

## A Case Report: COVID Vaccine-Induced Immune Thrombocytopenia

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Received: 19 May 2021

Accepted: 04 June 2021

Published: 11 June 2021

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### Citation:

Lwin, Zaw Thant, et al., A Case Report: COVID Vaccine-Induced Immune Thrombocytopenia. Clin Surg. 2021; 5(12): 1-3

### Keywords:

Coronavirus 19; Vaccine; Thrombocytopenia; Thrombosis

## 1. Abstract

We report a case of COVID-19 vaccine-induced thrombocytopenia in a healthy 52-year-old woman. COVID-19 has had a devastating impact on the lives of many; however, thanks to the tireless efforts of scientists, there are now highly effective vaccines available. Initial trials of these vaccines revealed side effects such as fatigue, headache, myalgia, and rarely, anaphylaxis. However, there has recently been reports of adverse events such as immune thrombocytopenia and thrombosis which can be life-threatening. This report chiefly aims to remind clinicians of these lesser-known side effects and, and to share our experience of diagnosis and management, along with the outcome, of this patient.

## 2. Introduction

Immune Thrombocytopenic Purpura (ITP) is a condition where immune-mediated destruction of platelets causes a reduction in their numbers. It is defined by a platelet count of less than  $100 \times 10^9/L$ , and classically presents with petechiae or purpuric rashes. Bleeding in patients is typically not seen unless platelet count drops below  $20 \times 10^9/L$ . A causative trigger is usually found, examples include infections such as hepatitis B, C, HIV, cytomegalovirus, Epstein Barr virus, etc. Recently, vaccine-induced thrombocytopenia or Vaccine Induced Thrombosis and Thrombocytopenia (VITT), has been observed in patients who have been administered either the Oxford-AstraZeneca or Johnson & Johnson COVID-19 vaccines, a rare but potentially life-threatening side effect. While management for thrombocytopenia is traditionally straightforward, VITT poses a new challenge for both clinicians and patients and warrants a careful balance of risk and benefits in order to provide the patient

with most appropriate management.

## 3. Case Report

A 52-year-old lady was referred by her GP to the acute medical unit for widespread petechiae which has been present for 3-4 days. 10 days prior, she has received the AstraZeneca COVID-19 vaccination. Her past medical history consisted of acquired hypothyroidism for which she is on levothyroxine 100 mcg daily. Clinical examination was unremarkable other than the presence of generalized petechiae over the trunk, arms, and legs. Initial blood tests revealed a platelet count of 6; however, other blood tests including D-dimer and fibrinogen were normal. Subsequent blood film confirmed true thrombocytopenia and revealed some reactive lymphocytes. Urgent CT brain and CT venogram were also carried out within an hour of initial assessment and were reported to have no evidence of thrombosis or acute haemorrhage. Haematology was contacted for advice and subsequently reviewed the patient, and further blood tests such as autoimmune screen, hepatitis screen and haemolytic screen were found to be unremarkable. Management was commenced by the haematology team, consisting of immunoglobulin 60mg with tranexamic acid. Steroids were not given. The patient was observed to have had a good response to the first dose of immunoglobulin, with her platelet count improving to  $20 \times 10^9/L$  on the second day of her admission. Thus, she was discharged home and was reviewed in outpatient haematology on day 3, where her platelet count was found to have further increased to  $66 \times 10^9/L$ . A week later, her platelet count has returned to normal at  $328 \times 10^9/L$ . In light of her history and symptoms, she was diagnosed by the haematology team to have likely had vaccine-in-

duced immune thrombocytopenia.

#### 4. Discussion

COVID-19 vaccines have been extensively studied through large scale clinical trials and observational studies. Pooled analysis of 4 international randomized controlled trials involving 23,745 participants showed that common adverse reactions with the Oxford-AstraZeneca vaccine were “injection site pain [and] tenderness, headache, fatigue, myalgia, malaise, pyrexia, chills, arthralgia, and nausea” [1]. These were observed in 1 in 10 people. Uncommon side effects ( $\geq 1$  in 1000 to  $< 1$  in 100) include dizziness, lymphadenopathy and decreased appetite. Initial trials also reported very rare cases of neuro-inflammatory disease [2].

