

Portal vein thrombosis after second Pfizer/BioNTech coronavirus disease 2019 vaccine

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ABSTRACT

We have reviewed a case of portomesenteric venous thrombosis that occurred shortly after the administration of the second Pfizer/BioNTech coronavirus disease 2019 (COVID-19) vaccine and discussed the literature surrounding the subject. Our report was generated after reviewing the patient's medical records and clinical images with his written informed consent. The literature review was conducted using PubMed and Google Scholar. Portomesenteric venous thrombosis after the Pfizer/BioNTech COVID-19 vaccine has previously been reported, although infrequently. We did not find enough information, given the paucity of the reported data, to assert a causative relationship between the Pfizer/BioNTech COVID-19 vaccine and the occurrence of portomesenteric thrombosis. (*J Vasc Surg Cases Innov Tech* 2022;8:667-9.)

Keywords: COVID-19; Portal vein thrombosis; Vaccine

Cases of portal vein thrombosis after adenovirus vector coronavirus disease 2019 (COVID-19) vaccines have been reported in association with thrombocytopenia.¹ Portal vein thrombosis after the Pfizer COVID-19 vaccine is a rare complication without many prior reported cases, especially cases without clear evidence of an underlying hypercoagulable state. We have described such a case, which had presented without thrombocytopenia and was successfully managed with anticoagulation therapy. The patient gave written informed consent for the report of his case details and imaging studies.

CASE REPORT

A 45-year-old never-smoker man with a body mass index of (BMI) 33 kg/m², no other significant medical history, and no family history of coagulable disorders had presented with an 8-day history of gradually worsening upper abdominal pain, malaise, nausea, vomiting, and anorexia that had started several hours after his second Pfizer/BioNTech BNT162b2 COVID-19 vaccine. His platelet count was normal, the hematocrit was 45%, the blood urea nitrogen/creatinine ratio was 14, and he had tested negative for COVID-19 via a polymerase chain reaction test at admission. A computed tomography (CT) scan of the abdomen and pelvis with intravenous contrast (*Fig. A and C*) revealed thrombosis of the superior mesenteric vein, main portal vein, and right portal vein and peripancreatic edema (his lipase and liver

function test results were within normal limits). Before beginning anticoagulation therapy, blood was drawn to perform a thrombosis panel, which revealed protein C activity of 54% (normal range, 60%-150%) and antithrombin III activity of 79% (normal range, 92%-136%). The thrombosis panel results were otherwise negative (including for paroxysmal nocturnal hemoglobinuria and JAK2 mutations). His symptoms gradually improved with intravenous fluids and parenteral anticoagulation therapy (intravenous heparin, which was transitioned to enoxaparin) during his 3-day hospital stay. His creatinine remained stable, and his hematocrit at discharge was 44.9%. He was discharged with rivaroxaban (15 mg twice daily for the first 21 days and 20 mg daily thereafter).

A contrast-enhanced CT scan performed 41 days after his second vaccine demonstrated continued thrombosis in the splenic, superior mesenteric, and portal veins, with new cavernous transformation and resolution of the peripancreatic edema. The liver function test and lipase results were normal at 45 days after the vaccine. A contrast-enhanced CT scan at 188 days after his second vaccine (*Fig. B and D*) was notable for cavernous vein transformation. Rivaroxaban was discontinued after 6 months in accordance with the hematology recommendations from another healthcare system after noting the cavernous transformation and improvement in symptoms. At the 6-month follow-up visit with our team, he endorsed intermittent vague mild right upper quadrant discomfort but felt overall well. At his 12-month follow-up visit, his symptoms had completely resolved, and the follow-up antithrombin III activity level was 77% without rivaroxaban. We plan to monitor him with annual clinical follow-up examinations and will order imaging studies as needed.

DISCUSSION

Our review of the literature found three cases that shared some similarity with our patient's case. The first was a report of a 66-year-old woman who had presented with lower extremity deep vein thrombosis within 24 hours after receiving the second dose of the Pfizer/BioNTech BNT162b2 COVID-19 vaccine.² Unlike our patient, this patient had had a heterozygous factor V Leiden

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Author conflict of interest: none.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the Journal policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

2468-4287

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<https://doi.org/10.1016/j.jvscit.2022.08.028>

