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Author contributions

All authors approved the final version of this manuscript. SO had full access to all the data. SH reviewed the skin findings. SO was responsible for the organization and coordination of the case.

Data availability statement

The data underlying this article will be shared upon reasonable request to the corresponding author.

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Unilateral linear purpuric rash heralding SARS-CoV-2 vaccine-induced immune thrombotic thrombocytopenia

Dear Editor,

Vaccine-induced immune thrombotic thrombocytopenia (VITT) has been a life-threatening complication since adenovirus-vectored vaccines, including ChAdOx1 nCoV-19 (AstraZeneca) and Ad26.COV2.S (Johnson & Johnson/Janssen), were used against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] VITT is characterized by thrombocytopenia, thrombosis, and presence of anti-platelet factor 4 (anti-PF4) antibodies.[1] Common reported symptoms include headache, abdominal pain, or swelling/pain of extremities, depending on the location of thrombosis.[1] Cutaneous manifestations in VITT have not yet been explored, but purpuric lesions may be observed in VITT cases with severe thrombocytopenia.[2]

A 29-year-old otherwise healthy male presented with linear purpuric rashes on the right leg for one week, followed by acute onset of painful swelling and weakness on the same leg within recent 2 days. Meanwhile, he also complained headache, nausea, and vomiting. The patient had received ChAdOx1 nCoV-19 vaccination 10 days before presentation. Physical examination showed linear erythematous-to-purplish palpable purpura along the right lower extremity (Fig. 1a,b). Duplex ultrasound examination revealed deep vein thrombosis (DVT), corresponding to the location of linear purpura from the level above right common femoral vein to right anterior/posterior tibial vein (Fig. 1c). Histopathology of linear purpura showed lymphocytic vasculitis and erythrocyte extravasation in the dermis and subcutaneous fat tissue (Fig. 1d,e). Magnetic resonance angiography study was arranged due to the neurologic symptoms and revealed dural sinus thrombosis at superior sagittal sinus (Fig. 1f), resulting in left parietal lobar hematoma, brain edema, and midline shift.

Laboratory testing showed thrombocytopenia (platelet count 42×10^9/L), elevated D-dimer level (>10 000 FEU ng/mL), and positive anti-PF4 IgG antibody ELISA tests [658.3 ng/mL (normal, 42.1–313.4 ng/mL)]. VITT was diagnosed, and the patient was treated with intravenous immunoglobulin (2 g/kg/day) for 2 days, intravenous methylprednisolone (80 mg/day) and apixaban (10 mg/day). Linear purpura diminished gradually after one-month VITT treatment.

Since global mass COVID-19 vaccination is in progress, the surveillance system by the Vaccine Adverse Events Reporting System (VAERS) had reported, despite a low incidence of VITT, several hundred patients developing this catastrophic adverse event.[1,3] Adenovirus-vectored COVID-19 vaccines induce the production of anti-PF4 antibodies which form immune complexes, triggering platelet activation and subsequent thrombotic events in VITT.[1] Venous thrombosis often occurs at multiple sites, such as cerebral venous sinus thrombosis, DVT, pulmonary embolism, splanchnic vein thrombosis, arterial thrombosis, and concomitant or secondary bleeding and/or intracerebral hemorrhage.[1]

Various cutaneous manifestations have been observed following COVID-19 vaccinations, including purpuric/petechial rashes.[2] Vasculitis is not the only etiology for COVID-19