VITT is some new phenomena that was not observed with the initial clinical trials, but has since been reported in a small number of patients who have been administered either the Oxford-AstraZeneca [3, 4] or the Johnson & Johnson vaccine, causing the latter to be suspended [5]. As of 21st April 2021, the Medicines and Healthcare Products Regulatory Agency (MHRA) has received 209 reports, with 41 being fatal, of possible VITT following the administration of the Oxford-AstraZeneca vaccine [6]. The MHRA estimates overall case incidence to be 9.3 per million doses.

Guidance from the British Haematology Society dictates that the following features suggest a “definite” case of VITT: thrombocytopenia (usually platelet count  $< 150 \times 10^9/L$ ), progressive thrombosis, extremely high D-Dimers, and low fibrinogen levels 5-28 days after vaccination (7). Other presenting features may include pulmonary embolism, arterial ischaemia, and bleeding. “Possible” case of VITT should also be suspected in patients presenting with “acute thrombosis and new onset thrombocytopenia within 28 days of receiving COVID-19 vaccination”. Consequences of VITT can range from thrombocytopenia to cerebral venous sinus thrombosis. Currently, VITT is believed to affect patients of all ages and genders.

The pathophysiology of VITT is currently thought to be associated with the development of anti-platelet 4 (PF4) antibodies [4], also observed in heparin-induced thrombocytopenia (HIT) [8]. Currently, patients with VITT have been reported to be positive for anti-PF4 antibodies without any previous exposure to heparin.

Traditionally, immune thrombocytopenia in healthy adults rarely require treatment unless they have a platelet count lower than  $50 \times 10^9/L$  or are symptomatic [9]. However, with VITT, the British Haematology Society (BHS) recommends giving urgent intravenous immunoglobulin (IVIG) at 1g/kg regardless of the degree of thrombocytopenia with ongoing review as this is most likely to “influence disease process” [7]. This differs with the American Society of Haematology guidelines which suggests starting IVIG if there are signs and symptoms of serious thrombosis along with positive imaging and/or low platelets [10]. BHS also suggests considering steroids if there will be a delay in administering intrave-

nous immunoglobulin. If necessary, fibrinogen should be corrected with fibrinogen concentrate or cryoprecipitate in order to maintain levels above 1.5g/L. Patients with fibrinogen levels above 1.5g/L should be anticoagulated with non-heparin-based therapies such as direct oral anticoagulants, fondaparinux, argatroban, or danaparoid; however, bleeding and thrombotic risks must be carefully weighed, and patients may need to start on lower doses. All heparin products, including heparin flushes, must be actively avoided. Avoiding the use of platelet transfusions, thrombopoietin receptor agonists, and antiplatelet agents is also advised.

Upon discharge, patients will need to be anticoagulated for an additional 3 months; however, they can be switched to an anti-platelet agent if their thrombosis was purely arterial, and platelets, fibrinogen, and D-Dimer levels have returned to normal. Platelet count will need to be monitored closely for signs of relapse, and the guidance suggests repeating anti-PF4 ELISA at day 28 from presentation [7]. If VITT has occurred after the first dose, patients should not receive the second dose.

The patient’s serum will also need to undergo ELISA testing for anti-PF4 antibodies, and if positive, treatment should continue, and patient’s serum should be sent for Covid-19 antibody testing and storage as well as for whole genome sequencing. Cases of VITT will also need to be reported to Public Health England as well as the MHRA via its yellow card reporting scheme [7].

Overall, VITT is a new phenomenon of which there is little guidance available to clinicians for its diagnosis and management. Current evidence suggests having a low clinical index of suspicion for VITT in patients presenting with easy bruising, bleeding, arterial or venous thrombosis within 28 days of receiving COVID-19 vaccination. ELISA assays for anti-PF4 antibodies can quickly help confirm diagnosis; however, this should not delay providing treatment with intravenous immunoglobulin which can combat against high levels of anti-PF4 antibodies that is driving the disease. Patients should also be appropriately anticoagulated based on their thrombosis and bleeding risks, and subsequent follow up is required to assess disease resolution. Reporting of cases is also essential so that more data is available to build robust guidelines for the identification and management of VITT. Given the life-threatening potential of this disease, it is crucial that both clinicians and patients stay abreast of this evolving situation in order to ensure the prompt diagnosis and treatment of VITT to prevent adverse outcomes.

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