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Genital necrosis with cutaneous thrombosis after COVID-19 mRNA vaccination

Editor

Thrombosis is a rare complication of COVID-19 vaccines that typically affects cerebral and visceral vessels.[1–4] However, skin involvement is largely unknown.[5,6] Here, we describe a case of genital necrosis associated with cutaneous thrombosis following COVID-19 vaccination.

An 84-year-old Japanese woman presented to our department with a three-day history of genital necrosis. She had received her first dose of Pfizer–BioNTech (New York, NY, USA; Mainz, Germany) BNT162b2 mRNA COVID-19 vaccine 26 days before admission. Nine days after the vaccination, she developed increasing pain in her genital region. She denied any trauma or precipitating event. Her medical history was significant for deep vein thrombosis after orthopaedic surgery, for which she had been receiving edoxaban over the past three years. She had no other risk factors for thrombosis.

On admission, she was well but febrile to 37.5°C. Dermatological examination revealed extensive necrosis with surrounding purpura that involved the mons pubis, labia majora and perineum (Fig. 1a). Laboratory investigations showed a leukocytosis (15.9×10^9/L) with a left shift. The platelet count was slightly elevated (359×10^9/L). The coagulation profile was unremarkable. Biochemical parameters were within the normal range except for an elevated C-reactive protein (11.6 mg/dL, normal <0.3 mg/dL). A thrombophilia screen—including antithrombin, protein C, protein S, lupus anticoagulant, anti-cardiolipin antibodies and anti-β-2-glycoprotein-1 antibodies—was unremarkable. Serological tests for rheumatoid factor, anti-nuclear antibody and anti-neutrophil cytoplasmic antibodies were all negative. Pelvic CT was performed to show subcutaneous fat stranding without fascial thickening. No haemorrhage or hematoma was noted. CT angiography detected no evidence of thrombosis. Skin biopsy showed epidermal necrosis, scattered neutrophils and lymphocytes in the dermis, and thrombotic occlusion of dermal vessels with mild perivascular infiltration (Fig. 1b,c). Immunohistochemistry revealed that the thrombi were positive for CD61, a platelet-specific marker (Fig. 1d,e). Based on the clinical and histopathological findings, a diagnosis of cutaneous necrosis with platelet thrombi formation and secondary infection was made. Treatment was started with ampicillin/sulbactam along with local wound care. Her fever, leukocytosis and genital pain resolved within the first week. The skin lesions also improved: more than 80% of the eschar had fallen off when she was discharged after one month of admission (Fig. 2a), and epithelization was almost completed another month later (Fig. 2b).

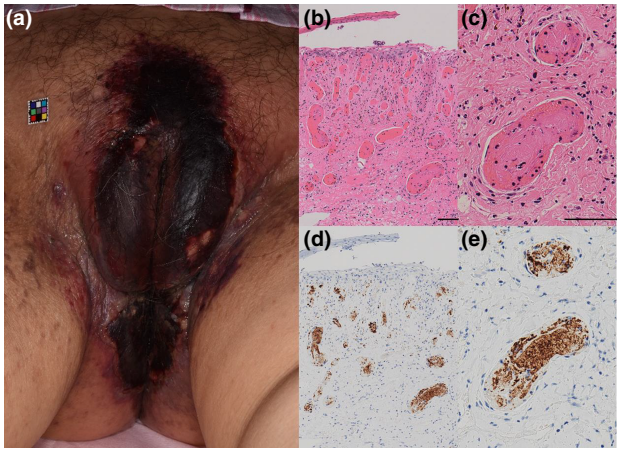

Figure 1 Skin lesions and histopathological findings at the time of admission. (a) Extensive necrosis with purpura in the genital region. (b,c) Histopathology showing epidermal necrosis and thrombotic occlusion of dermal vessels (haematoxylin-eosin stain, original magnification × 100 [b] and × 200 [c]). (d,e) Immunohistochemistry showing that the thrombi were positive for CD61 (original magnification × 100 [d] and × 200 [e]). Scale bar = 50 μm (b,c).