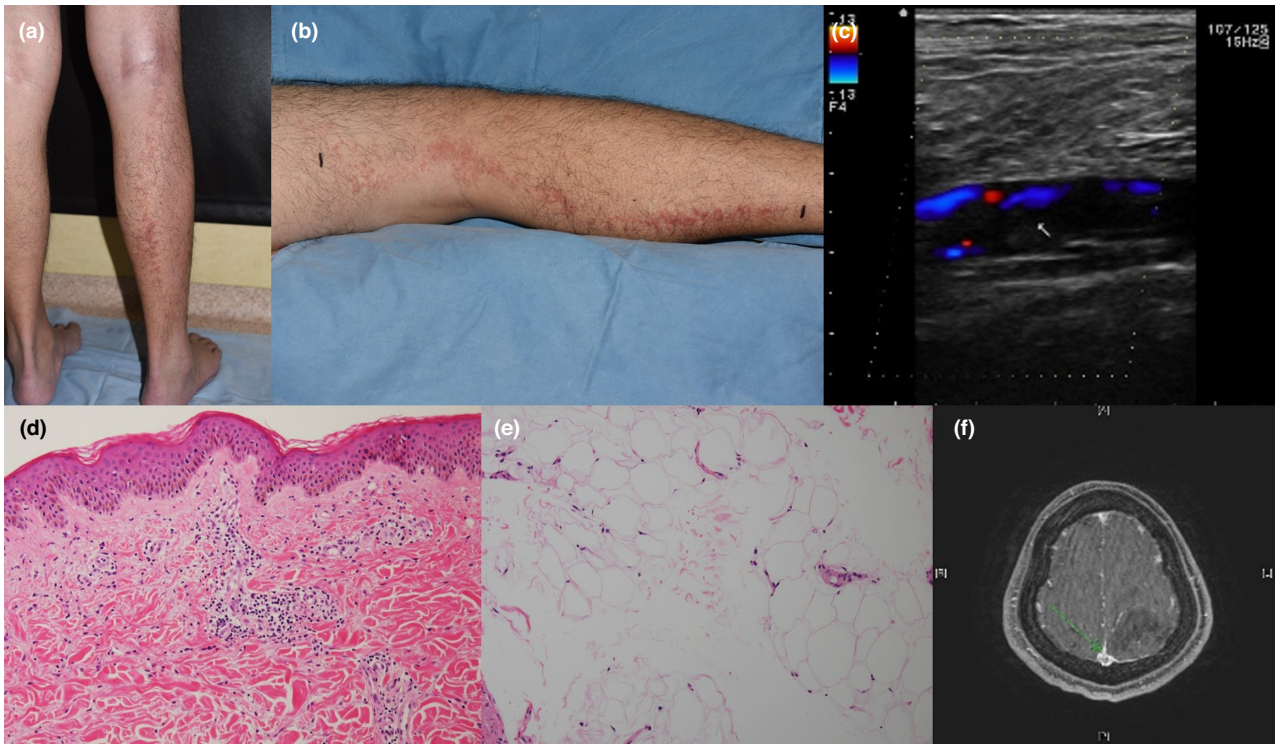

Figure 1 (a–b) Clinical manifestation of the 29-year-old male. Unilateral linear palpable purpura along the right lower extremity (a), extending from the middle part of the posterior thigh to the whole calf (b). (c) Thrombosis developing from the level above right common femoral vein to right anterior/posterior tibial vein in Duplex ultrasound examination (thrombus indicated by arrow). (d) Histopathology of linear purpura showing lymphocytic vasculitis in the dermis (H&E stain, original magnification ×100). (e) Erythrocyte extravasation in the subcutaneous fat tissue (H&E stain, original magnification ×200). (f) Dural sinus thrombosis at superior sagittal sinus in magnetic resonance angiography (irregular filling defect indicated by arrow, contrast-enhanced three-dimensional fast spoiled gradient-echo sequences).

vaccine-induced purpura.[2] In addition to COVID-19 vaccines, immune thrombocytopenic purpura also occurred in other vaccinations, manifesting with bleeding events and diffuse purpura due to severe thrombocytopenia.[2] However, purpura in this case developed in a unilateral linear pattern, which was a rare presenting sign of DVT.[4,5] In addition to activating platelets and coagulation reactions, anti-PF4 antibodies can cause a pancellular activation, including monocytes, neutrophils, endothelial cells, and other inflammatory cells, further posing a thrombosis risk.[1,3] Consequently, linear purpura may not only be associated with increased venous pressure due to stasis in DVT on a background of thrombocytopenia and coagulopathy, but also associated with vasculitis induced by maladaptive immune complex activation and deposition on the vessel walls following vaccination.[3–5] The area of rashes in correspondence to the extent of thrombosis shown in angiography and the therapeutic response to VITT treatments reinforce a relationship between unilateral purpura and DVT. During the era of COVID-19 pandemic, clinicians should be alert to a linear purpuric rash developing on the unilateral lower extremity after COVID-19 vaccination, especially accompanying with leg swelling or tenderness, which warrants further investigation for VITT.

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The patient in this manuscript has given written informed consent to publication of her case details.

