Received: 28 March 2022 | Revised: 19 May 2022 | Accepted: 2 June 2022

DOI: 10.1111/dth.15618

DERMATOLOGIC THERAPY WILEY

LETTER

A case of cutaneous arteritis after administration of mRNA coronavirus disease 2019 vaccine

Dear Editor,

Cutaneous adverse reactions after the administration of coronavirus disease 2019 (COVID-19) vaccine have been reported.[1] However, cutaneous vasculitis has only been described in a few cases. Here, we report a case of cutaneous arteritis following the administration of an mRNA COVID-19 vaccine.

A 63-year-old Japanese woman with no significant medical history and no history of infection with COVID-19, was admitted to our department with fever, skin rash, and anorexia. The skin rash was not painful or pruritic. Eighteen days earlier, she had received her second dose of an mRNA COVID-19 vaccine (BNT162b2 [BioNTech/Pfizer]). Seven days later, the patient complained of pharyngalgia. She had not taken any medications until she developed fever, skin eruption on the trunk, and anorexia 6 days afterward. Four days later, she visited a medical clinic and underwent a rapid influenza diagnostic test, which was negative.

On admission, she had a fever of 39.2°C. Disseminated purplish erythematous macules were observed on her trunk (Figure 1A,B). No exanthem was observed elsewhere on her body. Laboratory data revealed high serum levels of C-reactive protein, soluble interleukin-2 receptor, and D-dimer (Table 1). The serum levels of aspartate and alanine aminotransferases, creatine kinase, and ferritin were slightly elevated. Tests for anti-nuclear antibodies, rheumatoid factor, and myeloperoxidase and proteinase 3- anti-neutrophil cytoplasmic antibodies were negative. The anti-streptolysin O titer was not elevated. The results of the serological tests for Epstein–Barr virus were compatible with prior infection. Hepatitis B and C serologies and T-SPOT. TB test results were all negative. Her nasopharyngeal swab was tested for COVID-19 using reverse transcription polymerase chain reaction (RT-PCR) and the result was negative. Blood culture results were negative. Whole-body computed tomography revealed no signs of infection or malignancy. A biopsy specimen taken from the lateral thoracic skin exhibited an inflammatory infiltrate composed primarily of lymphocytes and histiocytes in the walls of arteries in the superficial subcutis with leukocytoclasia and fibrin thrombi (Figure 1C–F). These features were not observed in the dermal vessels. Together, the findings established the diagnosis of cutaneous arteritis following the administration of the mRNA COVID-19 vaccine.

Oral betamethasone, at a dose of 3 mg/day, was started on day 3. The fever subsided immediately, and the skin rash faded. The betamethasone course was completed within 3 weeks without any further flareups of arteritis.

In our case, a serological test of anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) immunoglobulin M was not performed to exclude RT-PCR-negative COVID-19. It follows that the cutaneous eruption in our patient might have been related to COVID-19. However, if delay time observed in cutaneous manifestation of arteritis after mRNA COVID-19 vaccination is similar across patients including further reported cases as well as our case, it would suggest that such arteritis might be at least temporally associated with the vaccination.

We reported here a case of cutaneous arteritis occurring after the administration of the mRNA COVID-19 vaccine, which suggests that there may be a potential association between the mRNA COVID-19 vaccine and the subsequent development of arteritis. Prior case reports have also shown the emergence of vasculitis following administration of the mRNA COVID-19 vaccine.[2–9] In some of these cases, the presence or absence of antibody deposition within a skin sample was examined using direct immunofluorescence.[5–7,9] Though in those cases, an antigen for the antibody was not identified. Thus, it remains unclear whether the onset of vasculitis after mRNA COVID-19 vaccination is caused by an anti-SARS-CoV-2 antibody.

