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LETTER TO THE EDITOR

Microvascular manifestations revealing vaccine-induced thrombotic thrombocytopenia after COVID-19 vaccination

KEYWORDS
Vaccine-induced immune thrombotic thrombocytopenia;
Raynaud disease;
Thrombosis;
thrombocytopenia;
Pernio;
Chilblain

Background

Since March 2021, cases of thrombocytopenia associated to thrombotic events have been described as a rare and serious adverse effects after vaccination with recombinant adenoviral vector anti-SARS-CoV-2 vaccines. This condition has been identified as vaccine-induced immune thrombotic thrombocytopenia (VITT) by Greinacher et al. [1]. The mechanism of VITT includes platelet activation by antibodies to platelet factor 4 (PF4) in a way that is similar to Heparin Induced Thrombocytopenia (HIT), but without previous exposure to heparin [1].

Recent reviews [2,3] on VITT have listed dermatological signs of potential VITT, sometimes without any thrombosis. Cutaneous manifestations, including unfrequent acral chillblain-like or pernio lesions were reported with COVID-19 infection, with mRNA (COMIRNATY® [Pfizer/BioNTech] or mRNA-1273 [Moderna]) and inactivated virus (CoronaVac® [Sinovac]) vaccines [2—4], but these latter findings were not associated with low platelet count or antiplatelet factor 4 (PF4) antibodies.

Objective

Report Raynaud's phenomenon, chilblain-like lesions, splinter hemorrhages as new features of vaccine induced thrombotic thrombocytopenia.

Case report

A 71-year-old woman presented with a recent Raynaud's phenomenon associated with thrombocytopenia. She was vaccinated on April 9, 2021 (day 0) by a first dose of ChAdOx1 nCoV-19, 8 days before symptoms onset. Her medical history included seronegative rheumatoid arthritis, colorectal cancer in 1990, arterial hypertension and dyslipidaemia. She was referred to our hospital on day 20 after vaccination.

Clinical examination showed chilblain-like lesions (Fig. 1, panel A) and splinter hemorrhages (Fig. 1, panel B) on the first two fingers associated with coldness and cyanosis of the left hand and a swollen left wrist (Fig. 1, panel C). Purpuric lesions were present on her legs. She reported a mild headache which prevailed in the morning. Her neurological exam was normal.

Laboratory tests performed on day 20 showed thrombocytopenia (54 G/L) associated with elevated D-dimers levels (9243 ng/mL) and fibrin degradation products (20 μg/mL). Hemoglobin, fibrinogen, and prothrombin time were normal at 122 g/L, 3.8 g/L and 12 seconds, respectively. Antiphospholipid antibodies were negative. Protein C activity, protein S antigen and antithrombin activity were normal at 108%, 89% and 91% respectively. Activated protein C resistance was ruled out by thrombin generation assay. Antiplatelet factor 4/heparin ELISA (Asserachrom HPIA Stago®) was positive (highest OD value 1.397, normal < 0.421).

Brain and chest thoracic computed tomography angiography ruled out cerebral vein thrombosis or pulmonary embolism. Arterial Doppler examination excluded large vessel occlusion. Nailfold capillaroscopy was normal except for splinter hemorrhages.

These features were highly suggestive of a likely vaccine-induced immune thrombotic thrombocytopenia (VITT) with an original, previously unreported, presentation.

The patient was successfully treated with high-dose intravenous immunoglobulins (total dosage1 g per kg) infused during 4 consecutive days, started on day 21, as suggested previously, associated with fondaparinux 2.5 mg per day [5].

Skin lesions rapidly improved as well as platelet count and D-dimers levels (Fig. 1, panel D). Antiplatelet factor 4/heparin ELISA were controlled negative on day 25 (OD 0.272,

