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CASE REPORT

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Upper extremity deep venous thrombosis after BNT162b2 mRNA COVID-19 vaccine case report

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Abstract

We describe a case of an otherwise healthy 60-year-old female patient who presented 6 days after receipt of the second dose of the BNT162b2 mRNA COVID-19 (Pfizer/BioNTech) vaccine and was found to have upper extremity deep venous thrombosis.

KEYWORDS

cardiovascular disorders, COVID-19, COVID-19 Vaccines, hematology, SARS-CoV-2

1 | BACKGROUND

More than 288 million doses of the novel BNT162b2 mRNA COVID-19 vaccine (Pfizer/BioNTech) have been administered in the United States, with 310,254 reported adverse events as of December 10, 2021.[1,2] A recent review of adverse reactions to COVID-19 vaccines illustrates that RNA-based vaccine recipients experience greater rates of reactogenicity events in comparison with recipients of adenovirus-based, inactivated, or pro-subunit COVID-19 vaccines.[3] It is postulated that these side effects, including site pain, fever, and chills, reflect the robust immune response after receipt of the vaccine. The review found that adverse side effects due to RNA-based COVID-19 vaccines are extremely rare. Furthermore, the original randomized controlled trial that demonstrated the efficacy of the Pfizer/BioNTech vaccine found similar incidence of adverse events between the placebo and vaccine groups.[4] Of the adverse events reported by study participants, none included deep venous thrombosis (DVT).

A recent prospective study investigated the presentations and outcomes in patients with venous thromboembolism (VTE), including DVT, pulmonary embolism, splanchnic vein thrombosis, or cerebral vein thrombosis, 4–30 days after vaccination against COVID-19 in comparison with historical controls.[5] The study found that VTE after COVID-19 vaccination is less frequently associated with major VTE risk factors, such as active cancer or recent surgery, in comparison with controls. When comparing patients with VTE after mRNA-based vaccination against historical controls, there was no difference in thrombosis site, major bleeding, or mortality. The sample included 74 patients who experienced VTE after mRNA-based COVID-19 vaccination. Of those, 64.9% were pulmonary embolism with or without DVT, 28.4% were isolated DVT, 2.7% were isolated cerebral venous sinus thrombosis, 2.7% were isolated splanchnic vein thrombosis, and 1.4% were venous thrombosis in multiple territories, although the investigators did not specify how many upper extremity DVTs occurred. As of December 10, 2021, the vaccine adverse event reporting system yielded 464 reports of "thrombosis" after the Pfizer/BioNTech vaccine in individuals with no reported current illness, 32 of which occurred in the upper extremity.[2] Despite these

32 reports, to our knowledge, no case reports detail this phenomenon. We describe a case of extensive upper extremity deep venous thrombosis (UEDVT) in an otherwise healthy patient shortly after receipt of the second dose of the Pfizer/BioNTech vaccine.

2 | CASE PRESENTATION

A 60-year-old woman with past medical history including hypertension, nephrolithiasis, and Covid-19 (4 months prior) presented to the emergency department with 3 days of substernal chest pain radiating toward the back and both shoulders 6 days after receiving her second dose of the Pfizer COVID-19 vaccine in her left deltoid. The patient tested negative for COVID-19 and denied shortness of breath, cough, fever, or dyspnea on exertion. Her ECG was notable for more pronounced t-wave inversions in III and aVF, prompting further workup (Figure 1). Troponin, CT angiogram of the chest, abdomen, and pelvis, and nuclear stress test were unremarkable. The patient was discharged the following day but noted her pain continued.

Once home, the patient additionally experienced pain, erythema, edema, and warmth in her left arm. Despite this, she continued to work as a hairdresser and engage in daily activities.

She re-presented to care 6 days after discharge. Notably, her left bicep circumference was 31 cm versus 28 cm on the right (Figure 2). Left upper extremity duplex ultrasound was remarkable for DVT of the internal jugular, subclavian, axillary, and basilic veins. Subsequent MRI angiogram was confirmatory (Figure 3). The patient had no previous personal or family history of thrombotic events. She had completed all age-appropriate cancer screening. She tested negative for Factor V Leiden, prothrombin gene mutation G20210A, lupus anticoagulants, beta-2-glycoprotein I antibodies, and anti-cardiolipin antibodies. Antithrombin III was within the reference range.