A small but increasing number of thrombotic events have been reported since the launch of mass vaccination campaigns against COVID-19. Adenovirus vector-based vaccines from AstraZeneca (Cambridge, UK) and Johnson & Johnson (Titusville, NJ, USA) are associated with severe thrombosis with thrombocytopenia, while mRNA-based vaccines from Pfizer–BioNTech and Moderna (Cambridge, MA, USA) are also associated with some thrombotic events, which do not always accompany thrombocytopenia.[1–4] The exact pathogenesis remains unknown, but platelet activation is thought to be a key feature underlying these events.[7] For both types of vaccines, thrombosis typically occurs in unusual locations such as cerebral and portal veins. However, only two cases of skin involvement have been reported, both of which manifested as local skin necrosis at injection sites.[5,6] To the best of our knowledge, this is

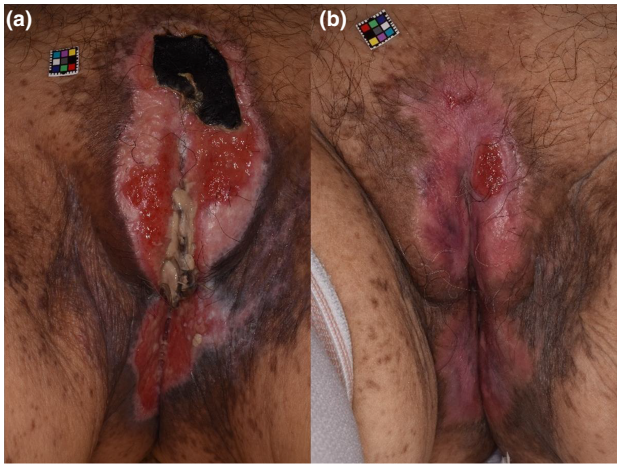

Figure 2 Improvement of the skin lesions. (a) Most of the eschar had fallen off one month after admission. (b) Epithelization was almost completed one month after discharge.

the first case of extensive skin necrosis after COVID-19 vaccination that developed outside the injection site. Although the mechanism of platelet thrombi formation in genital skin is unclear, the short time interval between the vaccination and the onset of symptoms may indicate a causal relationship. Therefore, our case extends the range of cutaneous manifestations associated with thrombosis after COVID-19 vaccination. In addition, it should be noted that she developed thrombosis despite receiving edoxaban, which highlights the need to consider the possibility of thrombosis even in patients under anticoagulant therapy. Although rare, skin necrosis should be recognized as a possible manifestation of thrombosis associated with COVID-19 vaccination.

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

Conflicts of interest
The authors have no conflict of interest to declare.

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Data availability statement
The data presented in this manuscript are available from the corresponding author upon reasonable request.

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Pityrosporum folliculitis in critically ill COVID-19 patients

Dear Editor,

During the *Coronavirus* disease 2019 (COVID-19) pandemic, dermatologists are dealing with challenging clinical scenarios in their clinical practice. A wide range of cutaneous manifestations has been described, either directly associated with the COVID-19, or as a consequence of management procedures, as well as an exacerbation of previous cutaneous conditions.[1]

We have read with great interest the paper published by Barrera-Godinez et al.,[2] in which they mention *Pityrosporum* folliculitis in COVID-19 patients. We have recently evaluated three patients in the intensive care unit (ICU), diagnosed with COVID-19 acute respiratory distress syndrome (ARDS) presenting similar cutaneous manifestations.

Initially, we were called to evaluate a 52-year-old obese man, with type 2 diabetes, under mechanical ventilation in a prone position and receiving systemic corticosteroids, due to a severe COVID-19 ARDS. He had also evolved with acute renal failure and septic complications (ventilator-associated pneumonia and septic shock by bloodstream infection), using several systemic antibiotics. A monomorphic eruption of follicular erythematous papules and pustules was observed on the chest, upper and lower limbs, on the back and abdomen after 6 days in the ICU. We

