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CASE REPORT

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Bullous pemphigoid in a patient with psoriasis after mRNA COVID-19 vaccination

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Abstract

Bullous pemphigoid and psoriasis are two well-characterised chronic autoimmune diseases that may be triggered by drugs, infections or vaccines. The coexistence of the two is a rare event but is more extraordinary if incited by messenger RNA (mRNA) COVID-19 vaccination. A 62-year-old Filipino male experiencing a flare-up of his long-standing psoriasis vulgaris presented with new onset tense blisters on the legs 2 days after his first booster dose of mRNA (Pfizer-BioNTech) vaccination. The clinical, skin punch biopsy, direct immunofluorescence and enzyme-linked immunosorbent assay were consistent with bullous pemphigoid. Complete resolution of the vesicles and bullae with no new lesions and flattening of psoriasis plaques were observed after 1 month of treatment of systemic corticosteroids and corticosteroid-sparing agents. An association may exist between bullous pemphigoid development and mRNA COVID-19 vaccination.

KEYWORDS

bullous pemphigoid, case report, mRNA COVID-19 vaccination, Pfizer, psoriasis

INTRODUCTION

Since the initiation of COVID-19 vaccination, several cutaneous adverse reactions have been reported with messenger RNA (mRNA) COVID-19 vaccinations. Most are local reactions but exacerbations of autoimmune inflammatory diseases such as psoriasis have occurred. We present a case of new-onset bullous pemphigoid (BP) in a patient with psoriasis following his first booster dose of mRNA (Pfizer-BioNTech) vaccine administration.

CASE PRESENTATION

A 62-year-old Filipino male experiencing a flare-up of his long-standing psoriasis vulgaris for 20 years presented with new onset tense blisters on the legs. Six weeks prior, the patient had developed a flare of psoriasis described as multiple erythematous plaques on the extremities, partially improved with clobetasol propionate 0.05% ointment. A few weeks after, he developed multiple pruritic tense vesicles and bullae, with erosions and serous crusting on the lower extremities 2 days after his first booster dose of mRNA (Pfizer-BioNTech) vaccination (Figure 1). He had two doses of AstraZeneca COVID-19 vaccine a year ago with no reported adverse reactions. The patient denied intake of any medication. A 4 mm-skin punch biopsy from the left anterior leg showed a subepidermal split with the predominance of eosinophils (Figure 2). Direct immunofluorescence (DIF) of the perilesional area on the left anterior leg showed a linear basement membrane staining pattern in IgG and C3 (Figure 3). Enzyme-linked immunosorbent assay revealed an

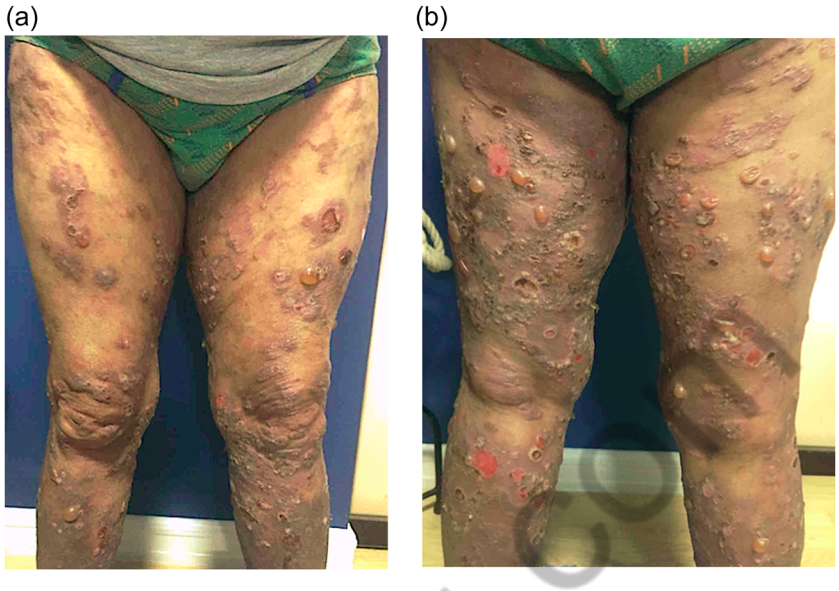

FIGURE 1 Cutaneous examination upon consultation shows multiple tense vesicles and bullae, approximately 0.5–3 cm in diameter, some ruptured and some intact on a slightly erythematous base, with erosions and serous crusting on the anterior (a) and posterior (b) lower extremities.

