullous pemphigoid with dipeptidyl-peptidase 4 inhibitors: a ten-year prospective observational study. *BMC Endocrine Disorders*, *21*(1), 1-5. https://doi.org/10.1186/s12902-021-00689-7
5. Goon, P. K. C., Bello, O., Adamczyk, L. A., Chan, J. Y. H., Sudhoff, H., & Banfield, C. C. (2021). Covid-19 dermatoses: Acral vesicular pattern evolving into bullous pemphigoid. *Skin Health and Disease*, *1*(1), e6. https://doi.org/10.1002/ski2.6
6. Tomayko, M. M., Damsky, W., Fathy, R., McMahon, D. E., Turner, N., Valentin, M. N., ... & Freeman, E. E. (2021). Subepidermal blistering eruptions, including bullous pemphigoid, following COVID-19 vaccination. *Journal of Allergy and Clinical Immunology*, *148*(3), 750-751. doi:10.1016/j.jaci.2021.06.026
7. Damiani, G., Pacifico, A., Pelloni, F., & Iorizzo, M. (2021). The first dose of COVID-19 vaccine may trigger pemphigus and bullous pemphigoid flares: is the second dose therefore contraindicated?. *Journal of the European Academy of Dermatology and Venereology*, *35*(10), e645. doi: 10.1111/jdv.17472. PMID: 34169578; PMCID: PMC8447358.
8. McMahon, D. E., Amerson, E., Rosenbach, M., Lipoff, J. B., Moustafa, D., Tyagi, A., ... & Freeman, E. E. (2021). Cutaneous reactions reported after Moderna and Pfizer COVID-19 vaccination: a registry-based study of 414 cases. *Journal of the American Academy of Dermatology*, *85*(1), 46-55. doi: 10.1016/j.jaad.2021.03.092. PMID: 33838206; PMCID: PMC8024548
9. Kong, J., Cuevas-Castillo, F., Nassar, M., Lei, C. M., Idrees, Z., Fix, W. C., ... & Mathew, A. (2021). Bullous drug eruption after second dose of mRNA-1273 (Moderna) COVID-19 vaccine: Case report. *Journal of Infection and Public Health*, *14*(10), 1392-1394. doi: 10.1016/j.jiph.2021.06.021. PMID: 34294590; PMCID: PMC8264280