Received: 26 June 2022 | Accepted: 27 July 2022

DOI: 10.1111/jdv.18503

LETTER TO THE EDITOR

Bullous pemphigoid and COVID-19 vaccination: Management and treatment reply to 'Bullous pemphigoid in a young male after COVID-19 mRNA vaccine: A report and brief literature review' by Pauluzzi et al.

Dear Editor,

We have read with great interest the article recently published by Pauluzzi et al.[1] who reported the case of a young male patient, who developed bullous pemphigoid (BP) after 15 days from COVID-19 vaccination with the mRNA vaccine BNT162b2 (Comirnaty®, BioNTech/Pfizer).

The authors speculated that this event may be related to an off-target immune activation following vaccine administration, although they clarify that further studies are needed to confirm the exact pathogenesis.[2,3]

In this context, at the Dermatology Centre of the University of Naples Federico II, we collected data on 43 patients with BP who performed three COVID-19 vaccine doses (mRNABNT162b2 and mRNA-1273 were the vaccines administered). In the majority of the cases (90.6%), no disease worsening or onset of new lesions was observed. In the remaining 4 (10.4%) cases, patients experienced disease worsening 5–8 days after the vaccination. Notably, all subjects were previously treated with oral corticosteroids ± azathioprine and they were all under control before undergoing vaccination. Table 1 shows patients' data with the type of vaccine received, the day of onset of disease worsening and the baseline treatment the patient was receiving. Fortunately, BP worsening was usually easily managed by increasing dosage or adding oral corticosteroids (prednisone) or azathioprine. A correlation between disease worsening and the type of COVID-19 vaccine received was not observed. Interestingly, we did not find any disease worsening after the third dose.

We agree with Pauluzzi et al. who correlate vaccination to an off-target immune activation; however, to date thanks to published studies,[4,5] we can speculate that the underlying pathogenesis could be explained by molecular mimicry between specific basement membrane proteins (e.g. BP-180 and BP-230) and the SARS-CoV-2 spike protein used by the virus to bind and fuse with host cells. Hence, COVID-19 vaccine may induce a large immunologic response in immunologically susceptible individuals and subsequent antibody production.[6] BP induced by vaccination against rabies[7] influenza, pneumococcus, tetanus, diphtheria[8] and pertussis has been reported in the literature, indicating that vaccination can trigger the disease. Therefore, our experience may further suggest a hyperimmune reaction induced in genetically predisposed individuals or a cross-reaction of vaccine antigens with BP antigens, supporting the possible worsening of BP manifestations to COVID-19 vaccination.

Moreover, given the partial similarity of BP pathogenesis with other dermatological conditions such as psoriasis suggested using biologicals for both conditions, the vaccine-induced activation of Th1/Th17 axis may further explain BP worsening.[9,10]

In conclusion, we would like to emphasize that in our experience, most BP patients (90%) showed no impact of COVID-19 vaccine on the disease, and even those who had a worsening of the disease were managed without significant complications and completed their vaccine schedule.

This finding reinforces the importance and safety of the COVID-19 vaccine campaign, especially in frail patients with rare diseases such as BP where management is often not

TABLE 1 Bullous pemphigoid flares after COVID-19 vaccine

	Sex	Age	Vaccine/dose	Days from vaccine/dose	Therapy before vaccination
1	M	60	mRNABNT162b2/3	7 days after second dose	Azathioprine 100 mg/die Prednisone 20 mg/die
2	M	74	mRNABNT162b2/3	5 days after second dose	Azathioprine 100 mg/die Prednisone 15 mg/die
3	F	80	mRNA-1273/3	6 days after first dose	Azathioprine 50 mg/die
4	M	78	mRNABNT162b2/3	8 days after second dose	Azathioprine 50 mg/die

easy.[11,12] Certainly, further studies will be needed to further investigate the impact COVID-19 vaccination may have on BP.

CONFLICT OF INTEREST

None to declare.

FUNDING INFORMATION

None.