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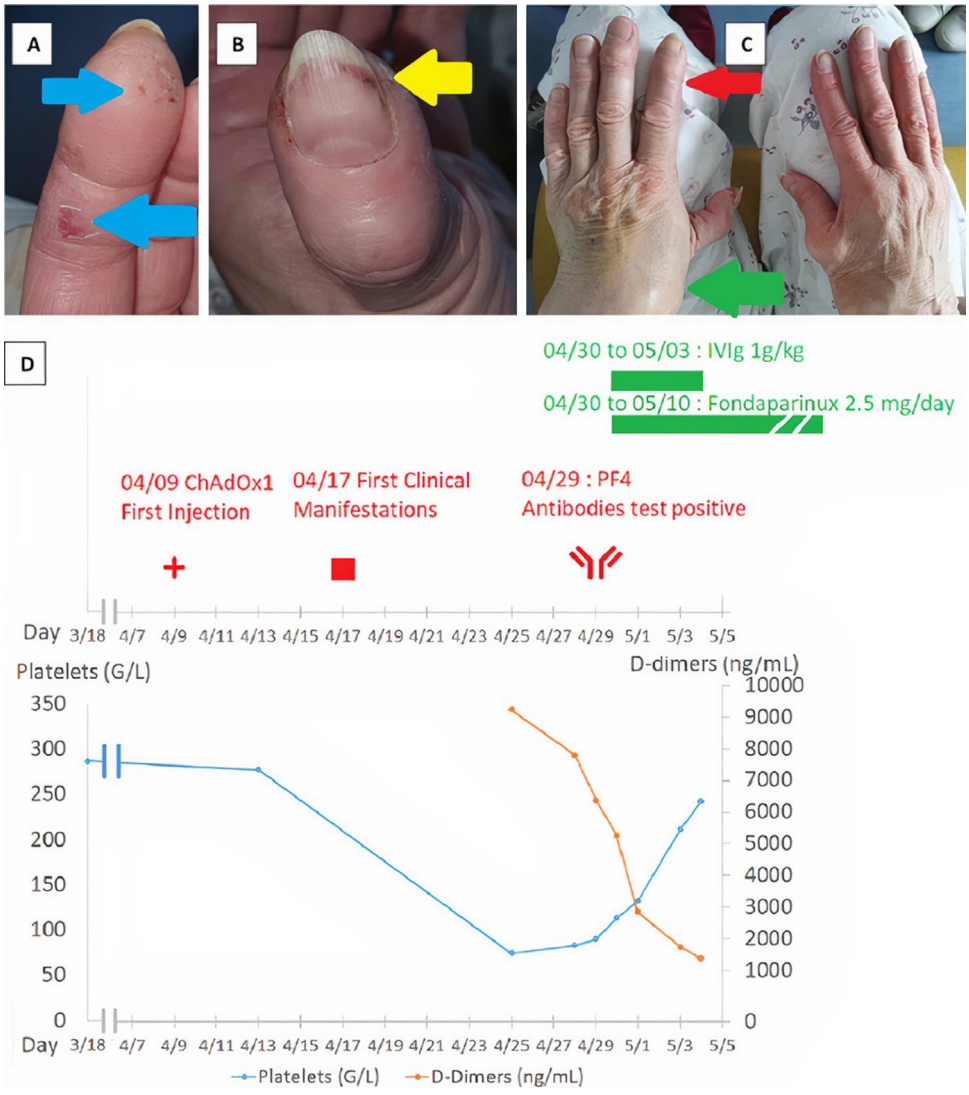

Figure 1 Microvascular manifestations after ChAdOx1 nCov-19 vaccination. Images show chilblain-like lesions on index (panel A, blue arrow), splinter hemorrhages on left thumb (panel B, yellow arrow) and swollen wrist (panel C, green arrow) associated with cold cyanosis of the left hand (panel C, red arrow). Diagram depicts the timeline of vaccination, symptoms, laboratory tests (Platelet count, D-dimers and anti-PF4/heparin antibodies) and treatment (panel D). PF4: platelet factor 4; IVIg: intravenous immunoglobulin.

normal < 0.401). The patient was discharged later the same day. All symptoms resolved completely and the 6-month follow-up was eventless.

Discussion

Although cutaneous manifestations have been reported in COVID-19 and after mRNA vaccines, to our knowledge (as of December 2021), this is the first report of Raynaud's phenomenon, chilblain-like lesions and splinter hemorrhages following ChAdOx1 nCoV-19 vaccination together with laboratory findings suggestive of VITT. These could be new and early features of VITT. Diagnosing this condition could lead to introduce a proper medical treatment before the onset of further complications.

Human and animal rights

The authors declare that the work described has not involved experimentation on humans or animals.

Informed consent and patient details

The authors declare that they obtained a written informed consent from the patients included in the article. The authors also confirm that the personal details of the patients have been removed.

Disclosure of interest

The authors declare that they have no competing interest.

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