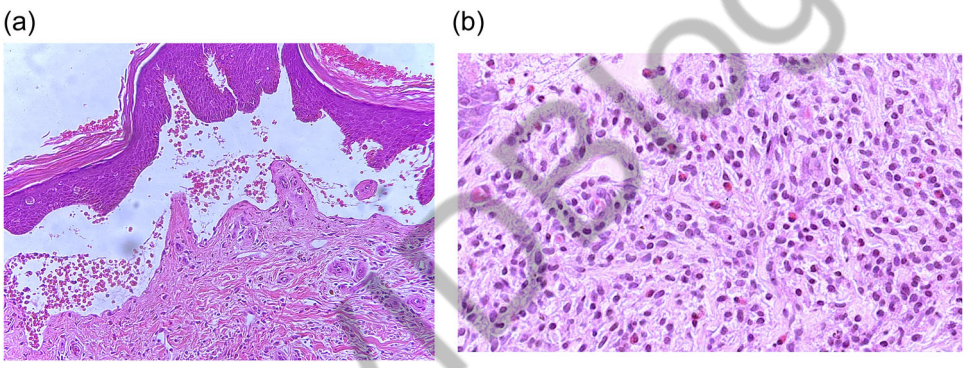

FIGURE 2 A skin biopsy of the left anterior leg shows subepidermal split and festooning of the dermal papillae (a) with superficial and interstitial infiltrates of lymphocytes and many eosinophils (b) (hematoxylin and eosin stain ×40).

anti-BP180 level of 37.18 RU/ml (normal value: <20 RU/ml) and an anti-BP230 level of 27.55 (normal value: <20 RU/ml). The clinical, histologic and serological findings were consistent with BP.

He was immediately started on prednisone 50 mg/day (0.8 mg/kg/day), tetracycline 500 mg/8 h, diphenhydramine 50 mg at bedtime, methotrexate 15 mg/week (0.3 mg/kg/day) and folic acid supplementation. There was a decrease in the number of tense vesicles and bullae and flattening of psoriasis plaques 1 week after the initiation of treatment. Tapering of steroids by 10 mg decrements was instituted after marked improvement of the lesions. Complete resolution of the vesicles and bullae with no new lesions and flattening of psoriasis plaques with postinflammatory hyperpigmentation were observed after 1 month of treatment (Figure 4). On subsequent follow-up after 3 months, the patient still had no new lesions and showed post-inflammatory hyperpigmentation.

DISCUSSION

BP is the most common autoimmune blistering disorder in the adult population. Most cases occur sporadically and are sometimes triggered by drugs, infections, UV radiation and vaccination.[1] Psoriasis, on the other hand, is the most common immune-mediated chronic, inflammatory skin disease that may also be precipitated by drugs, stress and infections.[2] The association between BP and psoriasis is infrequent. It is estimated to be around 2.1% and 5.3% in Taiwanese and Chinese general populations, respectively.[3,4] Donnelly et al.[5] reported the possible pathogenic relationship of the two. Although psoriasis predominantly involves the Th1 and Th17 pathways, while BP primarily involves the Th2 pathway, a serum shift toward a Th2 profile of patients with psoriasis may demonstrate the development of BP in psoriatic patients. Similarly, recent studies have identified the role of Th17/IL23, the main cytokines involved in psoriasis, in the pathogenesis of BP.[6]

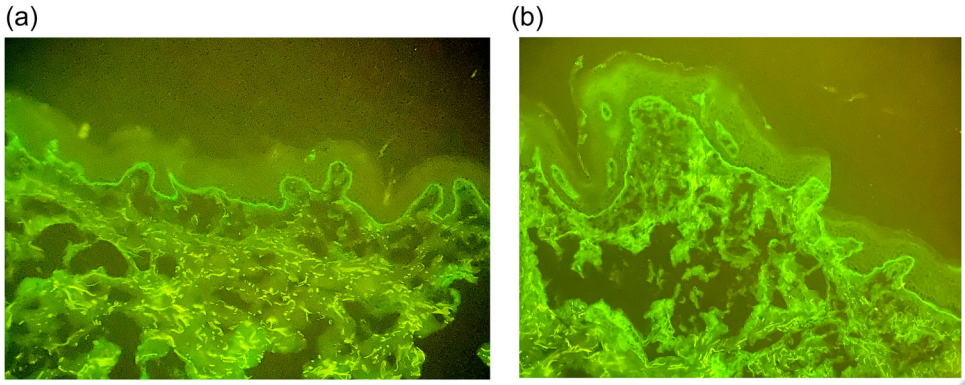

FIGURE 3 DIF of the perilesional skin on the left anterior leg shows a (a) +2 linear basement membrane staining pattern in C3 and (b) +1 linear basement membrane staining pattern in IgG. DIF, direct immunofluorescence.

