A case report of anti-P200 pemphigoid following COVID-19 vaccination

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INTRODUCTION

Anti-p200 pemphigoid is a rare autoimmune subepidermal bullous disease characterized by autoantibodies to laminin gamma-1 (p200). A few rare cases of autoimmune bullous dermatoses, mainly bullous pemphigoid (BP), have been reported following COVID-19 vaccination.[1,2] Only one case of anti-p200 pemphigoid postvaccination has been reported after a pneumococcal vaccination.[3] We report a case of anti-p200 pemphigoid subsequent to COVID-19 vaccination.

CASE REPORT

A 74-year-old man presented with sudden blisters of the extremities, hands, wrists, elbows, and feet, which appeared 48 hours after the second dose of the Moderna COVID-19 messenger (m)RNA vaccine. A few vesicles located only on his wrists appeared 10 days after the first dose with spontaneous resolution. His medical history included eczema and glaucoma. No additional treatment had been initiated.

Examination revealed numerous tense and flaccid blisters on inflammatory skin, on the extremities (Fig 1, *A-D*) and round erosion of the scrotum. Mucous membranes were unaffected. A local reaction site was also noted located at the injection area, with axillary lymphadenopathy. The patient did not have fever.

Laboratory evaluation showed only an elevated C-reactive protein concentration of 44 mg/L without leukocytosis. There was no eosinophilia. Histopathologic examination showed subepidermal separation. The dermal infiltrate was composed of numerous eosinophils and few lymphocytes. Direct immunofluorescence microscopy revealed linear C3 and immunoglobulin G (IgG) deposition along the dermo-epidermal junction (Fig 2). Indirect immunofluorescence microscopy of the patient sera on sodium chloride-split human skin showed IgG antibodies that were only bound to the dermal sides. Antibodies against BPAG-1, BPAG-2, and collagen VII were not detected by enzyme-linked immunosorbent assay. Immunoblot analysis of human dermal extracts revealed IgG4 that recognized a 200-kilo Dalton band corresponding to anti-p200 antibodies (Fig 3). A diagnosis of anti-p200 pemphigoid was established. The workup results for malignancy and for other autoimmune diseases based on computed tomography and laboratory tests were negative.

The patient was initially treated with clobetasol propionate 0.05% cream with a temporary effect. New lesions appeared during the decrease in topical corticosteroids. Colchicine (1 mg/day) and daily application of a topical corticosteroid led to a significant improvement after 15 days. Colchicine was stopped after 2 months because of hepatic cholestasis, and the use frequency of the topical corticosteroid was decreased over 4 months. Remission was sustained for 6 months after the treatment.

Abbreviations used:

BP:	bullous pemphigoid
IgG:	immunoglobulin G
mRNA:	messenger RNA

DISCUSSION

A broad spectrum of cutaneous adverse events has been described after mRNA COVID-19

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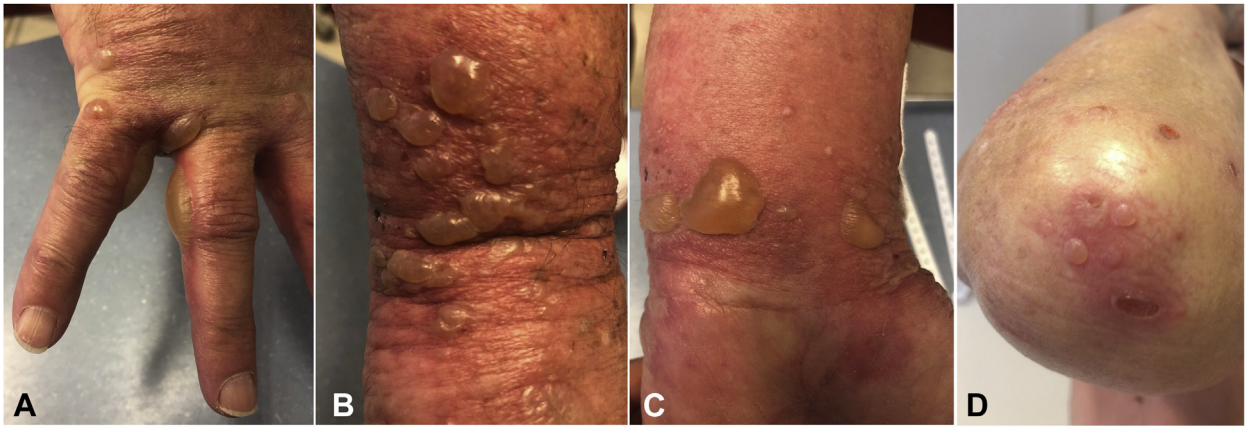

Fig 1. Clinical features of the wrist (**A-B**), lateral side of the fingers (**C**), and elbow (**D**).

