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CORRESPONDENCE

Immune thrombocytopenia in a 22-year-old post Covid-19 vaccine

To the Editor:

A 22-year-old healthy male with no medication use received the Pfizer-BioNTech BNT16B2b2 mRNA vaccine through his work as an emergency department employee. On day three, post-vaccination, he experienced widespread petechiae (Figure 1) and gum bleeding, which prompted his presentation. He was current on his vaccines, including yearly influenza, with no history of adverse reactions. He denied respiratory and gastrointestinal complaints or a history of infection. He had no personal or family history of bleeding or autoimmune disease. Vital signs and the remainder of his exam were normal. Laboratory tests revealed normal white-cell count, hemoglobin, and severe thrombocytopenia with a platelet count of 2×10^9/L.

Two months prior to receiving the vaccine, the patient was evaluated at an outpatient clinic for upper respiratory symptoms. His PCR assay returned negative for SARS-CoV-2, and complete blood count was unremarkable with a normal platelet count of 145×10^9/L (reference range, $140–400 \times 10^9$/L). The upper respiratory symptoms resolved within a few days, and the patient had no further complaints. However, as a precautionary measure, one-week post outpatient evaluation, he was again tested for SARS-CoV-2, which returned negative.

At the emergency department on day 3, post-vaccination, the following labs were normal or negative: prothrombin time, partial thromboplastin time, fibrinogen, BUN, creatine, electrolytes, bilirubin, LDH, alkaline phosphatase, albumin, globulin, total protein, and haptoglobin. The aspartate aminotransferase (42) and alanine aminotransferase (90) were mildly elevated; however, they normalized the next day. Additionally, he tested negative for HIV, Hepatitis B, Hepatitis C antibody, and Epstein–Barr Virus serology. A nasopharyngeal swab also returned negative for SARS-CoV-2 antigen. The patient was then admitted and given dexamethasone 40 mg daily for 4 days, a platelet transfusion, and intravenous immunoglobulin at 1 g/kg for 2 days.[1]

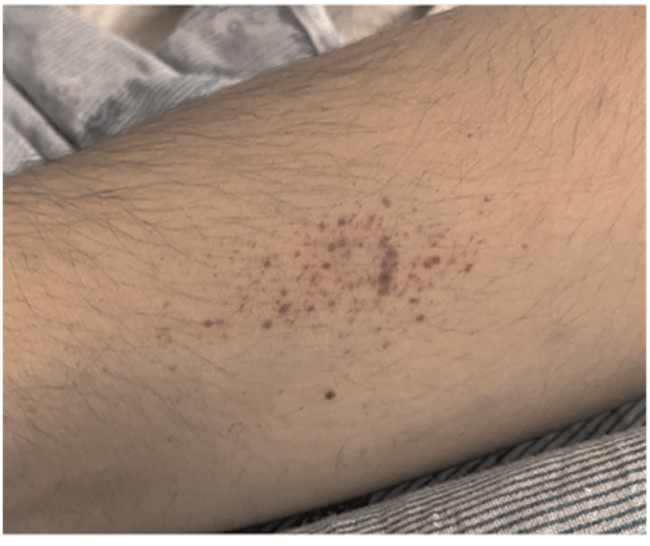

FIGURE 1 Purpuric lesions on the patient's upper extremity

Immunologic studies performed on day 6 for Rheumatoid factor, antibodies for Cyclic Citrullinated Peptide, Anti Centromere, Chromatin IgG, dsDNA, Jo1, Ribosomal P Protein, Ribonucleoprotein, Scleroderma, Smith, Sjogren's Syndrome B, Sm/Rnp IgG, Antinuclear Antibody (<1:80, normal <1:80) were normal. However, Sjogren's Syndrome A antibody (2.8) was elevated (normal <1 AI).

On day six, post-vaccination, petechiae and oral bleeding decreased, and the patient was discharged with a platelet count of 28×10^9/L. Based on the presentation, a platelet count $<100 \times 10^9$/L, and the exclusion of alternative causes, a diagnosis of ITP was made.[1]

At follow up, on day 11, the patient's platelet count normalized to 173×10^9/L, and the patient tested positive for plasma IIb/IIIa and Ia/IIa platelet autoantibodies. Sjogren's Syndrome A antibody decreased from 2.8 on day 6 to 1.5 (normal <1 AI). Moreover, complement C3 (94) was normal (reference range, 79–152 mg/dL), while complement C4 (10.9 mg/dL) was low (reference range, 16–38 mg/dL).

