Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Correspondence

Erythema nodosum, after Medigen vaccination against COVID-19?

Dear Editor,

The Medigen vaccine (MVC-COV1901) was launched in August, 2021 in Taiwan as the first Taiwanese-developed vaccine against COVID-19.[1] However, its real-world effect and safety remain largely unknown. Herein, we report a cutaneous eruption post Medigen vaccination.

A 27-year-old otherwise healthy man presented 3 days after the first dose of the vaccine with fever, malaise, headache, myalgia in extremities, nausea, abdominal discomfort, swelling of the ankles, and painful skin rash on the legs. He denied recent drug exposure or contact history. Physical examination revealed several tender erythematous deep-seated nodules on bilateral lower legs (Fig. 1A). Laboratory tests showed elevated C-reactive protein level (8.97 mg/dl) and prolonged erythrocyte sedimentation rate (22 mm/h). Complete blood count, hepatic and renal panels were within normal limits. Antinuclear antibody and anti-neutrophil cytoplasmic antibody were not detected. A SARS-CoV-2 rapid antigen test showed negative result. A tests for anti-streptolysin O antibody and QuantiFERON-TB Glod test were negative. Chest X-ray unraveled no pathological findings. Differential diagnoses included erythema nodosum (EN), neutrophilic dermatosis, and cutaneous vasculitis. A skin biopsy was performed. Histology demonstrated subcutaneous septal panniculitis with lymphocytic infiltrates and Miescher's granulomas (Fig. 1B). No other known risk factors for EN were identified in our patient, such as infections, sarcoidosis, malignancy, or other drug exposure. Therefore, EN associated with the Medigen vaccination was suspected. The patient was treated with oral prednisolone, colchicine, and topical fluocinonide, and the EN showed significant resolution after 10 days. The second dose of Medigen was not suggested.

To our knowledge, this is the first case of EN after a single dose of Medigen vaccination against COVID-19. The phase 2 trial of Medigen vaccine disclosed good safety profile with mostly mild adverse events and none serious adverse event.[1]

EN is characterized by painful erythematous subcutaneous nodules 1–5 cm in diameters on bilateral lower legs, and may be accompanied by fever, malaise, and arthralgia.[2] Cases of EN associated with different types of vaccination against various pathogens had been reported,

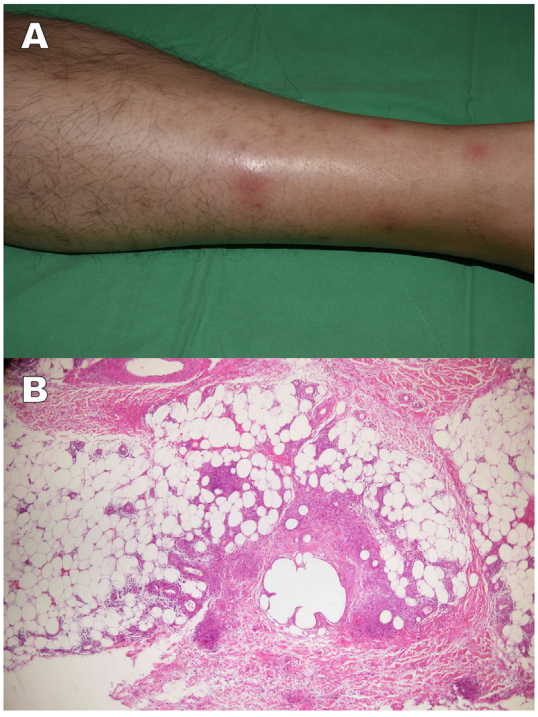

Figure 1 The dermatologic presentation and histology of the erythema nodosum in a 27-year-old male 3 days after receiving the Medigen vaccine against COVID-19. (A) Several ill-defined, non-blanchable, erythematous, and painful subcutaneous nodules on bilateral lower legs. (B) Histology revealed typical presentation of septal panniculitis with presence of Miescher's granulomas.

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and the onset of vaccine-associated EN could range from less than 24 h to 30 days after the first or the following dose.[2] In July, 2021, Hali et al. reported the first case of EN associated with the COVID-19 vaccine, in a 66-year-old female patient 48 h after the second dose of the Oxford AstraZeneca COVID-19 vaccine (AZD1222).[3] Furthermore, EN has also been associated with COVID-19 pneumonia.[4] However, the pathogenesis of vaccine-associated EN remains unknown, generally hypothesized as a delayed hypersensitivity reaction to the antigen.[2,3]

Most of the causes of EN were unknown, and common etiologies including streptococcal infection, sarcoidosis, drug exposure, tuberculosis, and inflammatory diseases were absent in our patient.[3] The present case report could not absolutely prove, though highly suspected, the causality between EN and the Medigen vaccine. Clinicians should be aware of possible EN as a Medigen-related adverse event. Since the adverse events are extremely rare and mild, the benefits of vaccination still overwhelmingly outweigh the risk of complications in the fight against COVID-19.

Causal inference requires both temporality and association. In this case, the association between EN and Medigen cannot be established in the absence of a re-challenge trial. The occurrence of EN after Medigen could be just a temporal coincidence. However, the absence of alternative etiologies, such as infections, autoimmune disease, or malignancy in this young patient support a possible association. It should be noted here that the pre-emergency use authorization phase 2 randomized placebo-controlled trial of Medigen vaccine, involving more than 3000 participants, disclosed good safety profile with mostly mild adverse events and none serious adverse event. Therefore, EN observed in this patient is likely an extremely rare event, even if we assumed an association.

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Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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Hui-Te Hsu
Hsuan-An Su
Yu-Chia Chen*
Department of Dermatology, Far Eastern Memorial Hospital, New Taipei City, Taiwan

*Corresponding author. No. 21, Section 2, Nanya South Road, Banciao District, New Taipei City, 220, Taiwan. Fax: +886 2 8966 5567.
E-mail address: ccyycc2408@gmail.com (Y.-C. Chen)

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