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Cerebral Venous Sinus Thrombosis without Thrombotic Thrombocytopenic Syndrome in a Male Patient after Ad26.COV2.S Vaccination

Kara L Heuvelhorst, Tyler Diener, Hana Manzoor*, Maher Khadra, Faisal Musa, Syed K Jafri

Departments of Radiology and Hematology-Oncology, Beaumont Hospital Dearborn,
18101 Oakwood Blvd, Dearborn, MI 48124
*Corresponding author: hana.manzoor@beaumont.org

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Abstract Objective: Here we present one of the first cases of Janssen (Johnson & Johnson Ad26.COV2.S vaccine-associated cerebral venous sinus thrombosis (CVST) in a male patient, and the presumed first case without associated thrombotic thrombocytopenic syndrome (TTS). Method: Patient was identified as a vaccine-related adverse effect due to the unusual presentation of CVST in a male following COVID-19 vaccination, though without thrombocytopenia. Results: Patient presented with left-sided weakness and transient dysarthria. Imaging revealed extensive CVST. Thorough coagulopathy work-up was negative and platelet levels remained within the normal range. Patient improved with non-heparin anticoagulation. Discussion: As more people worldwide continue to be vaccinated against COVID-19, the incidence of vaccine-related complications can be expected to rise. Multiple cases of CVST have been reported in patients following COVID-19 vaccination with associated TTS, nearly all in women. However, this is not the only presentation. Cerebral venous sinus thrombosis should be a consideration in patients who present with headache or altered mental status after COVID vaccination, despite normal platelet levels.

Keywords: *Cerebral Venous Sinus Thrombosis, Vaccine, Johnson & Johnson, Janssen, AstraZeneca, Clot, COVID-19, FDA, CDC, anti-PF4, Thrombotic Thrombocytopenic Syndrome, Ad26.COV2.S*

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1. Case

A 59 year old male presented to the emergency department on April 27, 2021 with left upper and lower extremity weakness and transient dysarthria. The patient had no history of stroke, coagulopathy, immobilization, family history or other risk factors. Physical exam confirmed left-sided weakness. The patient received the Janssen vaccine on March 20, 2021, not known at the time of presentation. The stroke protocol was activated and the patient underwent a non-contrast enhanced CT head, which demonstrated asymmetric hyperdensity within the left transverse sinus and confluence of sinuses, as well as a small right frontal subarachnoid hemorrhage (Figure 1). Subsequent CT angiography and MRI Brain confirmed extensive cerebral sinus thrombosis involving the posterior portion of the sagittal sinus and bilateral transverse sinuses with suspected extension into the left sigmoid sinus (Figure 2).

The patient was admitted to the intensive care unit and initially started on intravenous heparin. This was promptly exchanged for argatroban when the team became aware of recent vaccine administration in an effort to prevent the feared complication of Heparin-induced Thrombocytopenia (HIT). Platelet levels upon arrival were within the normal range, and, although they declined slightly during his hospitalization, remained within the normal range throughout the admission. Interestingly, thorough hematologic workup revealed a negative result for the Heparin Platelet Factor 4 antibody (anti-PF4) and Serotonin Release Assay. Antiphospholipid antibody, Factor V and Protein C and S activity were also within normal limits. D-dimer was elevated at 1,123 ng/mL. A negative COVID-19 test was also confirmed using the polymerase chain reaction method.

The patient continued to improve with anticoagulation and was discharged on a 3 month course of oral apixaban. A thorough workup is still in progress to exclude alternative etiologies to explain the hypercoagulable state, including malignancy.

