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CASE REPORT

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A Case of COVID-19 Vaccine-Induced Thrombotic Thrombocytopenia

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ABSTRACT

SARS-CoV-2, which originated in China in late 2019, has spread rapidly resulting in a global pandemic. Multiple vaccines have been developed to help prevent COVID-19 infection. Similar to other vaccines, common side effects including fever, fatigue, myalgias have occurred; however, episodes of more serious side effects have been noted. One such potentially serious sequalae is vaccine-induced thrombocytopenia (VITT), an autoimmune-mediated phenomenon hypothesized to occur due to molecular mimicry and the production of platelet PF4 antibodies, ultimately leading to thrombocytopenia and easy bruising. In this report, we present the case of a 34-year-old, otherwise, healthy female who presented with easy bruising and thrombocytopenia following completion of the two-dose Moderna COVID-19 vaccine, suspicious for a diagnosis of VITT. The patient was managed conservatively with steroids. Steroids and intravenous immune globulin therapy have been reported in the literature. This report highlights that VITT should be considered in the differential diagnosis for patient presenting with increased bruising in the setting of recent COVID-19 vaccine administration, and furthermore highlights the diagnostic workup and management options for such patients.

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1. Background

COVID-19 has caused a global pandemic, leading to the development and production of multiple vaccines. COVID-19 vaccine-related adverse events have become increasingly recognized. Though most adverse events are mild, including fever, fatigue, and myalgias, more serious events have been reported. Several vaccinated patients have developed a prothrombotic thrombocytopenic syndrome called 'vaccine-induced thrombotic thrombocytopenia (VITT)'[1]. Here, we describe a rare case of VITT in a 34-year-old patient after completion of the two-dose Moderna COVID-19 vaccine series.

2. Presentation and HPI

A 34-year-old woman with a history of postpartum subclinical hypothyroidism previously on levothyroxine presented to the emergency department after referral from her primary care physician for thrombocytopenia. The patient reported being in her usual state of health until approximately 2 weeks prior to presentation at which time she noted a petechial rash on the dorsal surface of the hands, as well as easy bruising. She denied new medications, occupational exposures, illicit substance use, or recent infection. The patient did, however, report the completion of the two-dose Moderna COVID-19 vaccine 3 days prior to the petechial rash. Given her symptoms, routine labs were ordered as an outpatient by her primary care provider, which demonstrated thrombocytopenia to 65,000 platelets/mcL (reference range 150,000–450,000 platelets/mcL), collected 5 days after the second dose of the vaccine, with further decline to 45,000 platelets/mcL 11 days later, compared to a prior historical baseline of 184,000 platelets/mcL.

Upon presentation to our facility, she remained hemodynamically stable. Physical examination was notable for a petechial rash localized to the dorsal surface of the bilateral hands with multiple bruises. Laboratory diagnostics demonstrated a further decline in the platelet count to 29,000 platelets/mcL without evidence of clumping, with a preserved white blood cell count and hemoglobin. Additional diagnostics (Table 1) were largely unremarkable, except for a mildly elevated aPTT (59.3 seconds; reference range 23.4–36.2 seconds), a positive lupus anticoagulant, and a mildly prolonged Dilute Russell's Viper Venom screen (57.7 seconds; reference range 36.1–50.8 seconds). Additional serologies including hepatitis panel, Human Immunodeficiency Virus, COVID-19 PCR, vitamin B12, folic acid, and morning cortisol were unremarkable. Intriguingly, heparin-induced thrombocytopenia (HIT) antibodies (anti-Platelet factor 4; anti-PF4), as measured by

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Table 1. Notable laboratory diagnostics at the time of presentation.

Lab test	Value	Reference range
Baseline platelet count	184,000 platelets/mcL	150,000–350,000 platelets/mcL
Platelets after first vaccine dose	65,000 platelets/mcL	150,000–350,000 platelets/mcL
Platelets after second vaccine dose	45,000 platelets/mcL	150,000–350,000 platelets/mcL
Platelets on presentation	29,000 platelets/mcL	150,000–350,000 platelets/mcL
Prothrombin Time	13.2 seconds	11.8–14.6 seconds
Partial Thromboplastin Time	59.3 seconds	23.4–36.2 seconds
Serum Sodium	142 mmol/L	136–145 mmol/L
Serum Potassium	3.9 mmol/L	3.4–4.5 mmol/L
Serum Chloride	110 mmol/L	98–107 mmol/L
White Blood Cell Count	4800/uL	4000–10,800/uL
Hemoglobin	13.5 g/dL	11–14.5 g/dL

enzyme-linked immunosorbent assay, were positive with an optical density of 0.505 (reference range 0.00–0.349), despite her lack of heparinoid exposure. She was managed conservatively with dexamethasone for presumed VITT and was ultimately discharged in stable condition with stable thrombocytopenia (35,000/mcL). On follow-up, the patient continued to remain asymptomatic without further episodes of petechiae or bleeding. Her platelet count recovered to 118,000/mcL, 6 weeks after discharge.