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Pityriasis lichenoides et varioliformis acuta after SARS-CoV-2 infection and relapse after vaccination

Editor

A 21-year-old, otherwise healthy, woman presented in emergency with a 4-week history of a widespread eruption. She had no past history of skin diseases, and her only medication was birth control pills. In early July, she had presented fever for 2 days and cough for 5 days. She was subsequently found a positive nasopharyngeal swab for SARS-CoV-2. She also reported sore throat 1–2 weeks after COVID-19 infection. She had not received COVID-19 vaccination. At the end of July, 2–3 weeks after COVID-19 infection, a rash started on the abdomen and spread widely from scalp to the lower limbs. Upon referral at the end of August, she presented with an itchy and painful eruption of monomorphous dark red papules. The skin lesions represented different stages, ranging from recent active papules to crusts and hypopigmented scars. They were distributed widely on the trunk, abdomen, back with a 'Christmas tree' pattern (Fig. 1a), upper arms, tights and legs (Fig. 1b). All mucosae were spared. The patient was in good general health with no systemic symptoms. A skin biopsy of a recent lesion revealed focal necrosis of the epidermis, parakeratosis, lymphocytic exocytosis and an inflammatory infiltrate of lymphocytes, macrophages and neutrophils as well as extravasation of red blood cells were found in the upper dermis (Fig. 2). The clinical presentation and histological findings were consistent with pityriasis

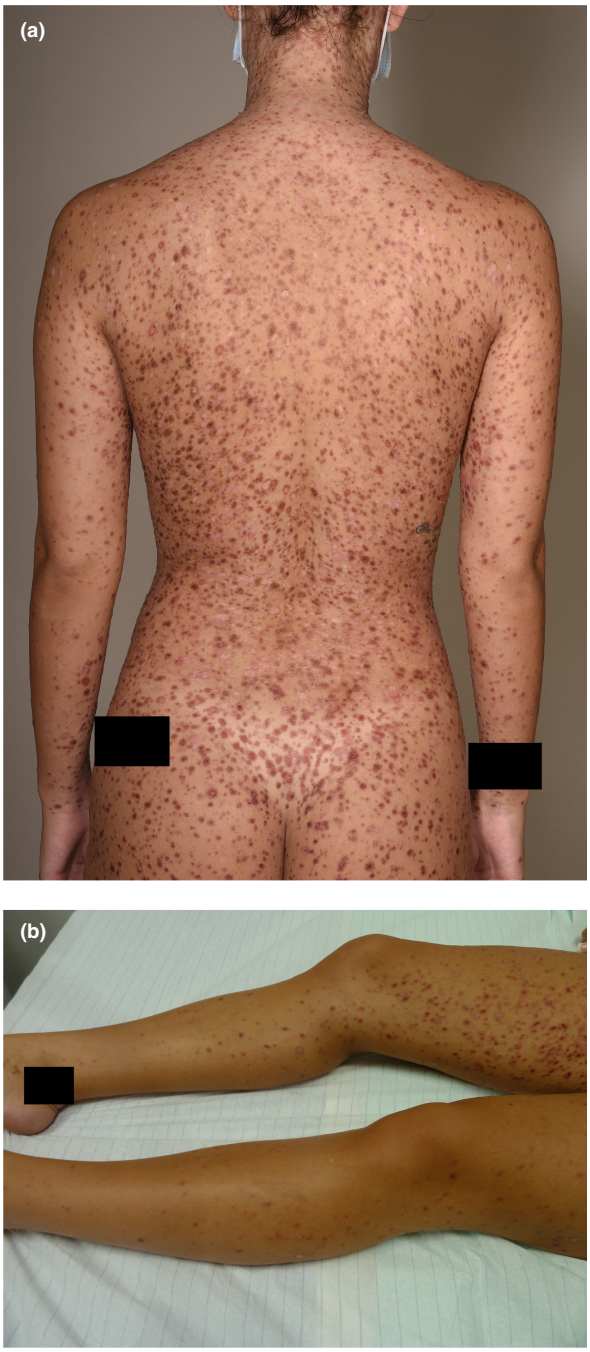

Figure 1 (a) Extensive eruption on the back, consisting of papules, crusts and hypopigmented scars with a Christmas tree distribution. (b) Dark papules of the tights and legs.