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Bullous pemphigoid after the second SARS-CoV-2 infection

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To the Editor:

Several dermatologic manifestations have been reported in association with SARS-CoV-2 infection, affecting 4 to 20.4% of patients [1]. Although immune-mediated dermatoses triggered by anti-SARS-Cov-2 vaccines have been published, very few bullous pemphigoids (BP) triggered by SARS-Cov-2 infection have been reported [2]. Herein, we describe a singular case of new-onset BP in a patient after the second SARS-CoV-2 infection.

A 75-year-old woman with Parkinson disease and hypertension presented to our dermatology department with a 2-month history of widespread itchy erythema involving the trunk and limbs with tense blisters and erosions (**Figure 1**). The dermatosis started with erythematous plaques 2-months before, during hospitalization for a severe SARS-CoV-2 infection. Notably, the patient had a previous SARS-CoV-2 infection one year before and had received two doses of the Moderna vaccine, the second eight months prior, without any cutaneous eruption. She had been taking levodopa/benserazide, levodopa/carbidopa, and valproic acid for 30 years. No other recent medicine had been administered. Dermatological examination showed tense bullae, superficial erosions, and hemorrhagic/seropurulent crust formation on the scalp, trunk, and limbs upon erythematous, confluent patches and plaques. The patient presented a high level of anti-SARS-CoV-2 specific antibodies (>12500U/mL, normal range <0.5). Skin biopsy showed subepidermal detachment with eosinophilic inflammatory cell infiltrate in the superficial dermis (**Figure 2**). Direct immunofluorescence revealed IgG and C3 deposition at the basement membrane zone. BP180/BP230 antibodies (>200/95U/mL, normal

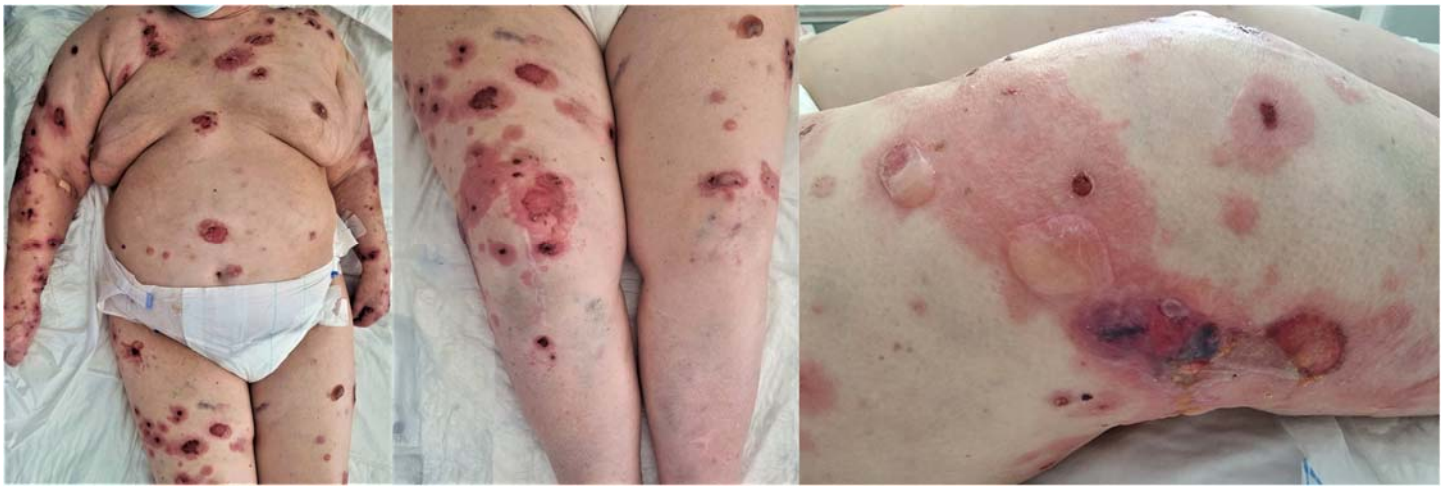

Figure 1. *Bullous pemphigoid, clinical image: tense bullae, superficial erosions and erythematous patches and plaques on the trunk and upper and lower extremities.*

