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10 RAPID COMMUNICATION

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Vaccine-induced thrombosis and thrombocytopenia with bilateral adrenal haemorrhage

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Dear Editor,

Vaccination to prevent severe acute respiratory syndrome coronavirus 2 infection offers the most promising approach for containment of the coronavirus disease 2019 (COVID-19) pandemic. Although the available vaccines are safe and effective, a prothrombotic syndrome in association with thrombocytopaenia (termed vaccine-induced thrombosis and thrombocytopaenia; VITT) has been observed in a small number of individuals receiving the adenoviral vector-based vaccines ChAdOx1 (Astra Zeneca, University of Oxford) and Ad26.COV2.S (Janssen; Johnson & Johnson). Whilst attention has largely been focused on cerebral venous sinus thrombosis in this disorder, thrombotic and bleeding complications can also occur at other sites. Here, we report the case of a patient with VITT in whom adrenal haemorrhage was the presenting pathology.

A 38-year-old male with no significant medical history and no family history of clotting disorders attended the emergency unit with sudden onset of severe abdominal pain and vomiting. He had received his first dose of the ChAdOx1 vaccine 8 days prior. Observations were normal and his abdomen was nontender.

Investigations revealed an elevated white cell count (19.1×10^9/L; predominantly neutrophils) and mild thrombocytopenia (139×10^9/L). Electrolytes, amylase, renal and liver function were normal, as was fibrinogen concentration and prothrombin/activated partial thromboplastin times. Blood lactate was elevated at 5 mmol/L. Plain abdominal X-ray was unremarkable but computed tomography abdomen showed retroperitoneal fat stranding and high-density fluid surrounding the adrenal glands, in keeping with haemorrhage (Figure 1A). A random cortisol immediately following the scan was 61 nmol/L, hence intravenous hydrocortisone 50 mg tds was commenced.

The platelet count fell profoundly over the following days to a nadir of 14×10^9/L. D-dimer concentration was markedly raised (>20,000 μg/L; normal <500) and heparin-induced thrombocytopenia (HIT) antibody screen (detecting antibodies to platelet factor 4) was positive. A diagnosis of VITT was made and treatment commenced with intravenous immunoglobulins, methylprednisolone, and the direct thrombin inhibitor argatroban. Thrombosis/emboli were subsequently noted in the sigmoid sinuses, straight sinus, and segmental pulmonary arteries, with the progression of the adrenal haemorrhage into organised haematoma (Figure 1B). Plasma exchange was eventually undertaken on account of resistant disease, leading to improved platelet count. He was maintained on hydrocortisone 20/10 mg and fludrocortisone 100 μg od on the presumption of long-term primary adrenal insufficiency, with a view to the formal assessment of the glucocorticoid and mineralocorticoid axes as an outpatient.

To our knowledge, this is the first published case of bilateral adrenal haemorrhage due to VITT. Our case serves as a reminder to clinicians that VITT may present with bilateral adrenal haemorrhage, with symptoms that are nonspecific and biochemistry at the presentation that is not classically 'Addisonian'. Prompt recognition and early treatment, including timely administration of glucocorticoid and mineralocorticoid replacement, is likely to lead to improved outcomes. Experience to date

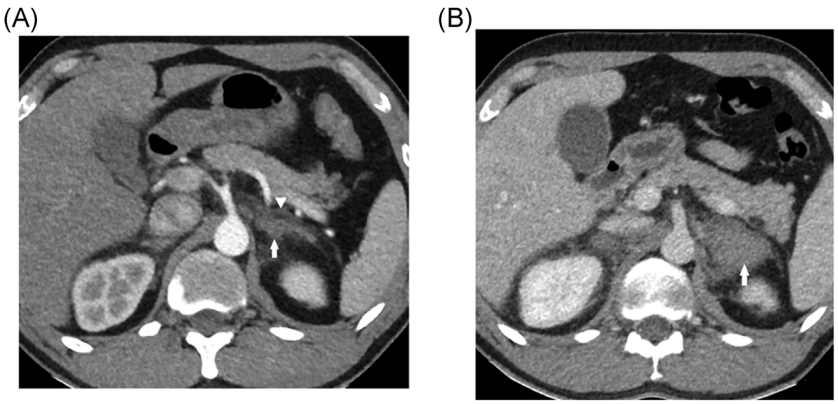

FIGURE 1 (A) Initial CT abdomen showing retroperitoneal fat stranding and fluid around the adrenals in keeping with adrenal haemorrhage. (B) Subsequent CT showing progression into an organised haematoma. CT, computed tomography

suggests that VITT behaves similarly to autoimmune HIT in which bilateral adrenal haemorrhage has been reported previously.[1–3] Adrenal infarction usually presents as a haemorrhage, with the unique vascular anatomy of a plentiful arterial inflow but only a single central adrenal vein accounting for the vulnerability of the gland to infarction. Whilst adrenal insufficiency in HIT is generally considered irreversible, recovery of adrenal function has been described.[4] Therefore, the need for ongoing steroid substitution in VITT-associated adrenal haemorrhage should be assessed at regular intervals. Finally, whilst our case illustrates a rare complication of the ChAdOx1 vaccine, the incidence of VITT is still very low, with the benefits of vaccination far outweighing any risk of thrombosis. Nevertheless, the predilection for VITT to affect young adults as in our case supports recent UK Governmental advice to use nonadenoviral-based vaccines in individuals under 40 wherever possible.

Additionally, given that the use of COVID-19 vaccines remains in the early stages, this case serves as a reminder that all such adverse outcomes should be reported to postadministration surveillance programs following national processes and Medicines and Healthcare products Regulatory Agency guidance. Endocrinologists therefore have a critical role in both reporting these cases and ensuring appropriate long-term monitoring. We also hope that this report will act as a stimulus for national and international collaborations to better define the demographics and natural history of VITT-associated adrenal haemorrhage and other potential endocrine complications.

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