INFORMED CONSENT

Patients gave consent for photograph acquisition and publication.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Fabrizio Martora
Angelo Ruggiero
Teresa Battista
Gabriella Fabbrocini
Matteo Megna

Dermatology Unit, Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy

Correspondence
Fabrizio Martora, Section of Dermatology – Department of Clinical Medicine and Surgery, University of Naples Federico II, Via Pansini 5, Napoli 80131, Italy.
Email: fabriziomartora92@libero.it

ORCID

Fabrizio Martora https://orcid.org/0000-0003-2523-050X
Angelo Ruggiero https://orcid.org/0000-0002-4658-7391
Matteo Megna https://orcid.org/0000-0003-1803-2046

REFERENCES

1. Pauluzzi M, Stinco G, Errichetti E. Bullous pemphigoid in a young male after COVID-19 mRNA vaccine: a report and brief literature review. J Eur Acad Dermatol Venereol. 2022;36(4):e257–9. https://doi.org/10.1111/jdv.17891
2. Tomayko MM, Damsky W, Fathy R, et al. Subepidermal blistering eruptions, including bullous pemphigoid, following COVID-19 vaccination. J Allergy Clin Immunol. 2021;148(3):750–1. https://doi.org/10.1016/j.jaci.2021.06.026
3. McMahon DE, Kovarik CL, Damsky W, et al. Clinical and pathologic correlation of cutaneous COVID-19 vaccine reactions including V-REPP: A registry-based study. J Am Acad Dermatol. 2022;86(1):113–21. https://doi.org/10.1016/j.jaad.2021.09.002
4. Gambichler T, Hamdani N, Budde H, et al. Bullous pemphigoid after SARS-CoV-2 vaccination: spike-protein-directed immunofluorescence confocal microscopy and T-cell-receptor studies. Br J Dermatol. 2022;186(4):728–31. https://doi.org/10.1111/bjd.20890
5. Maronese CA, Caproni M, Moltrasio C, et al. Bullous pemphigoid associated with COVID-19 vaccines: an italian multicentre study. Front Med (Lausanne). 2022;9:841506.
6. Pérez-López I, Moyano-Bueno D, Ruiz-Villaverde R. Bullous pemphigoid and COVID-19 vaccine. Penfigoide ampolloso y vacuna COVID-19. Med Clin (Barc). 2021;157(10):e333–4.
7. Jindal A, Nayak SUK, Shenoi SD, Rao R, Monappa V. Bullous pemphigoid triggered by rabies vaccine. Indian J Dermatol Venereol Leprol. 2020;86(1):66–8.
8. Maki N, Hashimoto T, Yamada T, Ishii N, Tsuruta D, Demitsu T. Case of pemphigoid with immunoglobulin G antibodies to BP180 C-terminal domain and laminin-γ1 (p200) developed after pneumococcal vaccination. J Dermatol. 2021;48(1):101–5.
9. Megna M, Potestio L, Gallo L, Caiazzo G, Ruggiero A, Fabbrocini G. Reply to "Psoriasis exacerbation after COVID-19 vaccination: report of 14 cases from a single centre" by Sotiriou E et al. J Eur Acad Dermatol Venereol. 2022;36(1):e11–3.
10. Martora F, Picone V, Fabbrocini G, Marasca C. Hidradenitis suppurativa flares following COVID-19 vaccination: a case series. JAAD Case Rep. 2022;23:42–5.
11. Martora F, Fabbrocini G, Nappa P, Megna M. Impact of the COVID-19 pandemic on hospital admissions of patients with rare diseases: an experience of a Southern Italy referral center. Int J Dermatol. 2022;61(7):e237–8. https://doi.org/10.1111/ijd.16236
12. Martora F, Fabbrocini G, Nappa P, Megna M. Reply to 'Development of severe pemphigus vulgaris following SARS-CoV-2 vaccination with BNT162b2' by Solimani et al. J Eur Acad Dermatol Venereol. 2022. Online ahead of print. https://doi.org/10.1111/jdv.18302