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CASE REPORT

COVID-19 Vaccine Acquired Haemophilia: A case study and literature review.

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Abstract

After viral infections and certain immunizations, a range of autoimmune diseases have been observed. Acquired antibodies against coagulation factor VIII cause acquired haemophilia A (AHA), a rare bleeding condition. AHA is likely under-diagnosed and often unrecognized due to limited data about incidence, diagnosis, and management. We report the case study of a 48-year-old Saudi male patient with acquired haemophilia after COVID-19 vaccination. He presented with hematuria and right loin pain. He was found to have prolonged aPTT not corrected by mixing study and his factor III level was low. He was managed by the insertion of a right ureter stunt and repeated infusion of factor VII concentrate. The etiologic, and pathologic basis of acquired haemophilia should be explored more in the future to clearly elucidate the disease. Exploration of better and optimal medical therapeutic regimens is a need for time to treat and prevent morbidity in the pandemic of COVID- 19.

Keywords: COVID-19 vaccine, Acquired Haemophilia

1 | INTRODUCTION.

Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been strongly

associated with immune mediated reactions, including the development of autoimmune disorders (1) . Acquired haemophilia A (AHA) is a rare autoimmune bleeding disorder caused by autoantibodies directed against coagulation factor VIII (2) . Limited information on AHA epidemiology is available, but it is estimated that its incidence approaches about 1.5 cases per million per year (3) . Clinical presentation in AHA is different from hereditary haemophilia A, as hereditary haemophilia A is an X-linked disorder that occurs in males at an earlier age, with positive family history and occasional hemarthroses. AHA often presents as spontaneous bleeding or hemorrhage in an otherwise healthy patient without a previous personal or family history of bleeding disorders (3) . The etiology of autoimmune disorders is largely attributable to an individual's genetic risk factors, exposure to environmental triggers, and underlying immune dysregulation (1) . Whereas a variety of autoimmune disorders have been reported after vaccination, specific vaccines elicit unique autoimmune pathology. SARS-CoV-2 infection has been shown to effect sustained dysregulation of adaptive and innate immunity (2) . The immunomodulatory effects of SARS-CoV-2 vaccination, however, are poorly understood. It is theorized that the spike protein S1 of SARS-CoV-2 may be responsible for this phenomenon by means of molecular mimicry (3) .

Case History:

We present a case of acquired haemophilia A (AHA) three months after application of Pfizer-BioNTech SARS-CoV-2 vaccine second dose. The patient was 48-year-old Saudi male, smoker medically free, began to experience right loin pain with gross hematuria for 3 days. He presented to the emergency department (ED) with above symptoms without any other urinary symptoms and admitted under urology team. He was evaluated by imaging (USG KUB & MRI abdomen) initially and later CT abdomen with iv contrast to rule out abdominal malignancy. Radiologically there was no structural pathology, no signs of abdominal malignancy, and no stone found in urinary system. He was referred to hematology team for more bleeding after stunt insertion and one episode of epistaxis. Physical exam was otherwise unremarkable. Vitally stable. He had a 96-second activated partial thromboplastin time (aPTT) (normal 23-39 seconds). His medical records showed normal aPTT in 2018 and 2019. His hemoglobin level was 9.4 g/dL (from a baseline of 12.8 g/dL three days back). A 1:1 mixing study combining the patient's plasma (aPTT of 96 seconds) with a normal control plasma (aPTT of 39 seconds) showed no significant correction of the aPTT (i.e., 80.5 seconds after Ist hour), suggesting the presence of an inhibitor other than factor deficiency. Factor VIII activity was undetected (<1%). Other laboratory tests were significant for: platelets 275x10^3/ul, WBC 9.5x10^3/ul, PT 12.9 seconds (INR 0.95), creatinine 98umol/l (eGFR>60mL/min), Urea 3.26 mmol/l, AST 20 u/l, ALT 28 u/l, total bilirubin 8.8 u mol/l. Antinuclear antibodies, ds-DNA antibodies, and rheumatoid factor, all were found negative. Due to continued active bleeding (hemoglobin drop), and one episode of epistaxis recombinant factor VIIa was also initiated with 90mcg/kg iv stat then repeated every 2 hours with dose of 30 mcg/kg till the hemostasis secured. Urgent referral was sent to higher centers because of non-availability of Bethesda test and factor eight inhibitor bypass activity (FEIBA). Patient hematuria was bit improved after 36 hours, and patient was referred to higher hematology center for further evaluation and management. Briefly we get information that he has high titre of Bethesda test, and was offered cyclophosphamide, methylprednisolone, and factor VIIa concentrate. His repeated Bethesda test improved, and patient was also clinically improved. No bleeding from any site and was discharged next week.

2 | DISCUSSION

Acquired haemophilia A is a life-threatening, rare autoimmune bleeding disorder that typically presents

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in another healthy patient with spontaneous hemorrhage involving the skin, soft tissue, and mucus membranes, but it can also present without any bleeding symptoms. While most cases reviewed were related to an underlying autoimmune process, pregnancy or post-partum, malignancies, and drug-related, only a limited number reported such a reaction after SARS-CoV-2 infection. There are two published case reports for post-COVID-19 vaccine induced AHA. The first case was reported in June 2021. He was a 69-year-old Saudi male who presented with bleeding symptoms after receiving the Pfizer-BioNTech SARS-CoV-2 vaccine. Laboratory testing showed isolated prolongation of the activated partial thromboplastin time, and normal von Willebrand factor & the presence of factor VIII inhibitor. He was treated with oral prednisolone for 4 weeks and improved (4) . The second case of AHA was published in August 2021. This was a 67-year-old African American male with a history of hypertension and asymptomatic pulmonary sarcoidosis not receiving any pharmacological treatment, presented with left thigh tightness and cramping pain 19 days after his second dose of Pfizer-BioNTech SARS-CoV-2 vaccine. It was proven that the left thigh hematoma was due to AHA after the COVID-19 vaccine. He was successfully treated with FEIBA, oral prednisolone, recombinant factor VII a, and rituximab (5) . The pathophysiology of AHA is unclear, although it is thought that T-lymphocytes and certain genetic polymorphisms may play a role (6) . Vaccines have long been implicated in generating autoantibodies. It has been suggested that vaccination may trigger an autoimmune response due to antigenic mimicry as well as due to activation of quiescent auto-reactive T and B cells (7, 8) . Moreover, there is growing evidence associating COVID-19 infection with hematological and non-hematological autoimmune disease, for example, cold agglutinin autoimmune hemolytic anemia, (9) thrombotic thrombocytopenic purpura, Guillain-Barre syndrome, (10) and immune thrombocytopenic purpura (11) .

3 | CONCLUSIONS

It is unclear that this new-onset AHA after COVID-19 vaccination association is causative or correlative. Although it is important to investigate any isolated prolongation of aPTT, especially after recent viral immunization, especially in the pandemic of COVID-19. Early diagnosis and optimal timely management of AHA is a fundamental and crucial step to decreasing the disease's morbidity and mortality.

Abbreviations:

AHA: Acquired Haemophilia A.

COVID-19: Coronavirus Disease 2019

aPTT: activated partial thromboplastin time.

SARScov-2: severe acute respiratory syndrome coronavirus-2

USG KUB: Ultrasonography kidney urinary bladder.

MRI: Magnetic resonance imaging.

CT scan: Computerized tomography scan

FEIBA: Factor eight inhibitor bypass activity

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Ethical Approval: NA

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