Acute Immune Thrombocytopenia (ITP) following Covid-19 vaccination in a patient with previously stable ITP

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Abstract

ITP (Immune Thrombocytopenia) is an autoimmune condition associated with multiple risk factors including viral infections (HBV/HCV/CMV, HIV and recently SARS-CoV-2) and vaccines. Though immune mechanisms have been proposed to explain the pathogenesis of acute ITP, autoimmunity with Covid-19 vaccine is still unclear and needs further research. We report a case of acute ITP after administration of Pfizer-BioNTech mRNA Covid-19 vaccine in a patient with previously stable ITP.

Key Words:
COVID-19, Immune thrombocytopenic purpura, Vaccination, Pfizer, SARS-CoV-2
Introduction

The Food and Drug Administration (FDA) issued Emergency Use Authorization (EUA) for the COVID-19 vaccine on December 11th, 2020. In New York, as of February 19, 2021, 2,147,076 first doses and 1,033,267 second doses of the COVID-19 mRNA vaccines have already been administered [1]. The FDA requires any vaccine related adverse events to be reported to the Vaccine Adverse Events Reporting System (VAERS). The VAERS currently has 15,865 reports of adverse events from the COVID vaccine ranging from mild symptoms to severe anaphylaxis [2].

“Immune thrombocytopenia” (ITP) is an autoimmune pathology which is defined by isolated platelet count below 100x10E9/L, petechiae or purpuric rashes and episodes of possible hemorrhage caused by anti-platelet antibodies. Typically, the disease follows a stable course with intermittent and episodic flares leading to relevant thrombocytopenia [3]. ITP has been described following several viral infections including but not limited to Hepatitis B/C, cytomegalovirus (CMV), and human immunodeficiency virus (HIV). More recently, there have been numerous cases of new-onset ITP in COVID-19 patients described in the literature [4]. Following the administration of the COVID-19 vaccine, rare cases of ITP have been reported to the federal government’s Vaccine Adverse Event Reporting System (VAERS). There has been reports for example of thrombocytopenia following the Pfizer vaccine with and without a history of ITP. Here we present a case of a patient with a known history of ITP and subsequent flare after the first dose of the Pfizer-BioNTech COVID mRNA vaccine.

Case Report

A 47-year-old female with a past medical history of hypothyroidism (secondary to Hashimoto’s thyroiditis), iron deficiency anemia (IDA), lymphadenopathy, and immune thrombocytopenic purpura (ITP) received her first dose of the Pfizer-BioNTech mRNA vaccine and experienced mild arm soreness for 2 days post-vaccination but did not experience any other adverse effects.

The patient had ITP diagnosed in 2002, during pregnancy, when platelets were decreased to as low as 4,000/mcL. After initial treatment with prednisone she had a response of CR (platelets >100,000 as described by Rodeghiero et al [5]. She had another ITP flare up 6 years later with platelets decreasing to 3,000/mcL which responded to Human Immune Globulin (IVIG) and dexamethasone in another CR response. Workup along this timeframe yielded a direct platelet antibody level of 1962 and a mildly elevated rheumatoid factor of 20.7 IU/mL. Negative tests included Anti-nuclear antigen (ANA), double-stranded DNA (dsDNA), anti-cardiolipin IgM and IgG, and Lupus anticoagulant. A bone marrow biopsy yielded no morphologic or immunophenotypic evidence of a lymphoproliferative disorder, increased blasts, or presence of clonal blast cells. Karyotyping showed a normal karyotype of 46XX. Her platelet count was recorded on many occasions in the interval years and ranged from 164,000 to 36,000. She was not maintained on any therapy for ITP during this time.

She was found to have an enlarged left axillary lymph node of routine mammogram in 2018 as well as left axillary and retroperitoneal adenopathy on chest in 12/2018 and abdominal pelvis CT in 6/2019. Biopsy of left axillary lymph node in 2018 showed no malignancy, and an excisional biopsy in 3/2019 of the area showed follicular hyperplasia without malignancy. Flow cytometry was negative for lymphocytic malignancy in 2018 and fine needle aspirate of adenopathy in the breast and two excisional biopsies were negative for malignancy in 2019.
Eighteen days post-administration, the patient presented to the emergency room with complaints of easy bruising, gum bleeding, and an episode of epistaxis. She denied any history of trauma, headache, visual changes, rectal bleeding, or gastrointestinal symptoms. Physical exam was remarkable for ecchymosis and petechiae on her bilateral upper and lower extremities and dried blood within her oropharynx. No splenomegaly or hepatomegaly was noted. A CT head was negative for hemorrhage and a chest radiograph was clear. Her platelet count was noted to be 1,000/mcL (her last platelet count 3 months prior was 62,000/mcL). Peripheral smear confirmed the thrombocytopenia and showed normal red blood cell (RBC) morphology (Figure 1 & 2). Her prothrombin time was 16.2 seconds and INR 1.5 mg/dL, reticulocyte count showed mildly elevated reticulocytes of 2.2%, lactate dehydrogenase (LDH) was mildly elevated a 310 U/L, a manual white blood cell differential showed 13 atypical lymphocytes. She had a mildly elevated alkaline phosphatase of 109 U/L, an antinuclear antibody screen (ANA) was negative. Her other cell lines and labs were within normal limits. Labs within normal limits included white blood cell count and differential, hemoglobin, red cell distribution width (RDW), aPTT, haptoglobin, basic metabolic panel, a point of care test was negative for SARS CoV-2 as well as Flu A and B. She had fibrinogen which was normal at 280 and denied headaches but no D-dimer or DVT study was done. She received dexamethasone and was admitted to the intensive care unit (ICU).

