LETTER TO THE EDITOR

A severe case of papulovesicular exthanthema with rhabdomyolysis after corona virus disease 2019 heterologous booster vaccination

Editor

A 66-year-old Japanese man was admitted for an emergency with skin rashes and muscle pain of his extremities. He had high fever over 39°C and difficulty in moving. He was taking bezafibrate 200 mg/day for hyperlipidemia for 3 months and received the third dose booster mRNA-1273 vaccine (Moderna) 8 months after the second vaccination with BNT162b1 (BioNTech-Pfizer). The present symptoms appeared 5 days after the third vaccination. At the second vaccination, he experienced no severe adverse events (AEs) other than temporary fever. On physical examination, widespread edematous and erythematous papulovesicles were seen on his trunk and extremities (Fig. 1a). Laboratory examination revealed elevated serum levels of creatine kinase (CK) at 801 U/L (normal range 59–248 U/L), myoglobin at 839 ng/mL (<154.9 ng/mL) and creatinine at 2.27 mg/dL (<1.2 mg/dL). His urine was reddish brown due to

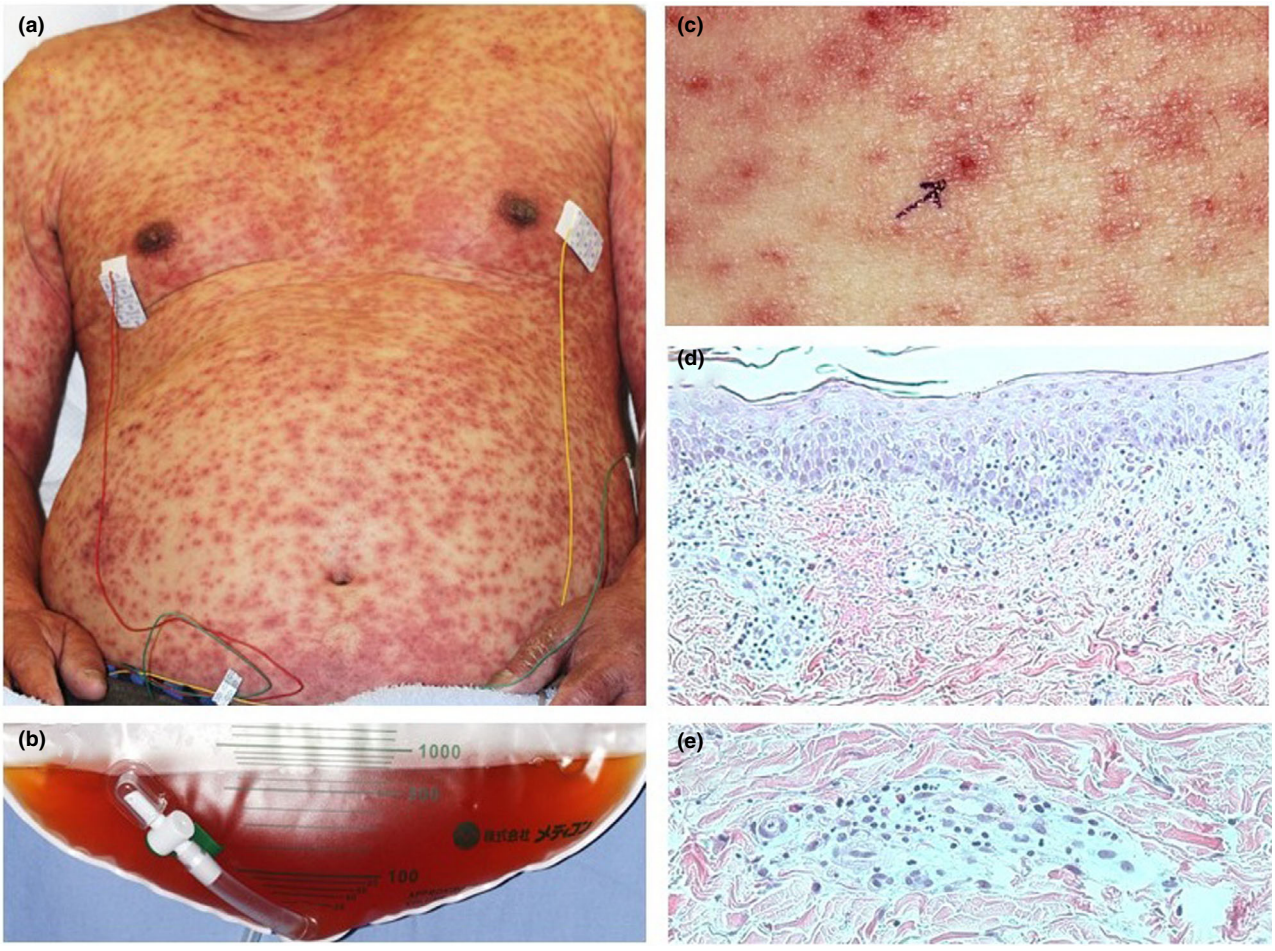

Figure 1 (a) Numerous widespread edematous and erythematous papulovesicles. (b) A reddish-brown myoglobinuria. (c) Erythematous papules on the abdomen. (d) Spongiosis of the epidermis and papillary dermal edema (HE, original magnification ×40). (e) Inflammatory infiltrates of lymphocytic with eosinophils in the vicinity of the small vessels in the upper dermis (HE, ×100).

myoglobinuria (Fig. 1b). Electrocardiogram and echocardiography demonstrated no findings of myocarditis. A biopsy from his abdomen (Fig. 1c) showed epidermal spongiosis, papillary oedema and perivascular lymphocytic infiltration with eosinophils in the upper dermis (Fig. 1d,e). We started oral prednisolone, 55 mg/day, and adequate fluid resuscitation and discontinued bezafibrate, resulting in rapid improvement of his cutaneous lesions and renal function in 5 days. CK and creatinine returned to normal. Both patch test and drug-induced lymphocyte stimulation test for bezafibrate were negative. Our diagnosis was papulovesicular-type vaccine-related eruption of papules and plaques (V-REPP) with rhabdomyolysis induced by the COVID-19 vaccine.