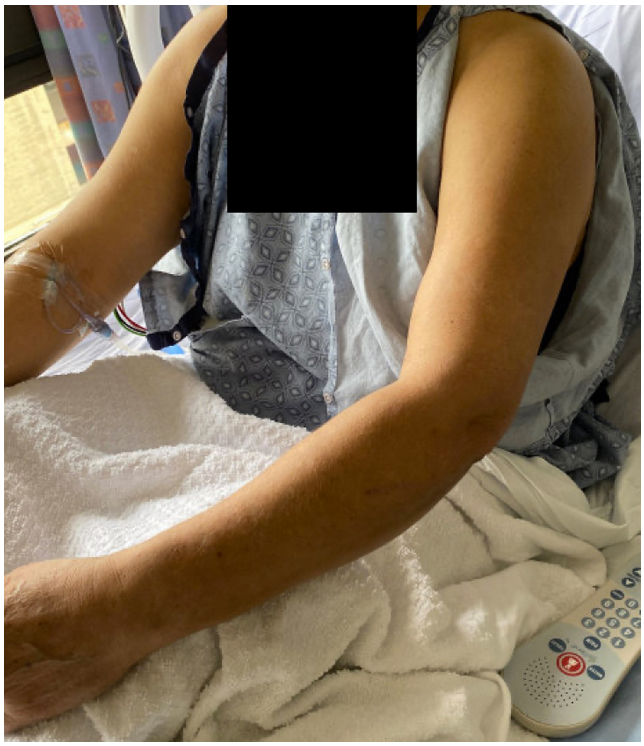

FIGURE 2 Patient with left upper extremity deep venous thrombosis 14 days after receipt of second dose of BNT162b2 mRNA COVID-19 vaccine

She had elevated factor VIII levels, which may have been elevated due to her inflammatory state. The patient was treated with a heparin drip, which decreased her pain and edema. The patient was considered for thrombolysis, but given improvement was discharged on apixaban. Eleven days later, a follow-up venogram showed persistent clot burden in the left axillary, mid-subclavian, and brachiocephalic veins. Thrombectomy, overnight tPA infusion, and ultimately left subclavian vein stenting resulted in some improvement in edema and pain. The patient was discharged with a left upper extremity compression wrap

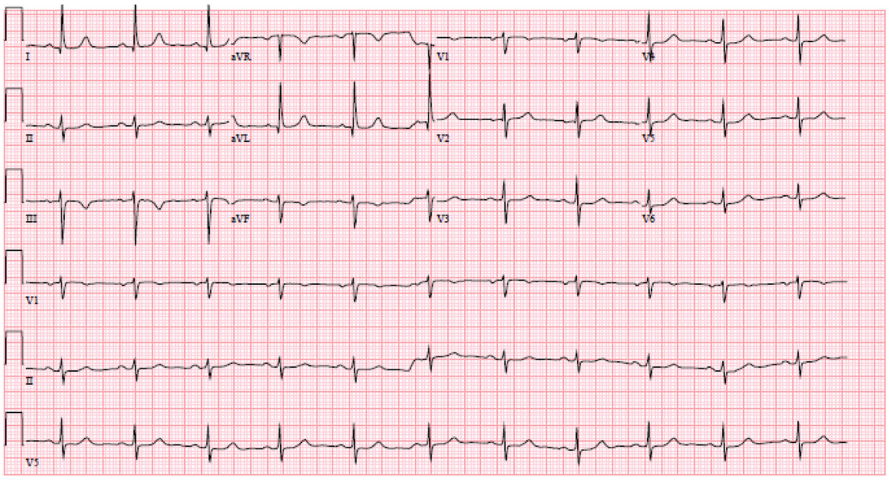

FIGURE 1 ECG for chest pain evaluation 6 days after receipt of second dose of BNT162b2 mRNA COVID-19 vaccine

and on daily apixaban and aspirin. A 3-week follow-up left upper extremity venous duplex ultrasound found no evidence of thrombosis and the patient reported resolution of pain (Figure 4). At a 4-month follow-up visit, the patient reported no pain or swelling of her upper extremities.