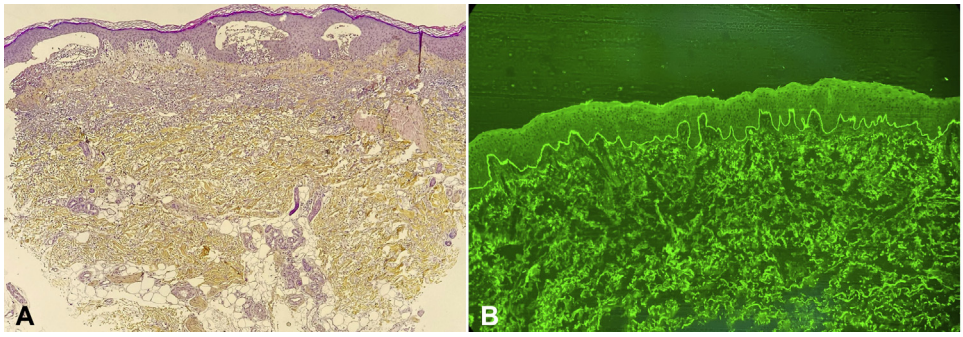

Fig 2. Histopathologic findings. **A,** Subepidermal blistering with dermal infiltrate with numerous eosinophils. Haematoxylin-eosin-stained section. **B,** Direct immunofluorescence microscopy.

vaccination, including subepidermal bullous disease, such as BP. The most frequently reported adverse effects were local injection site reactions, urticaria, morbilliform rashes, and pityriasis rosea-like reactions.[2,4] It appears that after the second dose, less than 50% relapse.[5]

Some cases of BP following COVID-19 vaccination have been described recently, highlighting the potential triggering role of the mRNA COVID-19 vaccine in autoimmune subepidermal bullous disease. Our anti-p200 pemphigoid case appears to be different from other BP cases, not only by these features, but also by its development. Indeed, the majority of described cases of BP following COVID-19 vaccination began after the second dose with a median onset on day 7.[1] In our clinical case, we noticed the first eruption 10 days after the first dose, with a more intense and rapid relapse after the second dose, and remission after 6 months, associated with a decrease in COVID-19-specific antibodies following immunization. The close temporal relationship between vaccination and the onset of anti-p200 pemphigoid in our patient reinforced the potential triggering role of the COVID-19 vaccine.

We suggest that vaccination may be the triggering factor of autoimmune subepidermal bullous diseases by stimulating the immune system with an unexplained mechanism. Indeed, vaccination could unmask subclinical disease defined by the presence of antibodies before clinical symptoms[6] through the immunostimulatory process of the vaccine and initiate rapid lesions after the first dose. In patients with more delayed kinetics, it could reflect a period of antibody production. COVID-19 vaccination represents the first use of mRNA vaccines in humans, and additional studies will be needed to understand the potential role of COVID-19 vaccination in initiating the development of autoimmune subepidermal bullous diseases.

Epidermolysis bullosa acquisita should be considered in the differential diagnosis, which was ruled out by immunoblotting and by lack of autoantibodies targeting type VII collagen. The diagnosis of anti-p200 pemphigoid can be challenging, as it shares clinical and histopathologic characteristics