Various COVID-19 vaccine-related cutaneous reactions have been reported. The acronym of the descriptive terms, V-REPP, was proposed for robust papules with overlying crust to pink papules with scales as seen in the present case. This type accounts for 3.0% of overall cutaneous reaction (n = 1364).[1] There are several case reports of rhabdomyolysis due to drugs or vaccines, most commonly to influenza vaccine, statins and fibrates.[2] According to the Vaccine Adverse Event Reporting System of the Centers for Disease Control and Prevention, 214 cases of rhabdomyolysis after COVID-19 vaccination were reported as of 14 January 2022.[3] Kamura *et al.*[4] reported a Japanese case of fatal thrombotic microangiopathy with rhabdomyolysis after the first dose of mRNA-1273. They suggested the involvement of an immunological mechanism such as vaccine-induced complement activation syndrome. To the best of our knowledge, there has been no report of concomitant development of rhabdomyolysis and papulovesicular-type V-REPP after COVID-19 vaccination.

The mRNA vaccines against COVID-19 are highly effective, whereas breakthrough infections are occurring. Many clinical trials are in progress and either homologous or heterologous prime-boost formats are proposed.[5] While the recent study demonstrated that heterologous booster vaccination induced the neutralizing antibody titres and spike-specific T-cell responses more effectively than homologous booster vaccination,[6] further studies are needed to confirm the effectiveness and safety of prime-boost vaccinations.

In the present case, it is unclear that which is the cause of the severe symptoms, a single dose of mRNA-1273 or a robust immune response elicited by heterologous booster vaccination. In addition, there is a possibility that the interaction of COVID-19 vaccine with other drugs plays a role in the development of AEs. Accumulation of similar cases will help to elucidate the underlying mechanisms of AEs caused by COVID-19 booster vaccination.

Funding source

None.

Conflict of Interest

The authors have no conflict of interest to declare.

Acknowledgements

The authors thank the resident doctors, Yuuki Kaida and Aya Hashimoto, for their excellent clinical assistance in emergency medical examination.

Patient consent

The patients in this manuscript have given written informed consent for the publication.

Data availability statement

No data are available.

A. Baba,[1,*] Y. Maki,[2] T. Kanekura,[3] H. Tsubouchi[4]

[1]Department of Dermatology, Kagoshima City Hospital, Kagoshima, Japan, [2]Department of Neurology, Kagoshima City Hospital, Kagoshima, Japan, [3]Department of Dermatology, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan, [4]Department of Gastroenterology, Kagoshima City Hospital, Kagoshima, Japan

*Correspondence: A. Baba. E-mail: baba-a16@kch.kagoshima.jp

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DOI: 10.1111/jdv.18420