



CASE STUDY

Cerebral venous sinus thrombosis associated with thrombocytopenia after the second dose of Chadox1 nCov-19 vaccination

Sagar R. Bhimani ^a, Harsha D. Makwana ^{b,*}, Supriya D. Malhotra ^c

^a Resident Doctor, Department of Pharmacology, Smt. NHL Municipal Medical College, Ahmedabad, Gujarat, India

^b Professor, Department of Emergency Medicine, L.G AMC MET Medical College, Ahmedabad, Gujarat, India

^c Professor and Head, Department of Pharmacology, Smt. NHL Municipal Medical College, Ahmedabad, Gujarat, India

ARTICLE INFO ABSTRACT



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Introduction: Reports of cerebral venous sinus thrombosis (CVST) after vaccination against SARS-CoV-2 have raised safety concerns and an emerging mechanism termed vaccine-induced immune thrombotic thrombocytopenia (VITT) was identified.

Objective: We aimed to estimate the frequency of CVST and other cerebrovascular events after vaccination.

Case study: We describe the case of a young male, who developed severe thrombocytopenia and CVST following the second dose of the covid 19 vaccine. He presented with a headache, with subsequent rapid neurological deterioration. The patient was successfully treated and discharged with the stable condition after 09 days of admission. We attribute this Adverse Event following Immunization (AEFI) of thrombotic condition to the vaccine due to the remarkable temporal relationship.

Conclusions: The proposed mechanism of VITT is the production of rogue antibodies against platelet factor-4 resulting in massive platelet aggregation. Radiologists and physicians should be aware and pay attention to early imaging signs of cerebral venous sinus thrombosis for timely diagnosis and treatment.

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Introduction

Global vaccination against severe acute respiratory syndrome-coronavirus-2 (Sars-cov-2) has become a priority for mitigating the COVID-19 pandemic. A breakthrough in managing the COVID-19 pandemic was the development and administration of vaccines against SARS-CoV2. Typical side effects of these vaccines were reported in clinical trials with several thousands of

volunteers but without evidence of a vaccine-associated increase in thromboembolic events (Schulz *et al.*, 2021).

Intracranial venous sinus thrombosis (IVST) is a potentially life-threatening condition with an incidence of about 15 per million per year in western countries (Devasagayam *et al.*, 2016; Coutinho *et al.*, 2012). It is associated with various types of thrombophilia, systemic diseases, or local causes such as trauma and infection (Silvis *et al.*, 2017). Thrombotic thrombocytopenic purpura (TTP) is observed



* Corresponding Author

Harsha D. Makwana

E-mail: drharsham@gmail.com

Contact: +919825899205

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with an annual incidence of 1 per 1,000,000 and is a potential sequela, among others, of virus infection and vaccination (Joly *et al.*, 2017; Yavaşoğlu *et al.*, 2020).

Signs and symptoms of CVST include headache, increased intracranial pressure, focal neurological deficits, encephalopathy, or cranial neuropathies (Furie *et al.*, 2021). 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 (Furie *et al.*, 2021). These clinical presentations often prompt clinicians initially to order a head computed tomography (CT) or brain magnetic resonance imaging (MRI).

Clinicians must be alerted to the emergence of such AEFI events to facilitate appropriate management. Patients presenting with CVST features and thrombocytopenia post-vaccination should undergo platelet factor 4 (PF4) antibody testing and be managed similarly as Heparin-induced thrombocytopenia (HIT), in particular avoiding heparin and platelet transfusions in case of positive PF4 antibody testing.

Here we describe a case report of an immediate complication in the form of cerebral venous sinus thrombosis after the second dose of the adenovirus-vector vaccines ChAdOx1 nCov-19 (Oxford-AstraZeneca) available in India branded as COVISHIELD with emphasis on the possible pathophysiology behind this complication.

Case Details

A 44 years old male patient was brought to the Emergency Medicine Department of a tertiary care hospital with complaints of severe headache for 5 days and nausea for 5

days. The patient was relatively asymptomatic before 5 days than he had complaints of tingling sensations over both arms, severe throbbing headaches on the occipital, b/l parietal region associated with nausea for 5 days. The patient was shifted to a private hospital for the same where a patient was managed conservatively.

The patient was Shifted to our hospital on the 9th day of his presenting complaints. No history of vomiting, neck rigidity, fever, cough, difficulty in breathing, altered sensorium, no focal neurological deficit. No history of fever, diarrhea, burning micturition, or alcohol intake. No history of DM, HTN, TB, or any surgical history. No history of any concomitant drug uses and no history of Covid-19 infection in past.

