Case of Exacerbation of Psoriasis Following COVID-19 Vaccination During Treatment with Brodalumab, Which Resulted in Secondary Failure

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A 43-year-old Japanese man who had suffered psoriasis vulgaris for eight years visited our hospital. His comorbidities were dyslipidemia, hyperuricemia, and obesity. He received phototherapy for six months, which did not result in improvement. Following treatment with brodalumab, his skin symptoms improved. However, seven months after brodalumab treatment, he received two doses of the mRNA-1273 COVID-19 vaccine, with a one-month interval between doses. One month following the second vaccination, his skin symptoms were exacerbated. He received additional NB-UVB therapy, but his skin symptoms did not improve. Nine months after the addition of NB-UVB therapy, treatment was switched to bimekizumab, and his skin became almost clear.

Psoriasis is often associated with comorbidities like metabolic syndrome. Currently, additional COVID-19 vaccination is recommended for high-risk cases such as those with metabolic syndrome. Therefore, it is essential to remain vigilant regarding the potential exacerbation of psoriasis following COVID-19 vaccination even during treatment with highly effective biologic therapy.

Key words: psoriasis, exacerbation, COVID-19 vaccination, brodalumab, secondary failure

INTRODUCTION

Psoriasis is an immune-mediated disorder characterized by the involvement of cytokines such as TNFα, IL-17, and IL-23 in the pathogenesis, and targeted biologic agents against these cytokines have shown significant clinical efficacy [1]. Various factors, including trauma, infections, medications, and vaccines, have been identified as exacerbating factors for psoriasis [2]. Vaccines such as influenza, pneumococcal, Bacillus Calmette–Guerin (BCG), and diphtheria vaccines have been reported as triggers for psoriasis exacerbation [2]. Since the onset of the global COVID-19 pandemic, cases of psoriasis exacerbation following the administration of the COVID-19 vaccines have been reported worldwide [3–9]. Herein, we report a case of exacerbation of psoriasis following COVID-19 vaccination during treatment with brodalumab, which resulted in secondary failure.

CASE REPORT

A 43-year-old Japanese man who had suffered psoriasis vulgaris for eight years, treated with topical corticosteroid and active vitamin D_3, oral apremilast (taken for 6 months) at another hospital, visited our hospital. His comorbidities were dyslipidemia, hyperuricemia, and obesity. His clinical features included scaly erythema on his head, back and extremities (Psoriasis Area and Severity Index [PASI] 11.8). He received phototherapy (NB-UVB) for six months (PASI 9.5). However, NB-UVB treatment did not show improvement (Fig. 1). He was treated with brodalumab and after three months, his skin symptoms improved (PASI 1.8) (Fig. 2) and were stable for the next five months. However, seven months after brodalumab treatment, he received two doses of the mRNA-1273 COVID-19 vaccine, with a one-month interval between them. One month following his second COVID-19 vaccination, his skin symptoms were exacerbated from the residual lesions and extended back to previously symptomatic areas (PASI 6.4) (Fig. 3). Despite receiving additional NB-UVB therapy, his skin symptoms did not improve. Nine months after the addition of NB-UVB therapy, the treatment was switched from brodalumab to bimekizumab in hopes of achieving additional therapeutic effects on skin lesions. After switching to bimekizumab, his skin became almost clear.

DISCUSSION

With the global COVID-19 pandemic, COVID-19 vaccination programs commenced in 2020. Following COVID-19 vaccination, there have been reported cases of psoriasis exacerbation [3–9]. Huang *et al*. conducted a comparative study involving 51 psoriasis patients who received the COVID-19 vaccine and 32 psoriasis patients who did not receive the COVID-19 vaccine. The study reported that there were 15 cases of psoriasis exacerbation among the vaccinated patients, which was significantly higher than the 2 cases observed in the unvaccinated patients ($p = 0.047$). The duration of psoriasis rash exacerbation following vaccination was reported to be 9.3 ± 4.3 days [3]. The longest period of psoriasis exacerbation following COVID-19 vaccination was 32 days, according to the reports we could find [4].