If the development of vasculitis after mRNA COVID-19 vaccination is mediated by an anti-SARS-CoV-2 antibody, what could be an antigen for the antibody? One potential antigen could be the SARS-CoV-2 spike protein that the host cells synthesize from the mRNA contained in the vaccine. However, one case report stated that the authors were unable to detect any SARS-CoV-2 spike protein deposition within the skin sample obtained from the patient developing post-COVID-19 vaccination vasculitis.[5] Another potential antigen could be a human tissue antigen. Instead of responding to a SARS-CoV-2 spike protein, an anti-SARS-CoV-2 spike protein antibody could react to a human tissue antigen with homology to the SARS-CoV-2 spike protein before developing post-COVID-19 vaccination vasculitis.[10] However, it has not been demonstrated whether such an antibody causes post-COVID-19 vaccination vasculitis.

Stimulation of the innate immune system by mRNA COVID-19 vaccination could induce the onset of vasculitis. The mRNA vaccine is

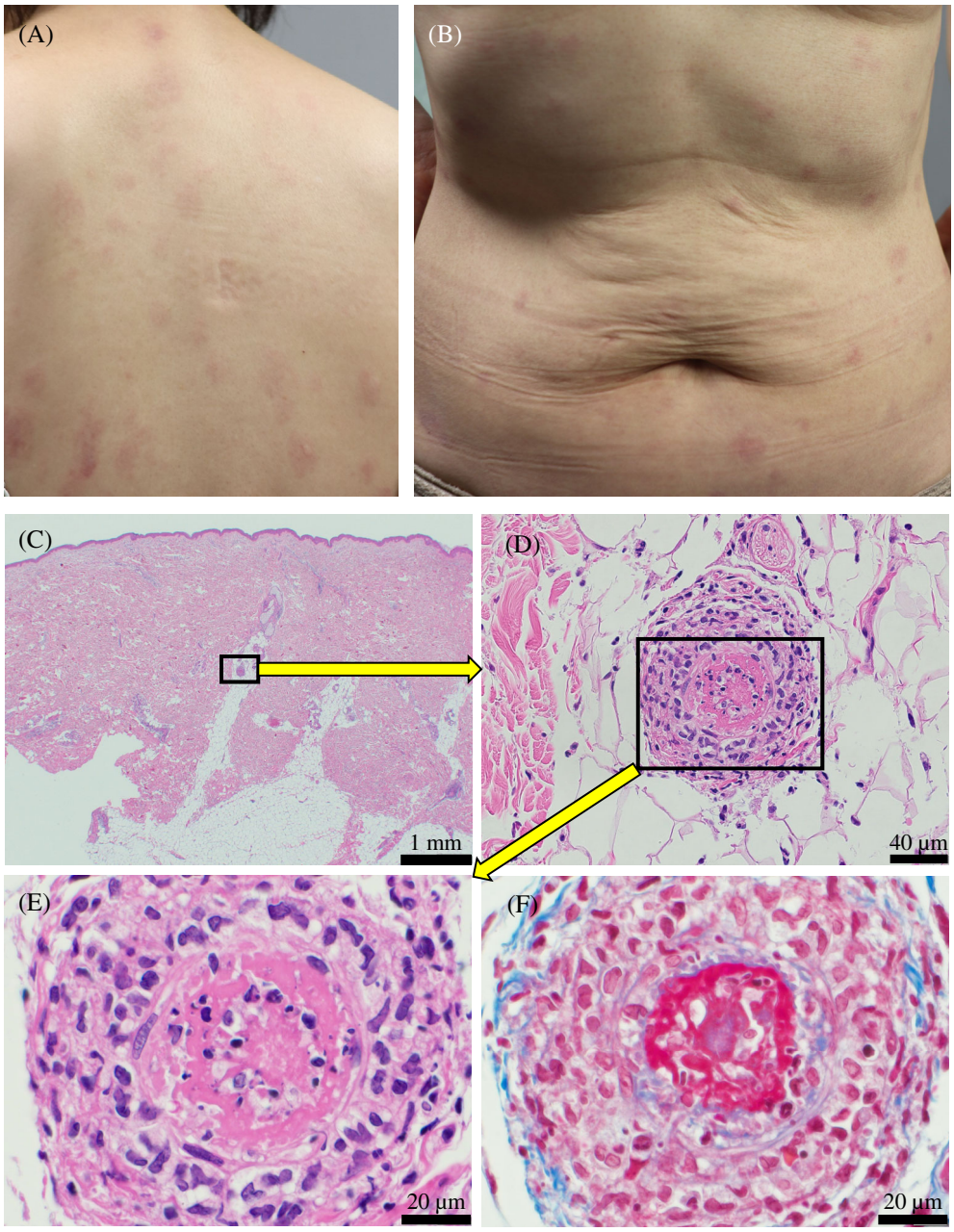

FIGURE 1 Clinical appearance and histopathological findings. Disseminated purplish erythematous macules are observed on the back (A), chest, and abdomen (B). A biopsy specimen taken from the lateral thoracic skin exhibited an inflammatory infiltrate composed mainly of lymphocytes and histiocytes in the walls of arteries in the superficial subcutis with leukocytoclasia and fibrin thrombi (C–F). (C–E) Hematoxylin–eosin stain. (F) Masson trichrome stain

thought to induce immune stimulation and cytokine secretion by activating signaling receptors of the innate immune system, including the Toll-like receptors, the natural role of which is to identify and respond to viral RNAs.[11] Thus, vasculitis could be triggered by the stimulation of the innate immune system by mRNA COVID-19 vaccination.