3 | DISCUSSION AND CONCLUSIONS

To our knowledge, our patient represents the first report of UEDVT shortly after receipt of the BNT162b2 vaccine in an otherwise healthy person. One case reported a lower extremity DVT shortly after BNT162b2 vaccination in a patient heterozygous for the factor V Leiden mutation.[6] Another case reported a patient with a DVT and pulmonary embolism (PE) after the first dose of the BNT162b2 vaccine with a positive heparin-induced thrombocytopenia screen, suggesting vaccine-induced immune-thrombotic thrombocytopenia (VITT).[7] Vaccine-induced immune-thrombotic thrombocytopenia has been described in recipients of the ChAdOx1 nCov-19 AstraZeneca[8,9] and Ad26.COV2.S (Janssen; Johnson & Johnson)[10] vaccines, but has not yet been described in recipients of the BNT162b2 vaccine. Our patient did not receive an ELISA assay for evaluation of VITT. The mRNA-1273 (Moderna) vaccine has also been associated with several reports of venous thrombosis. A case series reported one case of lower extremity DVT and PE, one case of PE, and one case of lower extremity DVT in

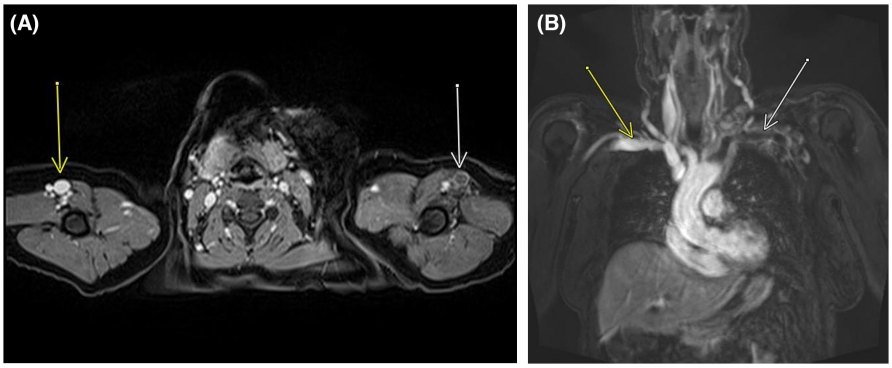

FIGURE 3 MRI Angiogram of upper extremity DVT 14 days after receipt of second dose of BNT162b2 mRNA COVID-19 vaccine. (A) Right brachial vein, patent (yellow arrow) and left brachial vein, thrombosed (white arrow). (B) Right subclavian vein, patent (yellow arrow) and left subclavian vein, thrombosed (white arrow)