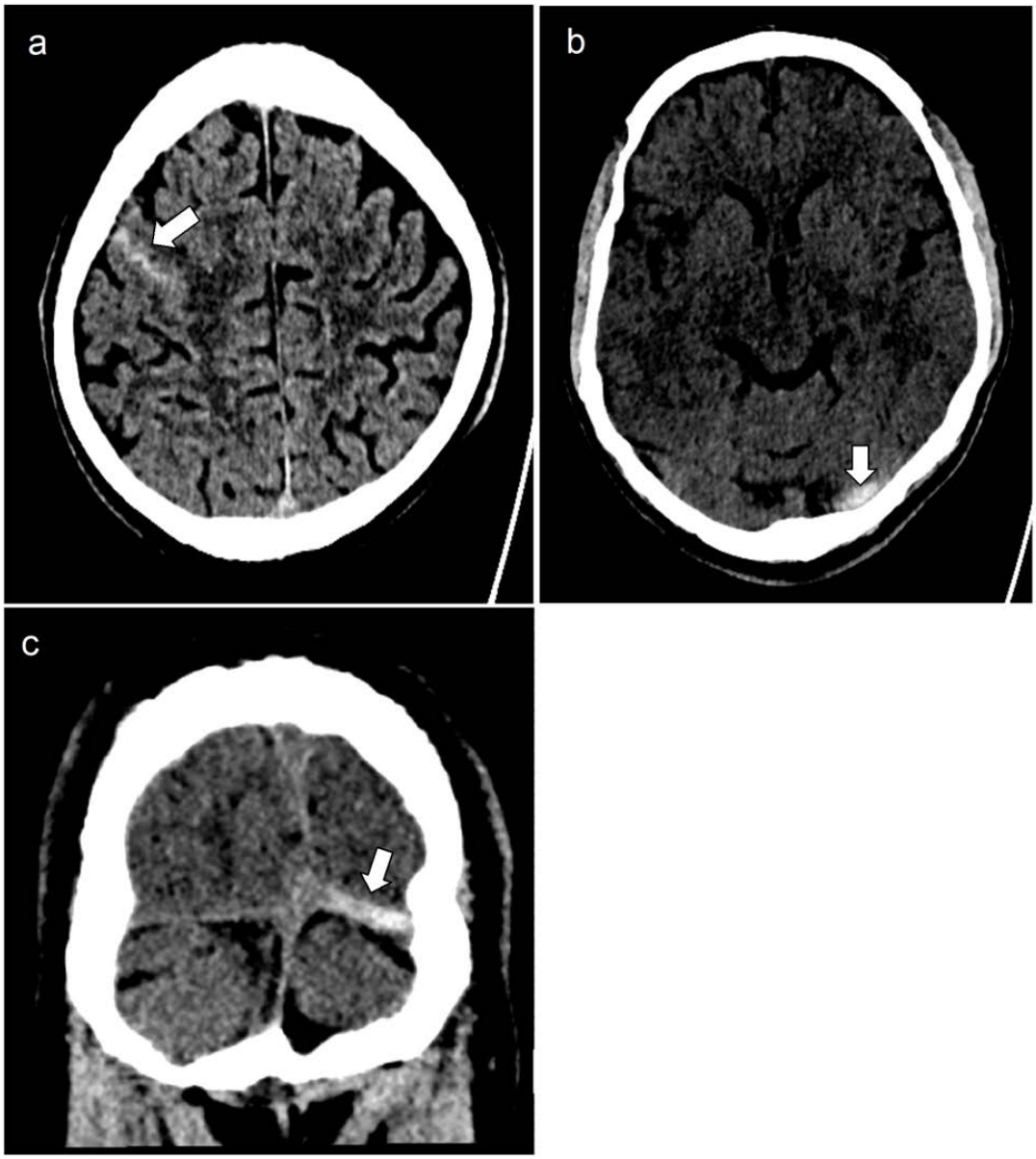

Figure 1. A, Unenhanced CT scan of head demonstrates subarachnoid hemorrhage in right frontal sulci (arrow). B, Unenhanced CT demonstrates hyperdense left transverse sinus (arrow). C, Coronal reformation of CT again demonstrates the hyperdense left transverse sinus (arrow).