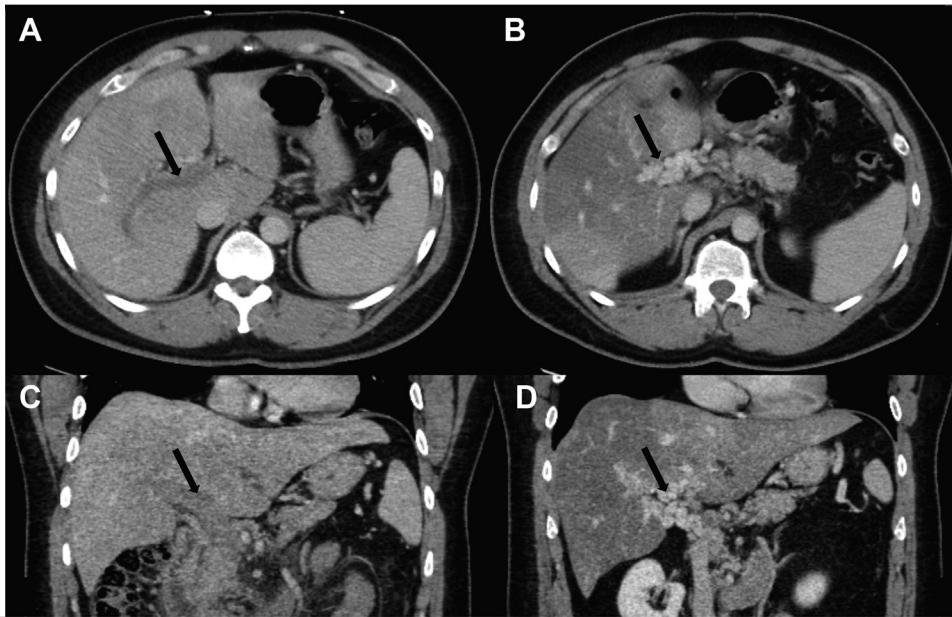


Fig. Computed tomography (CT) scan with intravenous contrast on the day of presentation showing a hypodense, thrombosed right portal vein in the axial plane with minimal evidence of collateralization (**A**) and the main portal vein in the coronal plane (**C**). CT scan on day 188 with intravenous contrast showing cavernous transformation of the main portal vein with mesoportal and portoportal collateralization in the axial (**B**) and coronal (**D**) planes.

mutation, which could have been contributory. A second patient, a 68-year-old woman with a BMI of 30 kg/m², was found to have isolated portal vein thrombosis after presenting with abdominal pain 14 days after her first dose of the Pfizer/BioNTech BNT162b2 COVID-19 vaccine and had evidence of antiphospholipid syndrome found on evaluation.³ The third patient was a 62-year-old woman with a BMI of 30 kg/m², who had presented with abdominal pain 1 day after the first dose of the Oxford/AstraZeneca ChAdOx1-S COVID-19 vaccine and was found to have thrombocytosis, extensive celiac trunk and portomesenteric thrombosis, and no evidence of a hypercoagulable disorder.⁴ A query to the Centers for Disease Control and Prevention (CDC) – Vaccine Adverse Event Reporting System (VAERS) yielded 185 reports of portal vein thrombosis (including porto-spleno-mesenteric venous thrombosis) associated with the Pfizer vaccine⁵; however, no details were available.

Because of the consumptive nature of thrombosis, proteins C and S and antithrombin can be mildly decreased in the setting of acute thrombosis and might not be reflective of a true innate deficiency.⁶ Dehydration has been shown to increase the risk of venous thromboembolism in certain patient populations but was not the case for our patient, who had had a low blood urea nitrogen/creatinine ratio and normal and stable hematocrit throughout his hospital stay.⁷

The mechanism by which COVID-19 vaccines might cause thrombosis remains to be fully elucidated.

Evidence regarding the AstraZeneca vaccine (an adenovirus vector vaccine) has suggested an immune (vaccine-induced) thrombotic thrombocytopenia (TTP) mediated by platelet-activating antibodies against platelet factor 4 and associated with thrombocytopenia, rather than thrombocytosis such as for patient 3.⁸⁻¹⁰ At least 18 cases of portal vein thrombosis have been reported after adenovirus vector COVID-19 vaccines (AstraZeneca and Janssen) and have tended to be associated with thrombocytopenia similar to TTP.¹

In contrast, the Pfizer vaccine uses mRNA to create a spike glycoprotein composed of an S1 and S2 subunit.¹¹ S1 has been shown to induce hypercoagulability via direct interaction with coagulation factors in platelet poor plasma, suggesting a mechanism that could induce aberrant clotting without the thrombocytopenia characteristic of TTP after adenovirus vector vaccines.¹² Although our patient's antithrombin III levels were only slightly decreased, true antithrombin III deficiency will tend to result in activity levels of 40% to 60%.¹³ It is plausible that an otherwise subclinical hypercoagulable state had contributed to his condition.

The mechanisms we have discussed could theoretically cause thrombotic complications other than portal vein thrombosis such as cerebral sinus thrombosis or lower extremity venous thromboembolism. However, a retrospective study of 13.6 million women aged <50 years using the CDC VAERS found no statistically significant increase in the rates of thrombosis after the Pfizer or

Moderna vaccines compared with that in the general population.¹⁴

CONCLUSIONS

As of July 2022, 933 million Pfizer, 356 million Moderna, 37 million Johnson & Johnson, and 67 million AstraZeneca doses have been administered in the United States and European Union combined,¹⁵ and >10 billion COVID-19 vaccine doses worldwide have been administered, with an excellent safety profile.¹⁶ Rare events can occur after vaccine administration, and clinicians should be aware of the possibility and how to address them. We have reported one such rare event after Pfizer COVID-19 vaccine administration.

Diligent event reporting via vaccine safety organizations, including the CDC VAERS in the United States, remains essential to monitoring the effects of the COVID-19 vaccines authorized via emergency use authorizations. We would also encourage the publication of case reports and series, in addition to reporting to the CDC VAERS, to allow for the evaluation of trends. Although additional events could affect how providers counsel and treat their patients, especially those with hypercoagulable disorders, our institution's practice has not been modified as a result of these cases.

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Submitted May 15, 2022; accepted Aug 30, 2022.