Flare-up of adult-onset Still's disease after receiving a second dose of BNT162b2 COVID-19 mRNA vaccine

Sirs,

Vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are essential for controlling the ongoing coronavirus disease 2019 (COVID-19) pandemic. At present, vaccination is continuing rapidly worldwide, and many individuals with rheumatic diseases have received vaccines to prevent SARS-CoV-2 infection. However, data on the safety of SARS-CoV-2 vaccines in patients with rheumatic diseases are insufficient (1). Herein, we report a case of adult-onset Still's disease (AOSD) that relapsed after SARS-CoV-2 vaccination.

A 37-year-old Japanese woman presented with a 2-month history of episodic fever (>39°C), rash, sore throat, and polyarthritis. These symptoms had appeared a few days after she received a second dose of BNT162b2 COVID-19 mRNA vaccine (Pfizer-BioNTech). She had been diagnosed with AOSD 13 years earlier and had experienced repeated remissions and relapses. Before SARS-CoV-2 vaccination, she had achieved a drug-free remission status for the previous 2 years. On presentation, joint examination showed swelling and tenderness of multiple joints bilaterally, including the hands, wrists, and knees. Skin examination revealed a salmon-pink maculopapular eruption on her arms and legs, which was most noticeable at fever peak (Fig. 1). Laboratory test results were as follows: white blood cell count, 9.8 × 10^3 cells/μL with 77.2% neutrophils; C-reactive protein level, 21.6 mg/L; and lactate dehydrogenase level, 325 U/L. Her serum ferritin level and liver function test results were normal. All autoimmune antibody tests were negative. Blood and urine cultures were negative. Virus tests, including Epstein-Barr virus, cytomegalovirus, and SARS-CoV-2, were negative. Computed tomography revealed generalised lymphadenopathy of the cervical, axillary, inguinal, and abdominal lymph nodes.

The patient's symptoms, including fever, rash, sore throat, polyarthritis, and enlarged lymph nodes, were similar to the findings of her previous AOSD flare-ups. Thus, she was diagnosed with a relapse of AOSD based on the Yamaguchi criteria. As the onset was immediately after SARS-CoV-2 vaccination and no infectious trigger had been identified, we suspected that the AOSD relapse was triggered by the vaccination. A low dose of steroid (prednisolone 15 mg/day) led to the partial relief of her symptoms, although she had fever again. After initiating tocilizumab (subcutaneously at 162 mg/2 weeks), all her symptoms were relieved. She was followed up for 2 months during which she did not experience further AOSD relapse (Fig. 2).

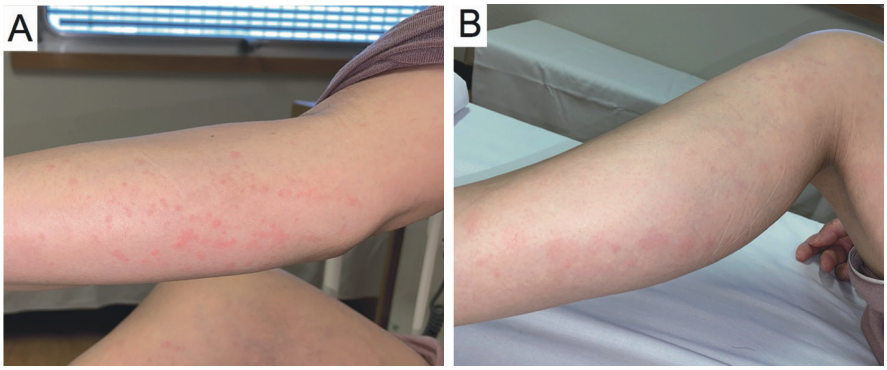

Fig. 1. Salmon-pink maculopapular rash on the patient's arms (A) and legs (B) that developed after receiving a second dose of the BNT162b2 COVID-19 mRNA vaccine.