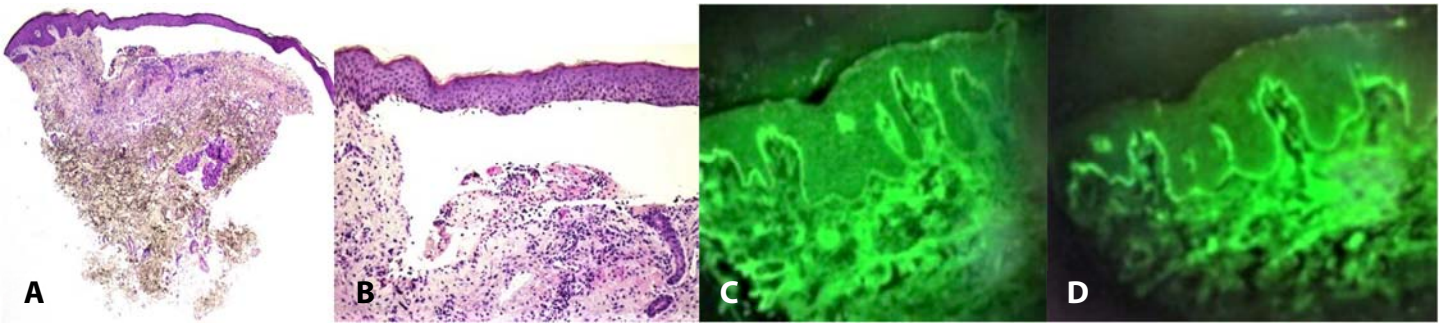

Figure 2. *Bullous pemphigoid, histopathological and direct immunofluorescence features:* ***A, B)*** *H&E histopathology showing subepidermal blister with an inflammatory infiltrate in the papillary dermis predominantly consisting of eosinophils and neutrophils.* ***C)*** *IgG, and,* ***D)*** *C3 deposition at the basement membrane zone.* ***A)*** *25×,* ***B)*** *100×,* ***C), D)*** *400×.*

<20U/mL) were also detected by enzyme-linked immunosorbent assay (**Figure 2**). Based on these findings a diagnosis of BP was reached. The patient was treated with oral prednisolone (30mg/day, with progressive reduction) and oral doxycycline (100mg/day) with clinical resolution after two months.

Bullous pemphigoids is an acquired autoimmune blistering bullous disease caused by circulating autoantibodies most commonly towards hemidesmosome antigens BP180 and/or BP230. Although most cases are idiopathic, several trigger factors have been described in the literature, such as drugs, ultraviolet radiation, burns, trauma, and vaccines. Furthermore, cases of BP developed following viral infections have been described [1].

A relationship between COVID-19 and the development of autoimmunity has been reported. Despite the fact that the molecular mechanisms underlying these putative associations are not well-understood, peptide sharing has been found between antigenic epitopes of SARS-CoV-2 and heat shock proteins (60 and 90) associated with autoimmune blistering diseases. Thus, it has been hypothesized that molecular mimicry may exist between basement membrane-specific proteins (e.g., BP180, BP230) and SARS-CoV-2 spike protein [3]. Furthermore, cytokines associated with COVID-19 included IL1B, IL17, and TNF, which have also been implicated in patients with bullous pemphigoid [4,5].

We describe this case of bullous pemphigoid triggered by SARS-CoV-2 infection and the particularity of having occurred only after the second SARS-CoV-2 infection, which was severe and led to hospitalization, unlike the first infection. We hypothesize that repeated exposures to SARS-CoV-2 antigens may lead to sensitization and immune cross-reactivity with similar self-antigens. Differing from the numerous cases recently described, bullous pemphigoid was not triggered by the administration of the mRNA vaccine (Moderna) alone. Nevertheless, we cannot exclude the fortuitous occurrence of bullous pemphigoid in a patient in whom other contributing factors may have played a role.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Massip E, Marcant P, Font G, et al. Cutaneous manifestations following COVID-19 vaccination: a multicentric descriptive cohort. *J Eur Acad Dermatol Venereol*. 2022;36:253-255. [PMID: 34927749].
2. Tomayko MM, Damsky W, Fathy R, et al. Subepidermal blistering eruptions, including bullous pemphigoid, following COVID-19 vaccination. *J Allergy Clin Immunol*. 2021;148:750-751. [PMID: 34275656].
3. Kasperkiewicz M. Covid-19, heat shock proteins, and autoimmune bullous diseases: a potential link deserving further attention. *Cell Stress Chaperones*. 2021;26:1-2. [PMID: 33196989].
4. Olson N, Eckhardt D, Delano A. New-Onset Bullous Pemphigoid in a COVID-19 Patient. *Case Rep Dermatol Med*. 2021;2021:5575111. [PMID: 34211788].
5. Riani M, Le Jan S, Plée J, et al. Bullous pemphigoid outcome is associated with CXCL10-induced matrix metalloproteinase 9

secretion from monocytes and neutrophils but not lymphocytes.
J Allergy Clin Immunol. 2017;139:863-872. [PMID: 27637385].