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3 **Abdominal pain and bilateral adrenal haemorrhage of COVID-19**
4 **vaccine-induced immune thrombotic thrombocytopenia**
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58 Running title: Adrenal haemorrhage of COVID-19 vaccine-induced immune
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4 thrombotic thrombocytopenia
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7 Key words: COVID-19 vaccine, ChAdOx1 COVID-19 (AstraZeneca) vaccine,
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10 platelet factor 4 antibodies, abdominal pain, adrenal haemorrhage, vaccine-associated
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13 immune thrombosis and thrombocytopenia
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16 Word counts: 367
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4 Dear Editor,
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7 It was our pleasure to respond to the comments made by Dr Jolobe in response to
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10 our article published on 25th August in the Quarterly Journal of Medicine: An
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13 International Journal of Medicine.¹ We appreciated the letter from Dr Jolobe and
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16 would like to make a brief comment on those suggestions.
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19 Heparin-induced thrombocytopenia (HIT) caused by the use of anticoagulants or
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22 heparin is a major risk factor of adrenal haemorrhage secondary to adrenal vein
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25 thrombosis. Immune thrombotic thrombocytopenia subsequent by coronavirus disease
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28 2019 (COVID-19) adenoviral vector-based vaccination is clinically mimics HIT.²⁻⁴
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31 This phenomenon is caused by the antibodies that recognize platelet factor 4 (PF4,
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34 also called CXCL4) bound to the platelets, resulting in thrombocytopenia and
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37 thrombotic events.⁴⁻⁶ The common clinical presentations of bilateral adrenal
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40 haemorrhage include hypotension or shock, abdominal pain, fever, nausea and
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43 confusion.⁷ Blauenfeldt RA, et al. reported a 60-year-old woman with severe
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46 abdominal pain and her computed tomography scan revealed bilateral adrenal
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49 haemorrhage and renal hematoma.⁸ The patient presented with shock, abdominal pain
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52 and altered mental status. Unfortunately, this patient died with multiple complications
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55 of vaccine-induced immune thrombotic thrombocytopenia (VITT). Laboratory data
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58 including corticotropin (ACTH), cortisol, renin, and aldosterone could be checked and
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4 timely treatment of glucocorticoid based on the suspicion of adrenal insufficiency or
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7 crisis caused by bilateral adrenal haemorrhage should be considered in these patients.
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10 Hydrocortisone and fludrocortisone were maintained for a period of time even in
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13 some advanced cases of adrenal haemorrhage caused by VITT.³
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16 In our patient, the computed tomography scan of abdomen demonstrated normal
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19 without haemorrhage in both adrenal glands. Blood analysis showed both cortisol and
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22 ACTH levels were within normal ranges. In addition, COVID-19 infection may cause
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25 a hypercoagulable state and lead to the complications of adrenal vein thrombosis and
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28 haemorrhage.^{9,10} During the hospital stay, we also performed a follow-up polymerase
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31 chain reaction (PCR) test for severe acute respiratory syndrome coronavirus 2
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34 (SARS-CoV-2) in our patient and the results were all negative.
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37 In conclusion, VITT can cause multiple organs involvements and devastating
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40 clinical features. Once the diagnosis of VITT is highly suspected, complete clinical
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43 examination and investigation should be taken as necessary. Early identification and
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46 appropriate management may prevent the catastrophic complications and improve
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49 patient outcomes.
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22 ***Conflict of interest***

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25 The authors declare that they have no conflict of interest.
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