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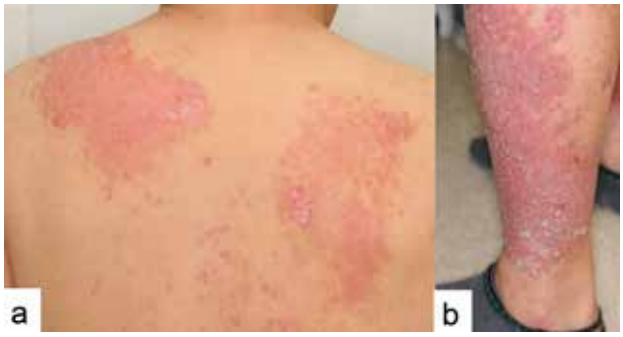

Fig. 1 (a), (b). Clinical features six months after NB-UVB treatment. NB-UVB treatment did not show improvement (PASI 9.5).

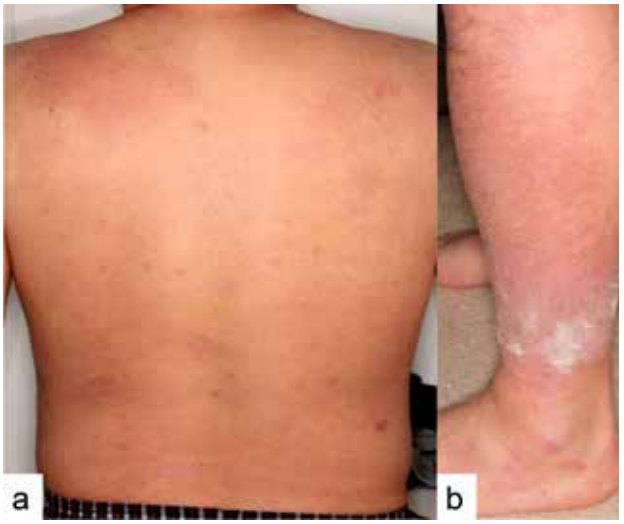

Fig. 2 (a), (b). Clinical features three months after brodalumab treatment. His skin symptom became almost clear (PASI 1.8).

Fig. 3 (a), (b). Clinical features one month after COVID-19 second vaccination. His skin symptom exacerbated on his back and legs (PASI 6.4).

In psoriasis patients undergoing treatment with biologic agents, there have been 12 reported cases of exacerbation following COVID-19 vaccination [5–9] (Table 1). The average age of the patients was 48 ± 10.1 years, with a higher prevalence in males (9 cases) compared to females (3 cases). Among the psoriasis types, there were 9 cases of plaque type, 2 cases of generalized pustular psoriasis (GPP), and 1 case of guttate type. Regarding the vaccine types, 7 patients received the Pfizer vaccine, and 5 patients received the AstraZeneca vaccine.

Exacerbation was observed in 6 cases after the first dose of COVID-19 vaccination and in 6 cases after the second dose of COVID-19 vaccination. The average duration from COVID-19 vaccination to psoriasis rash exacerbation was 10.5 ± 7.0 days. Additional treatments were administered in most cases, with 4 out of the 12 cases requiring a switch to alternative biologic agents. Among them, there was only one case report of a patient treated with brodalumab for GPP [5] and no reports of any patient with plaque type psoriasis vulgaris treated with brodalumab. In the patient with GPP who was treated with brodalumab and acitretin, increased dosing of acitretin following COVID-19 vaccine exacerbation resulted in improvement after 3 weeks [5].

In our case, the exacerbated skin symptoms did not improve despite adding NB-UVB. It has been reported that brodalumab can show good efficacy despite failure with previous agents and was superior to other approved therapies, including anti-TNFs, apremilast, secukinumab, and ustekinumab [10]. Nevertheless, our patient showed secondary failure triggered by COVID-19 vaccination. Although there have been many reports of COVID-19 vaccine-induced psoriasis exacerbations, this is the first case of exacerbation of plaque psoriasis during treatment with brodalumab, resulting in secondary failure triggered by COVID-19 vaccination. Both brodalumab and bimekizumab demonstrate high efficacy against skin lesions, but there is no direct clinical trial comparing the two drugs. PASI 100 indicates a 100% improvement and complete resolution from the baseline PASI score, which is used as a measure of treatment effectiveness in psoriasis. In brodalumab clinical trials, the proportion of patients achieving PASI 100 at 52 and 120 weeks was 64.8% and 61.1%, respectively [11]. On the other hand, in bimekizumab trials, the proportions of patients achieving PASI 100 at 56 and 104 weeks were even higher at 78.4% and 72.3%, respectively [12]. Therefore, bimekizumab is expected to have a greater effect on skin lesions compared to brodalumab, leading to a switch in treatment from brodalumab to bimekizumab in this case, resulting in improved skin lesions.