The patient took 2nd dose of ChAdOx1 nCov-19 (COVISHIELD) vaccine 10 days before admission. After 5 days of the last dose of the covid-19 vaccine, the patient developed the above-mentioned complaints.

On admission, the patient was conscious and oriented. The temperature was 96.4 F, BP-132/84 mmHg, RR-24/min, pulse-84/min, and SPO2-98% on room air. His investigations on the day of admission were as follows: Hb: 15.5 g/dl, WBC: 12053 cells/cumm, platelets: 94,000 cells/cumm, Creatinine: 0.86 mg/dL, Urea: 16.9 mg/dl, SGPT: 28 U/L, SGOT: 26 U/L, ALP: 117 U/L, Albumin: 4.5 g/dl, Prothrombin time (PT): 14.7 Second, activated partial thromboplastin time (aptt) plasma: 43.2 Second and D-dimer: 1.69 µg/ml (<0.5). Other investigations like Antinuclear Antibody and Anti Phospholipid Antibody were negative. Other relevant investigations and causes of thrombosis were conclusively ruled out. The platelet count during hospitalization was presented in **Figure 1**.

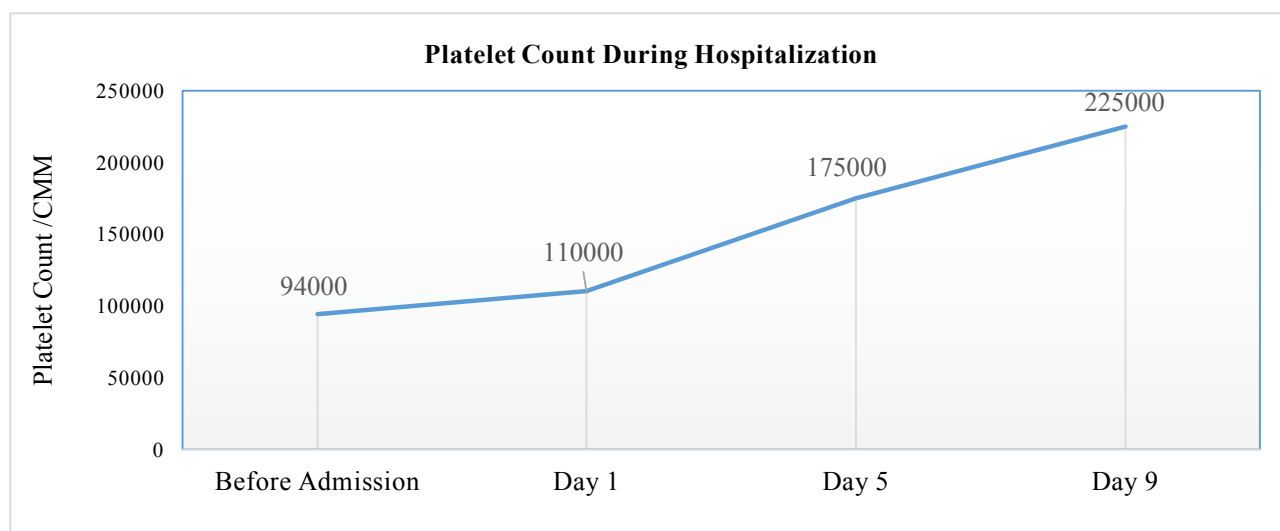


Figure 1: Trend of platelet count during Hospitalization shows improvement after initiation of treatment.

Radiological Investigation of MRI Brain and MR Venography report in **Figure 2**., shows "Multifocal patchy asymmetrical small acute hemorrhagic venous infarcts in

both high frontal lobes. Complete thrombosis of superior sagittal sinus left transverse and sigmoid venous sinuses. Partial to near-complete thrombosis of high transverse and

sigmoid venous sinuses. Bilateral high frontoparietal cortical vein thrombosis."

However, the patient was not tested for anti-PF4-antibodies. The patient tested negative for COVID-19 by Rapid Antigen Testing and RTPCR. Considering the temporal association, a probable diagnosis of vaccine-induced CVST was made.

He was treated with Injection of Mannitol 100 cc IV thrice a day, Injection of Pantoprazole 40 mg IV once a day,

Injection of Ondansetron 4 mg IV thrice a day, Injection LMWH 0.6 U SC twice a day, Tablet Levetiracetam 500 mg twice a day on the day of admission.

After conservative and symptomatic treatment patient's condition was improved. After 9 days of admission, the patient was discharged in hemodynamically and neurologically stable condition.

