Bullous hemorrhagic Sweet syndrome induced by SARS-CoV-2 Oxford AstraZeneca vaccine

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Competing interests

The authors declare that they have no competing interests.

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Informed consent was obtained from the patient for publication of this report.

To the editor,

Concurrent to the increasing use of COVID-19 vaccines, the number of vaccine-related adverse reactions has also increased[1]. We report a case of a 49-year-old male patient who presented with a 10-day-history of generalized painful cutaneous eruption. He denied any preceding respiratory or gastrointestinal symptoms or introduction of any medications, however, ten days before the rash onset, he received the first dose of the SARS-CoV-2 Oxford-AstraZeneca vaccine. Upon physical examination, we observed symmetrically distributed erythematous to violaceous vesicular papules and targetoid plaques on the lower part of the trunk and extremities, along with multiple grouped hemorrhagic blisters on both hands and feet (Figure

1A). Fingers of the right hand were edematous with large tense hemorrhagic bullae, while the left hand was less affected (Figure 1B). The patient was subfebrile and reported mild arthralgia, no other extracutaneous symptoms were present. Initial laboratory tests showed leukocytosis with neutrophilia, while C-reactive protein, liver and renal function tests, urine analysis, ANA, ANCA, cryoglobulins, rheumatoid factor were all within the reference range. The SARS-CoV-2 RT-PCR test was negative, while IgG SARS-CoV-2 antibodies were positive (895.3 AU/ml). Serology tests for viral and bacterial agents were all negative. Chest X-ray and abdominal ultrasound were unremarkable. Histopathological analysis revealed dense perivascular and periadnexal to diffuse neutrophilic infiltrate with marked leukocytoclasia involving the upper and mid-dermal layers. There was massive edema of papillary dermis resulting in subepidermal blister along with extravasated erythrocytes (Figure 2A-B). These findings were consistent with Sweet syndrome (SS). Thus, intravenous methylprednisolone (0.8 mg/kg/d) was initiated and most of the existing lesions started to recede in the next few days. Due to suspected secondary ischemia of the right-hand fingers, the vascular surgeon recommended antithrombotic prophylaxis with low-molecular-weight heparin and acetylsalicylic acid in addition to hyperbaric oxygen therapy. After two weeks of ongoing treatment, there was remarkable improvement in clinical status. The patient was discharged from the hospital with methylprednisolone 32 mg daily therapy and slow tapering over the following eight weeks.

Up to date, the most commonly reported cutaneous adverse events of SARS-CoV-2 vaccines are mild to moderate injection-site reactions occurring as a result of nonspecific stimulation of inflammation[1]. To our knowledge, there are only ten cases of SS induced by any vaccine reported in the literature, three with seasonal influenza, two with pneumococcal, two with tuberculosis, two with smallpox, one with influenza A[2]. Additionally, three cases of acute febrile neutrophilic dermatosis induced by SARS-CoV-2 Pfizer-BioNTech mRNA vaccines have been reported so far. In the reported cases, the time from vaccination to the onset of the skin lesions ranged from 12 hours to 15 days[1,3,4]. Our patient developed SS 10 days after the first dose of the Oxford-AstraZeneca vaccine. Generally, local and systemic reactions to the Oxford-AstraZeneca vaccine were mild and reported more often after the first dose and more frequently in adults aged 18-65[1]. Vaccination with Oxford-AstraZeneca is linked to thromboembolic events and very rarely to prothrombotic immune thrombocytopenia with cutaneous lesions similar to drug-induced cutaneous vasculitis[1].

The bullous variant of SS, seen in our case, is a rare form of the disease. Drugs, tumors or infectious agents may start a network of cytokines involved in the onset of SS[5]. SARS-CoV-2 infection may also trigger SS as reported recently[6]. To our best knowledge, this is the first case of SS induced by the Oxford-AstraZeneca vaccine. Balancing the possible link between vaccination and SS, we decided to contraindicate the second dose of vaccine for our patient. Because of the ongoing pandemic and introduction of new vaccines, it is of great importance that all potential side effects are reported and considered.

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Figure 1. Clinical presentation of Sweet syndrome; a) edematous red-violet papules and targetoid plaques

on the trunk and lower extremities, b) violaceous, edematous plaques and hemorrhagic blisters on hands.

Figure 2. Skin biopsy from the lower trunk showing (a) subepidermal blister and diffuse dermal inflammatory infiltrate (H&E, 100x) consisting of (b) predominantly neutrophils with pronounced leukocytoclasia (b, 400x).