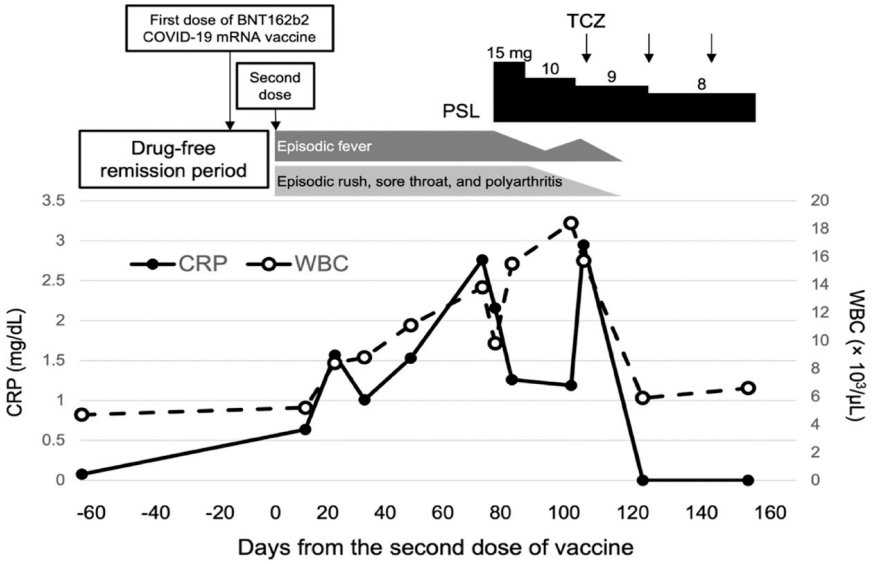

Fig. 2. Clinical course. Episodic fever, rash, sore throat, and polyarthritis appeared after a second dose of BNT162b2 COVID-19 mRNA vaccine (Pfizer-BioNTech). Although partial response to a low dose of steroid was observed, all her symptoms and laboratory data improved after initiating tocilizumab.
CRP: C-reactive protein; WBC: white blood cell; PSL: prednisolone; TCZ: 162 mg tocilizumab administered subcutaneously every 2 weeks.

The patient provided written consent for the publication of this case report, including copies of her clinical imaging results.

Although a case of AOSD that developed after SARS-CoV-2 infection was reported, to the best of our knowledge, there have been no previous reports of relapse after SARS-CoV-2 vaccination (2). Although the mechanisms related to vaccine administration and flare-ups of rheumatic diseases, including AOSD, are unknown, antiviral vaccination may induce a reaction similar to the mechanism of AOSD and exacerbate symptoms. In addition, there was a report of AOSD that developed following influenza vaccination (3). Moreover, the BNT162b2 COVID-19 mRNA vaccine activates $CD4^+$ type 1 helper T cells and various cytokines, including interferon-γ (4). As the levels of these cells and cytokines are elevated in the serum of patients with AOSD, these immune cells are considered to be involved in the pathogenesis of AOSD (5). Notably, in this patient, no symptoms developed after she received her first dose of SARS-CoV-2 vaccine. This may have been because the immune response is generally stronger after the second dose (6).

Rheumatologists should adjust the dose of immunosuppressive drugs before and after SARS-CoV-2 vaccination and monitor of its effectiveness. They should also be aware that SARS-CoV-2 vaccination may contribute to the development or relapse of rheumatic diseases.

S. Yamamoto, *MD*
K. Nishimura, *MD, PhD*
K. Yo, *MD*
D. Waki, *MD*
H. Murabe, *MD, PhD*
T. Yokota, *MD, PhD*

Department of Endocrinology and Rheumatology, Kurashiki Central Hospital, Okayama, Japan.

Letters to the Editors

Please address correspondence to:
Keisuke Nishimura,
Department of Endocrinology and Rheumatology,
Kurashiki Central Hospital,
1-1-1 Miwa, Kurashiki,
Okayama, 710-8602, Japan.
E-mail: keinishi@med.kobe-u.ac.jp

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