In the ICU, one unit of platelets and one unit of Human Immune Globulin (Privigen) (IVIG) was given with improvement of platelets to 61,000/mcL. On day two platelet level again fell to 19,000/mcL and one unit platelet transfusion and IVIG was again given with platelets subsequently rising to 72,000/mcL. CT chest, abdomen and pelvis were performed to evaluate lymphadenopathy and showed resolution of the previously noted adenopathy. Further workup was significant for Sjogren’s syndrome (SS-A antibody (RO) at 2.8 AI, a repeat ANA was positive 1:80 with a speckled pattern, an EBV DNA by PCR test was positive at 429 IU/ml, Hepatitis C, Hepatitis B, Human Immuno-deficiency virus (HIV), TSH were negative. She was discharged with clinic follow up. Up to the time of this report, she had received only the first dose of the vaccine.

Discussion

ITP (Immune thrombocytopenic purpura) is a rare autoimmune disease described by platelet count <100x10^9/L, which is associated with an increased risk of bleeding [6]. Risk factors include environmental factors (e.g., infections, drugs, and malignancy), genetic predisposition and viral infections as well. Moreover, some vaccines against infectious agents have also been associated with acute ITP including MMR (Measles, mumps and rubella), pneumococcus, Haemophilus influenzae B, hepatitis B virus, and varicella-zoster virus (VZV) [6,7]. Thrombocytopenia is being reported in association with SARS-CoV-2 infection and is a risk factor for increased morbidity and mortality. Thrombocytopenia in these patients may be caused by disseminated intravascular coagulation (DIC), sepsis, drug induced as well as acute ITP have been reported [6]. Multiple mechanisms are reported including infection of the bone marrow cells leading to inhibition of platelet production or by direct effect on platelets by the virus (conceivably via CD-13 receptors), virus induced liver damage resulting in thrombopoietin synthesis, pulmonary endothelial injury with formation of platelet clumps in the lungs, resulting in formation of micro thrombi and thrombocytopenia, degradation of platelets by immune system [7]. There is not adequate discussion on these immune mechanisms up till date. Certain phenomenon which can explain this
autoimmunity by viruses include molecular mimicry, cryptic antigen expression and epitome spreading. Molecular mimicry has been well explained with viruses including HIV, HCV, VZV and H. Pylori. However, between SARS-CoV-2 and platelets this sequence homology has yet to be identified [8].

Vaccines are now required for prevention of diseases such as SARS-CoV-2 in the general population and for those who are at high risk of complications [9]. Up till Dec 2020, 212 vaccines were developed across the globe including 4 non-replicating viral vector vaccines, three inactivated vaccines, two protein subunit vaccines and two RNA vaccines which had entered in phase III clinical trials. Among these companies, the leading companies, Moderna, BioNTech/Pfizer, and Inovio generated nucleic acid-based vaccines. Early studies from BioNTech/Pfizer and Moderna are associated with a strong antibody response [10,11]. Pfizer generated a BNT162b2 COVID-19 vaccine which is a lipid nanoparticle–formulated, nucleoside-modified RNA vaccine that encodes a prefusion stabilized, membrane-anchored SARS-CoV-2 full-length spike protein [12]. Side effects reported include local reactions like redness, swelling, pain at injection site and systemic like fever, chills, fatigue, headache, new or worsening muscle pain, vomiting [12,13]. Lymphadenopathy in arm and neck region particularly was also reported but was not common. Rarely reported side effects included Bell’s palsy, appendicitis, acute MI, and cerebrovascular accident [13]. There are very few reports of ITP exacerbation following Covid-19 vaccine administration. There was one reported case with of acute ITP, in patient with stable chronic ITP, within 2 weeks of administration of Moderna vaccine (14).

Our patient with previous history of ITP received first dose of Pfizer -BioNTech mRNA vaccine. Her last ITP flare was 13 years ago and has been having stable platelet count above 30,000/mcL since then. After 18 days of vaccine administration, she presented with acute on chronic ITP. Work up ruled out any other etiology of thrombocytopenia, including active COVID-19 infection. Patient did not complain of any headaches, and thus the likelihood for thrombosis was very low. Although the positive EBV DNA PCR may have been a factor contributing to the acute on chronic ITP, there is no way to tell if the vaccine may have caused a reactivation of EBV which triggered the acute ITP. However, given her infrequency of ITP flares and the fact that the event occurred after receiving vaccine, association of thrombocytopenia with COVID-19 vaccine should be considered. The underlying mechanism requires further research.

Conclusion:

The temporal relation of ITP exacerbation after receiving the Pfizer-BioNTech mRNA Covid-19 vaccine in this patient, especially considering infrequency of flare ups and stable platelet count for many years, is of considerable significance. Best available evidence from all clinical trials and reported side effects from vaccinated individuals suggest ITP secondary to the covid vaccine is an exceedingly rare reportable adverse effect but the benefits of vaccination outweigh the risks of covid infection in these patients. Considering few similar cases recently reported it is advisable that patients with chronic ITP should be monitored closely for any suspicious symptoms following
vaccination. The underlying mechanism of this autoimmunity is still unclear and needs further research.

Potential Conflicts of Interest
No conflicts of interests were declared by any of the authors listed.

Patient Consent Statement
Written Consent obtain from patient for the Case report
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