3. Discussion

The patient in this report presented in the context of asymptomatic thrombocytopenia shortly following the second dose of the Moderna COVID-19 vaccine. The incidence of VITT has been noted to be exceedingly rare with only a few cases being reported after tens of millions of vaccines [1]. The highest incidence has been reported in Norway where five cases were reported from among approximately 130,000 individuals vaccinated with the Oxford AstraZeneca vaccine, suggesting an incidence of 1 in 26,000 [2]. An initial report from the Centers for Disease Control (CDC) in the USA identified 15 cases from among approximately 8 million individuals vaccinated with the Johnson & Johnson vaccine, suggesting an incidence of 1 in 533,333 [3]. A prior study demonstrated evidence of thrombocytopenia following COVID-19 vaccination at 5–28 days post vaccination [1].

The patient presented here reported no antecedent history of underlying rheumatological disease, immune thrombocytopenic purpura, or recent infections. Intriguingly, lupus anticoagulant and HIT antibody screens were noted to be positive, despite a negative antinuclear antibody and a lack of heparinoid exposure, respectively. Antiphospholipid syndrome (APS) and HIT are caused by different antibodies (lupus anticoagulant, anticardiolipin antibodies, or beta-2 glycoprotein, and platelet factor 4 (PF4) antibodies, respectively); however, due to similarities in the pathophysiology, it is postulated that these two autoimmune antibody-mediated disorders may be related [4]. Indeed, Lasne et al. reported that 3 out 20 patients with APS also tested positive for anti-PF4 antibodies, the causative agent of HIT. One of the patients had a positive serotonin release assay with a level of 26% (normal, <20%). None of these patients reported history of HIT or received heparin in at least thirty months [5]. APS antibodies have been shown not only to induce platelet activation but also to lead to the activation of monocytes, endothelial cells, and complement, as well as the elaboration of numerous cofactors and procoagulant/adhesion molecules that facilitate the production of a procoagulant state encourage thrombosis [6]. Similarly, IgG anti-PF4 platelet antibodies bind with heparin in the bloodstream, resulting in platelet activation and formation of platelet microparticles and microthrombi [7]. This could indicate that patients who have a prior history of APS have a higher risk of developing VITT, given that there is a possible correlation between the two diseases.

In cases of VITT, antibodies against platelet factor 4 have been identified [1]. While the presence of these antibodies is often encountered in the setting of heparin exposure, in rare cases, these antibodies have been described as an autoimmune phenomenon in those not exposed to heparin products [8]. Molecular mimicry between pathogen and host antigens is believed to contribute to the pathogenesis of VITT. There is a suspected strong sequence homology between specific viral and bacterial proteins and beta-2 glycoprotein 1 [9]. Data from the Society of Thrombosis and Haemostasis Research hypothesized that post-vaccine thrombocytopenia arises secondary to autoantibody formation in the setting of immune stimulation with resultant antibody formation against platelet PF4 antigen [10]. Preliminary theories suggest that vaccine components bind to the PF4 antigen to generate a neoantigen [1].

Although there are prior reports of improvement in the clinical condition of patients with evidence of thrombosis with administration of low molecular weight heparin, it may be advisable to choose from the non-heparin anticoagulants, given the same pathophysiological antibody-mediated mechanism [11]. The British Society of Hematology recommends the treatment of VITT with intravenous immunoglobulin for 2 days and steroids [12]. Most patients have had rapid recovery of platelet count within 1–3 days after receiving IVIG [1]. IVIG has also been shown to inhibit platelet antibodies in HIT [13].

4. Conclusion

We describe a rare case of VITT in a 34-year-old patient after completion of the two-dose Moderna

COVID-19 vaccine series. Patients presenting with increased bruising, in the setting of recent COVID-19 vaccine administration, should be screened for VITT. If present, patients should be made aware of this phenomenon and it would be advisable to avoid heparin administration. If thrombosis is present, then anticoagulation with non-heparin anticoagulants should be initiated. Patients with a prior diagnosis of antiphospholipid syndrome should be cautioned regarding the possible effects of the vaccine.

Disclosure statement

No potential conflict of interest was reported by the author(s)

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