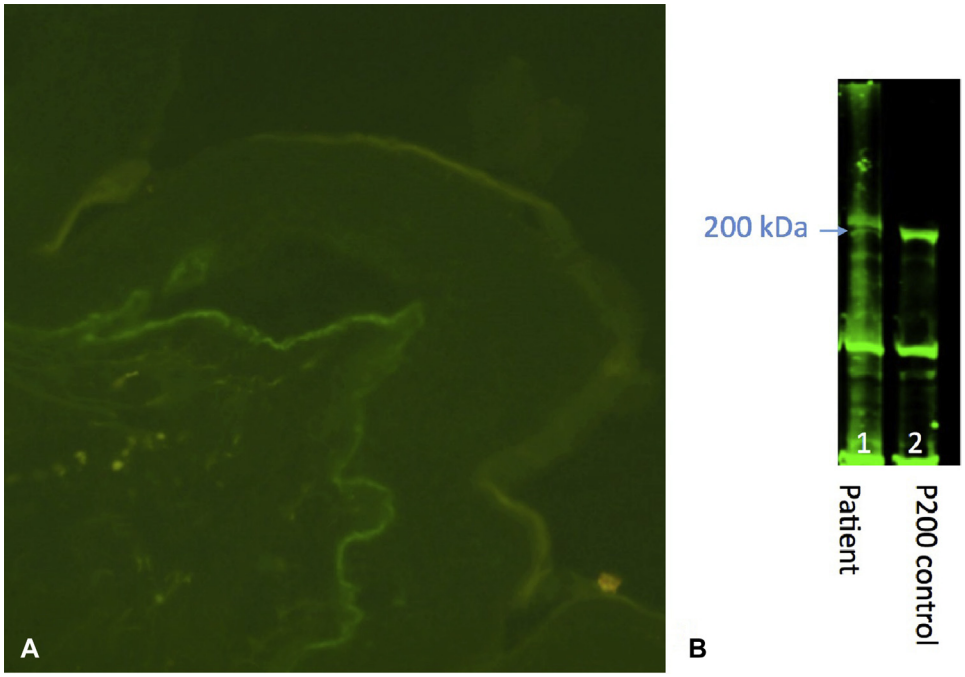

Fig 3. A, Indirect immunofluorescence microscopy using salt-split skin showed bound immunoglobulin G (IgG) on the dermal side. **B,** Immunoblotting with dermal extracts confirmed that the patient's IgG autoantibodies reacted with a 200-kDa protein.

with other blistering diseases. Some cases of anti-p200 pemphigoid closely resemble epidermolysis bullosa acquisita, with lesions on extremities. Mucosal involvement has also been described. Patients are younger than those with BP. Detection of autoantibodies recognizing a 200-kilo Dalton protein by immunoblotting of human dermal extract, corresponding to laminin gamma-1, confirmed the diagnosis.[7]

Of the 12 cases of bullous eruption following COVID-19 vaccination described by Tomayko et al,[1] 3 had negative immunologic testing. Nevertheless, detection of anti-p200 antibodies was not performed, possibly underestimating the cases of anti-p200 pemphigoid, as it resembles BP.

In this same series of 12 patients reported by Tomayko et al,[1] the clinical course was variable. The authors suggest that these different developments may reflect different pathophysiologic mechanisms; BP-like disease and BP unmasked by vaccination, which require stronger treatment.

Anti-p200 pemphigoid is usually a chronic disease, with a more severe and relapsing course than BP, despite the use of systemic treatment.[3,7] In our case, systemic treatment with colchicine was required, combined with a topical corticosteroid due to the recurrent course. Complete remission was obtained for 6 months, despite the discontinuation of colchicine after 2 months of treatment due to the appearance of cholestasis.

Cases of disease flare were described following vaccination during a period of remission in patients with BP.[8] In our case, a worsening of the lesions appeared after the second dose.

In conclusion, this rare autoimmune bullous disease was associated with the Moderna COVID-19 mRNA vaccine. For this specific patient, another dose of the vaccine may be accompanied by a risk of relapse of the dermatosis. The risk-benefit ratio must be carefully assessed with the patient.[8,9]

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Conflicts of interest

None disclosed.

REFERENCES

1. 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):750-751. https://doi.org/10.1016/j.jaci.2021.06.026
2. Larson V, Seidenberg R, Caplan A, Brinster NK, Meehan SA, Kim RH. Clinical and histopathological spectrum of delayed adverse cutaneous reactions following COVID-19 vaccination. *J Cutan Pathol*. 2022;49(1):34-41. https://doi.org/10.1111/cup.14104

3. 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):101-105. https://doi.org/10.1111/1346-8138.15626
4. Blumenthal KG, Freeman EE, Saff RR, et al. Delayed large local reactions to mrna-1273 vaccine against SARS-CoV-2. *N Engl J Med*. 2021;384(13):1273-1277. https://doi.org/10.1056/NEJMc2102131
5. McMahon DE, Amerson E, Rosenbach M, et al. Cutaneous reactions reported after Moderna and Pfizer COVID-19 vaccination: a registry-based study of 414 cases. *J Am Acad Dermatol*. 2021;85(1):46-55. https://doi.org/10.1016/j.jaad.2021.03.092
6. Raneses E, McGinley Simpson M, Rosenberg A, Coffman M, Meyerle J. A retrospective review of autoimmune bullous disease antibody positivity before clinical symptoms. *J Am Acad Dermatol*. 2022;86(1):237-239. https://doi.org/10.1016/j.jaad.2021.02.003
7. Commin MH, Schmidt E, Duvert-Lehembre S, et al. Clinical and immunological features and outcome of anti-p200 pemphigoid. *Br J Dermatol*. 2016;175(4):776-781. https://doi.org/10.1111/bjd.14629
8. Damiani G, Pacifico A, Pelloni F, Iorizzo M. The first dose of COVID-19 vaccine may trigger pemphigus and bullous pemphigoid flares: is the second dose therefore contraindicated? *J Eur Acad Dermatol Venereol*. 2021;35(10):e645-e647. https://doi.org/10.1111/jdv.17472
9. Sokolowska M, Eiwegger T, Ollert M, et al. EAACI statement on the diagnosis, management and prevention of severe allergic reactions to COVID-19 vaccines. *Allergy*. 2021;76(6):1629-1639. https://doi.org/10.1111/all.14739