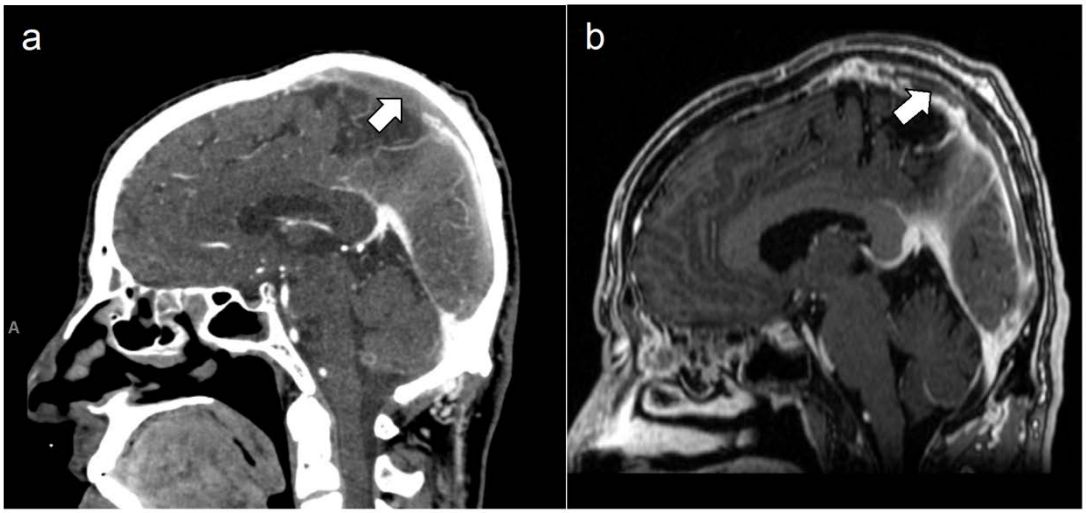

Figure 2. A, CT Angiogram demonstrates extensive filling defects (arrows) within the superior sagittal sinus. B, MRI Brain with contrast confirms the findings

2. Discussion

The Janssen COVID-19 vaccine (Johnson & Johnson, Ad26.COV2.S) received emergency use authorization on February 27, 2021 [1,2]. Over the proceeding weeks, several cases of CVST with TTS were reported, nearly all in women under the age of 50 years old [1,2,3,4,5]. The use of the Janssen vaccine was temporarily suspended from April 13-21 while these cases were under investigation [6]. The CDC and FDA have since recommended resuming use of the vaccine with a warning for women younger than 50 years old [6,7].

Several hospitalizations and a small number of deaths have been reported related to CVST with TTS associated with the Janssen and AtraZeneca (ChAdOx1 nCoV-19) vaccines, the vast majority in female patients less than 50 years of age [1,2,6,8]. It appears that of those tested, all were positive for the presence of heparin-platelet factor 4 HIT antibody (anti-PF4) [1,2,4,5,8,9,10] via enzyme-linked immunosorbent assay (ELISA). Our patient, however, tested negative for anti-PF4. To our knowledge, this is the first reported case of Janssen vaccine-associated cerebral venous sinus thrombosis without thrombotic thrombocytopenia syndrome.

As the number of patients who receive COVID-19 vaccines increases worldwide, there should be a continued high index of suspicion for CVST in patients who present with headache or altered mental status after administration [1], despite normal platelet levels.

Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient. A copy of the consent form is available for review by the Editor of this journal.

Abbreviations

FDA, Food and Drug Administration; CVST, Cerebral Venous Sinus Thrombosis; TTS, Thrombotic 1Thrombocytopenia Syndrome; DVT, Deep Venous Thrombosis; CDC, Centers for Disease Control; Anti-PF4, Platelet Factor 4 antibody; HIT, Heparin-induced Thrombocytopenia

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Declarations of Interest

No relevant relationships.

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