Case Report

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Cerebral venous sinus thrombosis associated with vaccine-induced thrombotic thrombocytopenia

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Abstract

Thrombosis-thrombocytopenia syndrome and cerebral venous sinus thrombosis have been rarely reported in patients who have received severe acute respiratory syndrome coronavirus 2 adenoviral vector vaccines. Awareness of this potential adverse effect, recognizing early clinical symptoms and subtle signs of cerebral venous sinus thrombosis on head computed tomography and brain magnetic resonance imaging, appropriate vascular imaging, and unique treatment for this condition is critical. This is a report of a case of vaccine-induced thrombotic thrombocytopenia and associated cerebral venous sinus thrombosis with emphasis on imaging and clinical course.

Keywords

SARS-CoV-2, COVID-19, vaccine, thrombosis thrombocytopenia, dural venous sinus thrombosis, CT venography, magnetic resonance venography

Introduction

There have been recent reports of a rare occurrence of cerebral venous sinus thrombosis (CVST) associated with thrombocytopenia in patients who have received severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) adenoviral vector vaccines including Ad26.COV2.S (Janssen) coronavirus disease 2019 (COVID-19) vaccine in the United States[1,2] or ChAdOx1nCoV-19 (AstraZeneca)[2] vaccination[3,4] in Europe. In the USA, the initial report of six reports of CVST with thrombocytopenia following 6.86 million doses administered (0.87 cases per million doses administered) resulted in pausing immunization using Jensen vaccine on 13 April which was later lifted on 23 April 2021, with a total 15 cases reported.[5] Both vaccines carry replication-incompetent adenoviral vectors encoding the spike glycoprotein on SARS-CoV-2. Patients are reported to have high levels of antibodies to platelet factor 4 (PF4)–polyanion complexes 1–3 as a result of auto-antibody production to the leaked DNA bound to PF4.[6]

Signs and symptoms of CVST include headache or increased intracranial pressure, focal neurological deficits, encephalopathy, or cranial neuropathies.[7] About 90% of patients present with headaches. Focal neurological deficits depend on the location of the brain involved and include hemiparesis, aphasia, and visual loss.[7] These clinical presentations often prompt clinicians initially to order a head computed tomography (CT) or brain magnetic resonance imaging (MRI). Radiologists need to pay attention to early imaging signs of cerebral venous sinus thrombosis for timely diagnosis and treatment.

Case

A woman in her 30s developed headaches 10 days after receiving Ad26.COV2.S Janssen vaccine followed by thrombocytopenia (platelet $80 \times 10^3/\mu L$) and worsening head and neck pain 15 days after vaccination. Head CT (Figure 1(a)) was negative for acute infarct or hemorrhage but demonstrated subtle increased density of the right transverse and sigmoid sinuses suspicious for dural venous sinus thrombosis. A week later, she developed left lower extremity pain and weakness. Duplex ultrasound demonstrated acute deep venous thrombosis involving posterior tibialis and popliteal veins. Magnetic resonance venography (Figure 1(b)) and CT venography (Figure 1(c)) performed demonstrated a large near occlusive thrombus in the right transverse sinus extending to the right sigmoid sinus and jugular bulb ('empty delta sign'). A direct

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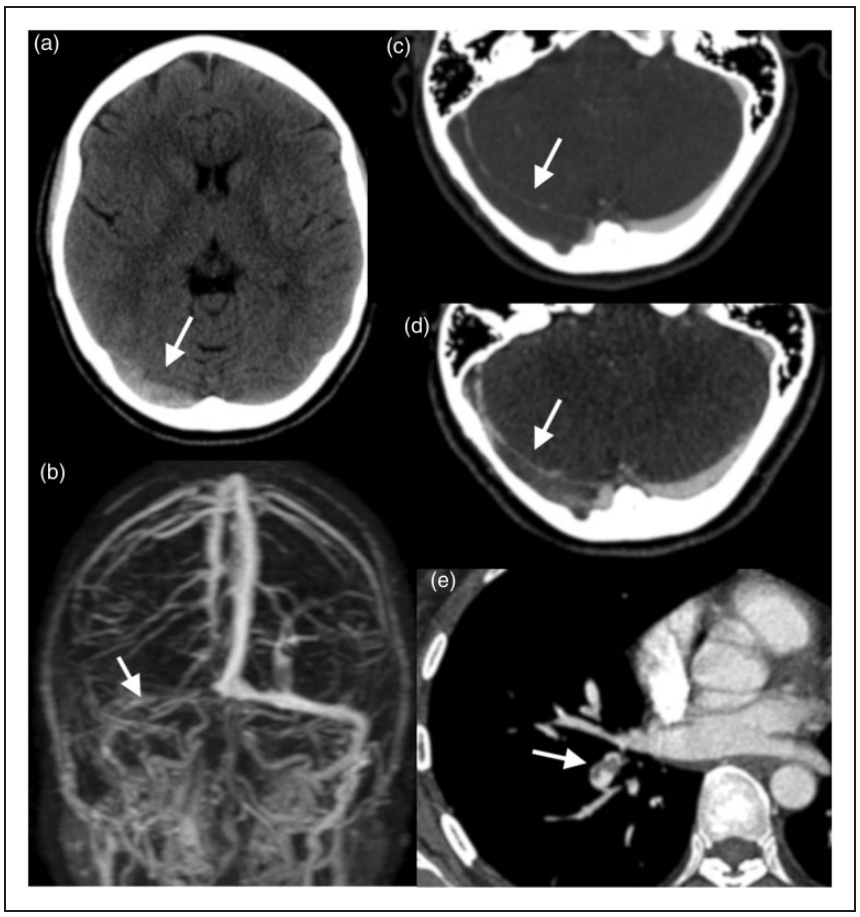