On day 34 a repeat of the patient's abnormal immunologic studies showed a normal value of both Sjogren's syndrome A antibody (SSA AB: <0.2) and Complement C4 (27.6 mg/dL).

Additionally, SARS-CoV-2 IgG antibody testing was performed to rule out that a previous COVID-19 infection elicited the ITP experienced on day 3. However, SARS- CoV-2 IgG was negative.

As of February 16, 2021, and since the patient's discharge on day 6, he remains healthy without any evidence or symptoms of autoimmune disease. [Correction added on 22 February 2021, after first online publication: 11 February 2021].

Previous studies reported only mild or moderate adverse events following the Covid-19 vaccine.[2-4] To our knowledge, outside of a report in the press,[5,6] this is the first case published in the medical literature of an individual, with no other cause identified and no associated illness, experiencing ITP after receiving the Pfizer-BioNTech vaccine. The temporal relationship of the patient's presentation 3 days post-vaccine administration suggests, but does not prove, the vaccine may be linked to the patient's ITP. Additionally, the rapid and severe drop in platelet count to 2×10^9/L is reminiscent of the abrupt onset observed in drug-induced thrombocytopenia, which further suggests a recent etiology.[7]

However, it must be noted that the incidence of ITP is about 3.3 per 100 000 adults/year.[8] Therefore, it is also plausible that this patient's diagnosis was purely coincidental, given that the United States has administered over 12 million vaccines to date.[9] Additionally, 43 448 participants were included in the Pfizer-BioNTech trial, and no ITP was reported.[2] Moreover, considering the low complement C4 (10.9 mg/dL), mildly elevated SSA Ab (1.5), and 2 months prior, the platelet count (145×10^9/L) was near the lower limit, it is difficult to exclude alternative causes, such as an underlying autoimmune condition with pre-existing ITP. In this scenario, the ITP became clinically apparent following the vaccine, though this patient never manifested symptoms suggestive of autoimmune disease.

This case was reported to the FDA's Vaccine Adverse Events Reporting System (VAERS) and is valuable both for post-approval pharmacovigilance and as a foundation for clinicians to evaluate future patients with suspected ITP. Rare vaccination events are important, but do not diminish the enormous utility of vaccination and the well-documented safety profile[2] of the Pfizer-BioNTech BNT16B2b2 mRNA vaccine.

CONFLICT OF INTEREST

The authors report no conflict of interest.

DATA AVAILABILITY STATEMENT

Data sharing not applicable - no new data generated

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Familial thrombocytopenia flare-up following the first dose of mRNA-1273 Covid-19 vaccine

To the Editor:

A 36-year-old female with a past medical history of thrombocytopenia, previously classified as immune thrombocytopenic purpura (ITP), presented to the hospital with diffuse petechiae, easy bruising, bleeding gums and a mild headache. She has a history of excessive bleeding after dental procedures but denied heavy menstrual bleeding. She was diagnosed with "ITP" as a child with a baseline platelet count of 40-60 K/μL. Previously, her work up was negative for autoimmune and nutritional disorders. Her family history included multiple generations of both genders reporting similar low platelet counts since birth. Prior evaluations included a bone marrow biopsy of a male sibling with thrombocytopenia, which demonstrated normocellular trilineal hematopoiesis with slightly increased small size megakaryocytes, normal flow cytometry; FoundationOne Liquid CDx Next Generation Sequencing testing showed multiple variants of unknown significance seen in 14 different genes including GATA2. Additionally, two younger family members had been investigated for possible ANKRD26-related autosomal dominant thrombocytopenia though no testing was available for review in these cases. The last exacerbation of her chronic thrombocytopenia was 12 years prior during her second pregnancy for which she received intravenous immunoglobulin (IVIg) and steroids with minimal increase in her platelet count but no serious bleeding reported. Since that time, she has required no treatment; her blood counts are monitored every 6 months by her primary care doctor.

Patient received the first dose of SARS-CoV-2 mRNA-1273 Moderna Covid-19 vaccine 2 weeks prior to presentation. One week post receipt the patient experienced mild headaches for which she took three ibuprofen capsules as she is allergic to acetaminophen. The headaches persisted and the patient took sumatriptan with improvement of her symptoms. She had taken ibuprofen and sumatriptan in the past with no adverse events. Also, she had a vaginal ring