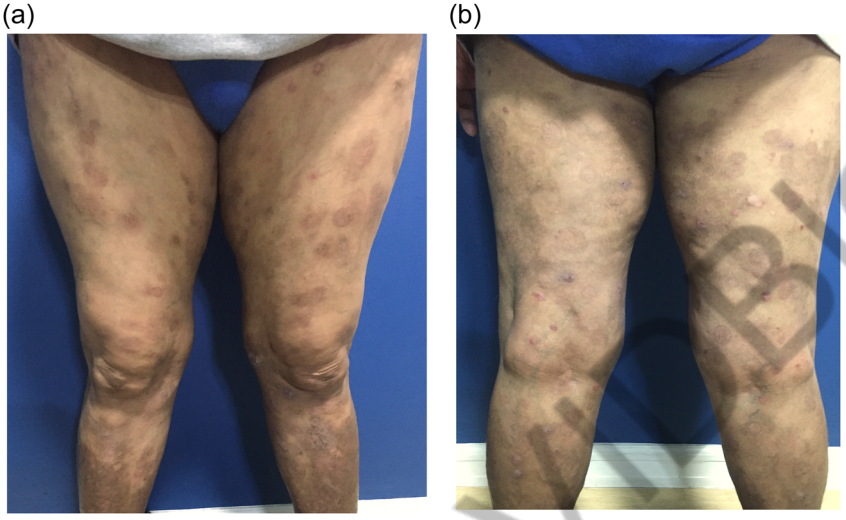

FIGURE 4 Cutaneous examination after 3 months of treatment of prednisone, tetracycline, and methotrexate shows complete resolution of vesicles and bullae on the (a) anterior and (b) posterior lower extremities.

The disruption of laminin within the basement membrane zone (BMZ) may also promote instability and proliferation of keratinocytes leading to the development of psoriasis.[4] This damage to the BMZ in psoriatic patients may also induce the generation of anti-BMZ antibodies causing BP.[4]

Since the introduction of COVID-19 vaccination, few reports on the development of new-onset or flares of existing BP after the administration of mRNA vaccinations (Pfizer and Moderna) have been published.[7] These observations have raised several theories on the role of COVID vaccines in BP initiation. One theory suggested that individuals who developed BP after COVID immunization harboured subclinical or undiagnosed BP that was unmasked by vaccination. Transitory bystander immune cells may have stimulated an existing subclinical autoreactivity.[8] Garcia-Montero et al.[9] believed that mRNA molecules of the vaccine elicit both humoral and adaptive responses. These molecules are recognized by toll-like receptors that activate type I interferon production and stimulate the Th1 response. BP occurs by off-target immune activation postvaccination. Intriguingly, Gambichler et al.[10] proposed that molecular mimicry exists between the vaccine and human proteins that could trigger the generation of autoreactive lymphocytes and cross-reactive antibodies leading to autoimmune reactions. Gambichler et al.[11] also investigated two patients with BP and found that some of the expanded T-cell clones detected in the patients might be reactive to other SARS-CoV-2-derived epitopes including nucleocapsid proteins. However, whether these T-cell clones might hint at an undocumented previous infection with SARS-CoV2 or some other mechanism remains unclear at this point. Whether the development of BP in our patient is a coincidence or is triggered by COVID-19 vaccination is still difficult to elucidate at this time.[12]

Treatment of coexistent BP and psoriasis can be a challenge. Oral corticosteroids such as prednisone have reported to induce remission of both BP and psoriasis with a risk of psoriasis rebound when stopped.[13] Hence, corticosteroid-sparing agents such as methotrexate, azathioprine and dapsone are usually administered.[14] Methotrexate has shown an excellent response in patients with coexistent BP and psoriasis.[15]

Although a true association may exist between BP development and mRNA COVID-19 (Pfizer-BioNTech) vaccination, additional reports and studies are needed to prove their association. Physicians must be aware of these atypical occurrences following vaccination. Even if vaccines may initiate new or trigger autoimmune diseases, the benefits of COVID-19 vaccination in preventing fatal COVID-19 infection still outweigh the risks.

AUTHOR CONTRIBUTIONS

We certify that all authors have participated sufficiently in the intellectual content, conception, and design of this article. All authors agree to be accountable for all aspects of the manuscript.

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CONFLICT OF INTEREST

The authors declared no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analysed in this study.

ETHICS STATEMENT

Exemption from the ethical review was obtained from Rizal Medical Center, Pasig City, Philippines. Verbal and written informed consent were obtained from the patient.

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