The detailed mechanism of exacerbation of psoriasis following COVID-19 mRNA vaccination remains unclear. However, Sureshchandra *et al.* examined immune responses using PBMCs from healthy individuals

Table 1 Psoriasis exacerbation following COVID-19 vaccine during biologic treatment

Case	Age	Sex	Type of psoriasis	Vaccine	Dose	Days	Previous treatment	New treatment	Reference
1	36	Male	Plaque	AZD1222	1	18	Adalimumab	Adalimumab, cyclosporine 200 mg/day	Chao JP, *et al.*[5]
2	50	Female	Plaque	AZD1222	1	7	Ixekizumab	Ixekizumab	Chao JP, *et al.*[5]
3	40	Female	GPP	AZD1222	1	1	Brodalumab, acitretin 20 mg/day	Brodalumab, acitretin 50 mg/day	Chao JP, *et al.*[5]
4	45	Male	Plaque	AZD1222	1	10	Secukinumab	Secukinumab*	Megna M, *et al.*[6]
5	61	Male	Plaque	BNT162b2	2	12	Adalimumab	Ixekizumab	Megna M, *et al.*[6]
6	47	Male	Guttate	BNT162b2	2	9	Ixekizumab	Ixekizumab*	Megna M, *et al.*[6]
7	39	Female	Plaque	AZD1222	2	7	Guselkumab	Guselkumab*	Megna M, *et al.*[6]
8	58	Male	Plaque	BNT162b2	2	5	Secukinumab	Secukinumab*	Megna M, *et al.*[6]
9	59	Male	Plaque	BNT162b2	1	14	Etanercept	Ixekizumab	Megna M, *et al.*[6]
10	65	Male	GPP	BNT162b2	2	12	Infliximab	Secukinumab	Yatsuzuka K, *et al.*[7]
11	42	Male	Plaque	BNT162b2	1	28	Secukinumab	Ixekizumab	Durmus O, *et al.*[8]
12	34	Male	Plaque	BNT162b2	2	3	Risankizumab	Risankizumab	Tsunoda K, *et al.*[9]

*Biologic treatment associated with topical calcipotriol/betamethasone combination and/or phototherapy.
Abbreviations: AZD1222, AstraZeneca-Oxford AZD1222; BNT162b2, Pfizer mRNABNT162b2; GPP, Generalized pustular psoriasis.

following COVID-19 mRNA vaccination [13]. They stimulated PBMCs with SARS-CoV-2 spike-overlapping peptide from four healthy individuals who received either the BNT162b2 or the mRNA-1273 vaccines. Spike-specific polyfunctional IFNγ + IL2 + and IFNγ + TNFα + (Th1) CD4+ were evident, along with increased expression of TCF7 and vaccination induced Th17 responses in CD4 + T cells in agreement with an increased expression of *RORA*. This result strongly suggested that mRNA vaccines facilitate the development of a Th1/Th17 response [13]. We speculate that this mechanism caused the exacerbation of psoriasis in our case following COVID-19 vaccination. To the best of our knowledge, there have been no reports linking the underlying data from the BNT162b2 or the mRNA-1273 COVID-19 vaccines to any aspect of the mechanism of psoriasis exacerbation.

Psoriasis is often associated with comorbidities like metabolic syndrome. Currently, additional COVID-19 vaccination is recommended for high-risk cases such as those with metabolic syndrome. Therefore, it is essential to remain vigilant regarding the potential exacerbation of psoriasis following COVID-19 vaccination even during treatment with highly effective biologic therapy.

CONFLICT OF INTEREST

All authors have no conflict of interest to declare.

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