Figure 1. Images illustrating cerebral and pulmonary venous thrombosis. Axial non-contrast computed tomography (CT) examination of the head. (a) Subtle increased density in the right transverse and sigmoid sinuses. Magnetic resonance venography (b) and CT venography (c) demonstrate large near occlusive thrombus involving the right transverse and sigmoid sinuses extending to the jugular bulb. CT venography (d) following treatment demonstrates improvement in clot burden. CT angiography of the chest (e) illustrates right-sided subsegmental pulmonary emboli.

thrombin inhibitor (argatroban) was initiated and the patient was transferred to a tertiary care center with the clinical diagnosis of vaccine-induced thrombotic thrombocytopenia (VITT). On admission, the platelet count had improved to $143 \times 10^3/\mu L$. Heparin PF4-IgG (immunoglobulin G) antibody was positive. The patient received bivalirudin with a rise of the platelet count to $180 \times 10^3/\mu L$ and improvement in headache. Intravenous immunoglobulin was not given due to the improvement in platelet count. The patient was discharged home on apixaban.

One week later, she developed chest pain and CT angiography of the chest demonstrated subsegmental pulmonary emboli (Figure 1(e)) with no heart strain. Duplex ultrasound showed resolution of left popliteal vein thrombosis suggestive of clot embolization. Repeat CT venogram demonstrated improvement in dural venous sinus thrombosis with a decrease in clot burden (Figure 1(d)). The patient was instructed to continue apixaban.

Discussion

In this report, we described the imaging and clinical course of a rare case of CVST associated with VITT. Clinicians need to be aware of this rare adverse event and on the look out for severe headaches or new neurological symptoms, backache, severe abdominal pain, shortness of breath, leg swelling, or petechiae after Jansen vaccine administration.[6] Radiologists need to be aware of early signs of CVST on initial CT or MRI of the head, which are often performed as the first diagnostic imaging examinations. Although non-contrast CT of the head is often not sensitive for detection of CVST, increased attenuation (>70 Hounsfield units (HUs)) of the thrombosed vein/sinus is a reliable sign that warrants further imaging. This leads to the 'dense triangle sign' and 'cord sign' in cases of dural venous sinus and cortical venous sinus thrombosis, respectively.[8] Expansion or convex margins of sinuses, focal asymmetry, or increased density of the dural venous sinuses or cortical veins should raise the suspicion for CVST.[8] Other detectable complications include edema of the brain parenchyma, venous infarct and hemorrhage. Cerebral infarcts in a non-arterial distribution also warrant further vascular imaging.

Findings suggestive of CVST on routine MRI brain include an absence of expected flow void on T2 weighted imaging, presence of T1 hyperintensity related to a

subacute thrombus, and hypointensity on gradient echo T2* weighted imaging or susceptibility-weighted imaging. CT venography, contrast-enhanced magnetic resonance venography, or volumetric high-resolution gradient echo T1 post-contrast imaging of the brain have a high sensitivity for detecting CVST8 and differentiating it from its mimics such as arachnoid granulations. A catheter angiogram is rarely needed for diagnosis.

Additional recommended work-up includes complete blood count with platelet count, a prothrombin time, partial thromboplastin time, fibrinogen, D-dimer, and a PF4 antibody enzyme-linked immunosorbent assay (ELISA). If the PF4 antibody is positive or is unable to obtain, treatment with non-heparin anticoagulants and high-dose intravenous immune globulin should be considered.[6] Anticoagulation follows guidelines for heparin-induced thrombocytopenia-associated thrombosis, which includes non-heparin anticoagulants such as argatroban, bivalirudin, danaparoid, fondaparinux, or a direct oral anticoagulant at therapeutic anticoagulant dose intensity. Anticoagulation is recommended even in the presence of secondary intracranial hemorrhage to block the progression of thrombosis. All cases of thrombosis after a COVID-19 vaccine should be reported to the US Department of Health and Human Services vaccine adverse event reporting system.[7]

Conclusions

Thrombosis-thrombocytopenia syndrome (TTS) and CVST is a very rare adverse event in patients who have received SARS-CoV-2 adenoviral vector vaccines. Radiologists need to be aware of early signs of CVST on routine imaging of the brain and raise suspicion for this rare entity. Clinical work-up includes measurement of anti-PF4 antibody and treatment excludes heparin products.

Conflict of interest

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