

Cerebral Venous Sinus Thrombosis in a Patient With a History of COVID-19 mRNA Vaccination

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A 43-year-old woman with no significant medical history was admitted to our hospital's step down unit with a headache secondary to a cerebral venous sinus thrombosis (CVST), which had been discovered on computed tomography (CT) scan and confirmed with CT angiography.

History

She had had COVID-19 infection in November 2020 and had received 2 doses of the Pfizer BioNTech COVID-19 vaccine in March/April 2021. The patient reported experiencing a headache with sudden onset while bending over to tie her shoes as she was getting ready for work on the morning of admission, about 1 month after receiving the second dose of the COVID-19 vaccine. She stated that the headache "flushed" over from the back of her head to the front and that she had begun experiencing blurry vision, which felt different than any headache she had ever experienced.

She denied smoking cigarettes, drinking alcohol, or using illicit drugs. She denied taking any medications including oral contraceptives. Findings from a physical examination, including a neurological examination and her vital signs, were within normal limits.

Diagnostic testing

An initial CT scan of the brain showed hyperdense material noted in the right transverse sinus, greater than in the left, and the confluence of sinuses measuring 6.0 cm × 1.5 cm, which was highly suspicious for a sinus venous thrombosis. A CT angiogram of the Circle of Willis showed extensive venous sinus thrombosis within the torcular herophili and right transverse sinus with a small amount of thrombus within the medial left transverse sinus. A repeat CT scan of the head on hospital day 2 showed mild interval progression of intracranial venous thrombosis compared with the prior examination, but no

intracranial hemorrhage or midline shift were noted.

Findings from a hypercoagulable workup showed elevated levels of homocysteine at 0.14 mg/dL, protein C at 187%, and cardiolipin antibody at 13 MPL. Results were negative for anti-thrombin antigen, anticard phospholipid antibody, phospholipid antibody, protein S antigen, lupus anticoagulant, lupus hexagonal phase, and heparin-induced platelet antibody. However, given that this bloodwork was performed after the heparin drip was initiated, the results were not accurate and had to be repeated in the outpatient setting.

Treatment and management

The patient was initially started on a heparin drip, which was then transitioned to fondaparinux 7.5 mg subcutaneous daily and was ultimately switched to apixaban 10 mg orally every 12 hours. For her headaches, the patient was administered tramadol and butalbital/acetaminophen/caffeine.

On hospital day 3, the patient had an episode of emesis, which was an acute change from the patient's baseline. A CT scan of the head at that time showed a stable venous thrombosis. Once she remained clinically stable and the venous thrombosis remained stable, she was medically cleared to be discharged home on anticoagulation therapy for 6 months (apixaban 10 mg orally every 12 hours for 7 days and 5 mg orally every 12 hours thereafter) and the need for a repeat CT scan of the head in 4 weeks for reassessment of the venous thrombosis.

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Discussion

CVST is a rare but important cause of stroke in adults with an average age of onset of 32.9 years and is about 3 times more common in women than in men.^{1,2} It is characterized by either complete or partial blockage of a major cerebral venous sinus or the smaller feeding cortical veins. It is frequently misdiagnosed or diagnosed late, since it presents similarly to other neurological conditions and requires high-quality and well-timed brain imaging.³ Noncontrast CT scanning is useful initially to rule out bleeding in a suspected stroke or acute headache, and the diagnosis can be confirmed with magnetic resonance imaging or CT venography (sensitivity 95%; specificity 91%).⁴ The most common risk factors are estrogen-containing oral contraceptives, puerperium, and pregnancy.² Other systemic inflammatory conditions such as iron-deficiency anemia, malignancy, inflammatory bowel disease, and lupus as well as genetically acquired thrombophilia also increase the risk.² CVST has a generally good prognosis if discovered and treated early with anticoagulation with parenteral heparin.² Patients who are refractory to treatment with anticoagulation may require endovascular procedures (thrombolysis or thrombectomy) or a decompressive craniotomy.^{5,6} The recurrence risk after a CVST is low, although patients with thrombophilic disorders are at a greater risk.²

With recent evidence showing similar venous thromboses in several patients receiving Johnson & Johnson's COVID-19 vaccine, our case is clinically relevant and warrants further discussion and investigation.⁷ Given our patient's history, presentation, and extensive diagnostic workup, it seems less likely that our patient's COVID-19 vaccination played a role in her diagnosis. Her hypercoagulable workup showed elevated homocysteine, protein C activity, and cardiolipin antibody, so she may have a hypercoagulable disorder. However, this cannot be said with certainty as these laboratory tests were conducted after the heparin drip was

initiated. If these markers are elevated on repeat bloodwork in an outpatient setting, then the patient may have a hypercoagulable disorder.

The incidence rate of CVST in the general population is quite low. Observed cases of CVST following administration of Johnson & Johnson's COVID-19 vaccine appear to exceed expected cases, based on the background rates of CVST among women aged 20 to 50 years (3-fold or greater).⁷ According to the Centers for Disease Control and Prevention, 28 cases of CVST and 3 deaths were reported out of the 6.8 million Johnson & Johnson's vaccine doses administered.⁸ These numbers are relatively within the range of the normal incidence rate. Furthermore, these individuals were all women between the ages of 18 and 48 years whose symptoms occurred 6 to 13 days after vaccination.⁸ Our patient had received the second dose of the Pfizer BioNTech COVID-19 vaccine about 1 month prior to developing symptoms.

The patients with CVST from Johnson & Johnson's COVID-19 vaccine had also experienced thrombocytopenia, but our patient's platelet count was within normal limits and remained steady throughout her hospital stay. Although as of April 12, 2021, there have been 3 cases of CVST without thrombocytopenia reported with the Moderna COVID-19 vaccine, there have been no reported cases of CVST with thrombocytopenia linked to either mRNA vaccine.^{7,9} While it is possible that our patient is the first to have experienced a CVST related to the Pfizer BioNTech vaccine, there is strong evidence suggesting that this is highly unlikely.

Alternatively, having COVID-19 infection has been shown to put patients in a hypercoagulable state. In the absence of evidence supporting other etiologies, it is possible that our patient's CVST was linked to a prolonged hypercoagulable state because of a COVID-19 infection in November 2020. Another issue worth discussing is how long the hypercoagulable inflammatory state of COVID-19 persists in the body. Studies have shown a direct

relationship between the progression of COVID-19 and patients' D-dimer and IL-6 levels, but researchers have not been able to measure the duration of patient's hypercoagulability risk in the post-acute phase of COVID-19.¹⁰

It is important to be observant for symptoms signifying potential thrombotic events in patients with recent vaccination against COVID-19, and strides can be made in patient education and clinical practice to promote early detection, as this greatly influences morbidity and mortality.

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