Our case report suggests that there may be a potential association between the mRNA COVID-19 vaccine and the subsequent development of cutaneous arteritis. However, it remains to be proved that the mRNA COVID-19 vaccine causes arteritis. Further studies may help elucidate the underlying mechanisms of post-COVID-19 vaccination arteritis.

AUTHOR CONTRIBUTIONS

Jun-ichi Iwata acquired, analyzed, and interpreted the patient's data. Afterwards, He designed and drafted the work. Yukiko Kanetsuna, Aiko Takano, and Yoshihito Horiuchi contributed to the acquisition of the patient's data for the work and revised the work critically.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The authors declare that they do not have any research data.

TABLE 1 Laboratory parameters of the patient

Parameter	Result	Normal value
Leukocytes	8000/μl	3300–8600/μl
Neutrophils	6512/μl	
Hemoglobin	13.2 g/dl	11.6–14.8 g/dl
Platelets	22.5 × 10^4/μl	15.8–34.8 × 10^4/μl
Aspartate aminotransferase	42 U/L	13–30 U/L
Alanine aminotransferase	29 U/L	7–23 U/L
Lactate dehydrogenase	223 U/L	124–222 U/L
Creatine kinase	212 U/L	41–153 U/L
Blood urea nitrogen	12 mg/dl	8–20 mg/dl
Creatinine	0.72 mg/dl	0.46–0.79 mg/dl
C-reactive protein	12.0 mg/dl	< 0.14 mg/dl
Ferritin	309 ng/ml	21–274 ng/ml
D-dimer	2.6 μg/ml	<1.0 μg/ml
CH50	48.5 U/ml	25–48 U/ml
Soluble interleukin-2 receptor	1130 U/ml	157–474 U/ml
Anti-nuclear antibody	Negative	
Myeloperoxidase ANCA	Negative	
Proteinase 3- ANCA	Negative	
Rheumatoid factor	Negative	
Anti-streptolysin O titer	10 IU/ml	<239 IU/ml
EBV anti-VCA IgM	Negative	
EBV anti-VCA IgG	Positive	
EBV anti-EBNA IgG	Positive	
HBsAg	Negative	
Anti-HBs	Negative	
Anti-HCV	Negative	
T-SPOT. TB test	Negative	

Abbreviations: ANCA, anti-neutrophil cytoplasmic antibody; anti-HBs, hepatitis B surface antibody; anti-HCV, hepatitis C virus antibody; EBNA, Epstein–Barr virus nuclear antigen; EBV, Epstein–Barr virus; HBsAg, hepatitis B surface antigen; IgG, immunoglobulin G; IgM, immunoglobulin M; VCA, viral capsid antigen.

ETHICS STATEMENT

Informed consent was obtained from the patient for the publication of her clinical data.

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