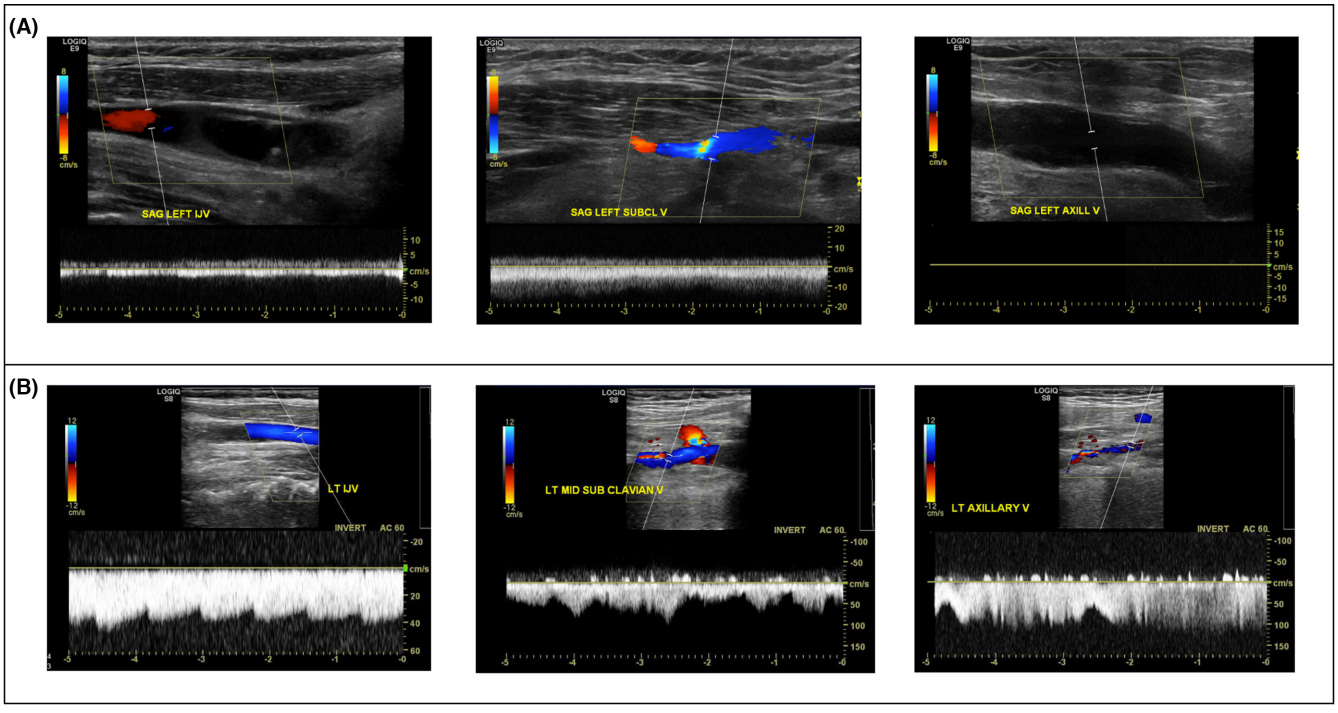

FIGURE 4 Venous Duplex Ultrasound of upper extremity at patient presentation (A) and at 3-week follow-up (B). (A) From left to right: Duplex US of thrombosed left internal jugular vein, left subclavian vein, and left axillary vein 13 days after receipt of second dose of BNT162b2 mRNA COVID-19 vaccine (B) From left to right: Duplex US of patent left internal jugular vein, left subclavian vein, and left axillary vein at 3-week follow up

Moderna vaccine recipients with no thrombotic disorders.[11] In a case presentation similar to ours, an otherwise healthy patient with a negative thrombophilia screening experienced an ipsilateral upper extremity DVT after the second dose of the Moderna vaccine.[12] Given the similar mechanism of action between the mRNA-1273 (Moderna) and BNT162b2 (Pfizer/BioNTech) vaccines, it is possible that the same pathophysiology underlies the DVT in these patients. One proposed mechanism is that mRNA binds to pattern recognition receptors (PRRs) in endosomes or cytosol, subsequently activating a pro-inflammatory cascade.[12,13]

Other than her occupation,[14] our patient did not have other known risk factors for DVT: no personal or family history of thromboembolism, no tobacco use, took no prescription medications, and had received all age-appropriate cancer screening. During the patient's hospitalization, an MRI Angiogram found moderate stenosis of the contralateral right subclavian vein during hyperabduction, which was concerning for thoracic outlet syndrome. However, follow-up MRI angiogram found bilaterally patent subclavian and axillary arteries and bilateral mild compression of the subclavian veins at the level of the costo-clavicular space during hyperabduction that resolved completely when in the neutral position. Furthermore, there was no mass found in the thoracic outlet that could lead to compression of arteries or veins. Thus, thoracic outlet syndrome is unlikely to have caused the patient's UEDVT. COVID-19 infection is associated with venous and arterial thrombosis;[15] therefore, the patient's COVID-19 infection 4 months prior may have increased the risk of thrombosis.

UEDVT occurs in about 0.4 to 1 per 10,000 people per year and <20% of incidents are idiopathic.[16] Idiopathic UEDVT is relatively rare and given the scarcity of potential causes, our case may simply reflect expected background incidence. Furthermore, an analysis of upper and lower DVT venous duplex ultrasound reports found no increased risk of DVT in recipients of the Pfizer, Moderna, and Janssen vaccines.[17] Nevertheless, UEDVT after vaccination should remain on the differential as clinicians assess chest and arm pain following vaccination. Altogether, our case suggests a possible association between the BNT162b2 vaccine and UEDVT that requires further research.

AUTHOR CONTRIBUTIONS

Susan Gonzalez: SG had full access to all of the data in the study, takes responsibility for the integrity of the data and the accuracy of the data analysis, drafted the manuscript, and provided administrative, technical, or material support. David Levine: DL provided study supervision. All authors contributed to study concept and design, acquisition, analysis or interpretation of data, critical revision of the manuscript for important intellectual content, and read and approved the final manuscript.

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None.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

CONSENT

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

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