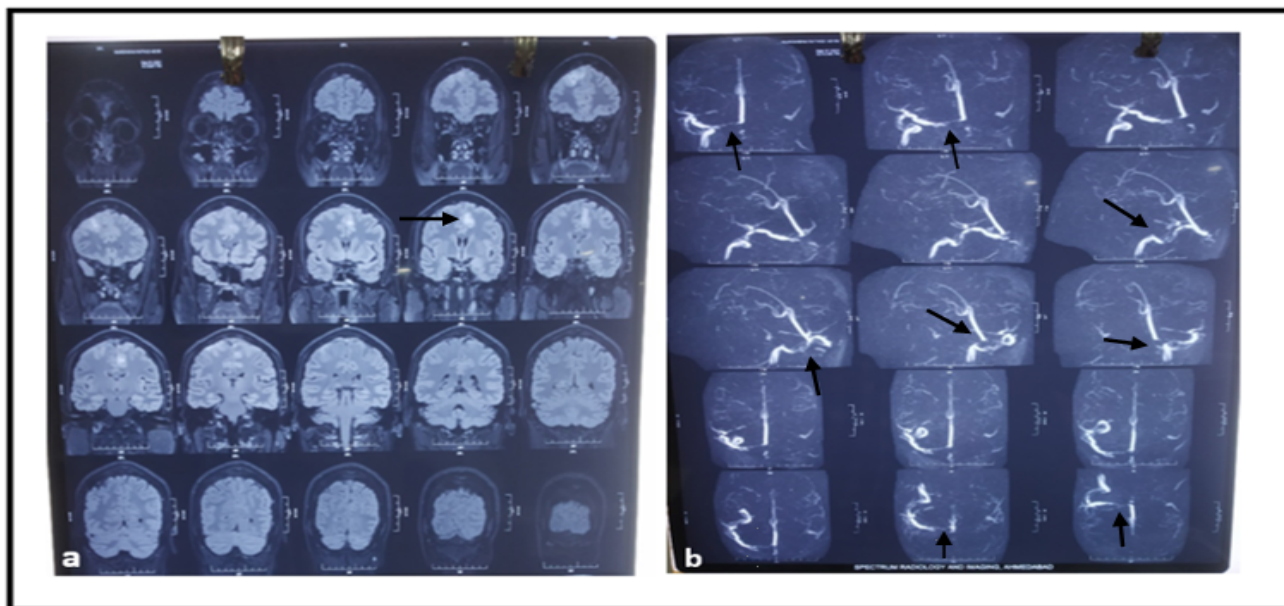


Figure 2: a) MRI Brain of the patient shows "Multifocal patchy asymmetrical small acute hemorrhagic venous infarcts in both high frontal lobes" b) MR Venography of the patient shows Complete thrombosis of superior sagittal sinus, left transverse and sigmoid venous sinuses. Partial to near-complete thrombosis of high transverse and sigmoid venous sinuses. Bilateral high frontoparietal cortical vein thrombosis.

Discussion

The COVID-19 pandemic is challenging the global public health and health care sectors in many ways. A rapid vaccination program is essential in helping to control the COVID-19 pandemic. Hence, it is vital that such COVID-19 vaccine-associated events, which at this stage appear to be very rare, are viewed through this lens. VITT is a newly emerging phenomenon with different COVID-19 vaccines. However, further studies are required to understand whether these antibodies are autoantibodies against PF4 induced by the strong inflammatory stimulus of vaccination or antibodies induced by the vaccine that cross-reacts with PF4 and platelets. In addition, mRNA vaccines have been linked with severe thrombocytopenia and bleeding (Nazy et al., 2021; Lee et al., 2021).

Cerebral venous sinus thrombosis (CVST) is a rare form of cerebrovascular disease. Symptoms are mostly neurological, as in the present case, including severe and persistent headache, blurred vision, vomiting, seizures, focal neurological deficits, and altered sensorium. CVST

with thrombocytopenia was entirely unexpected as a much rarer complication associated with certain types of COVID-19 vaccination

We present a case of cerebral venous thrombosis and concomitant thrombocytopenia in a young healthy adult male within 5 days from vaccination against SARS-CoV-2 with ChAdOx1 nCov-19 Vaccine. We were unable to identify other causes of the CVST. In this case, the temporal relation between the vaccination and the onset of CVST suggests that the events were associated. Considering the temporal association and potential thrombotic potential of ChAdOx1 nCoV-19 (COVISHIELD) vaccine, a probable diagnosis of vaccine-induced CVST was made.

The mechanism of thrombosis is that the viral proteins and free DNA in the vaccine bind to PF4 to generate a neoantigen that subsequently leads to the development of antibodies against PF4 which activate platelets aggregation and promotes clotting (Scully et al., 2021).

Several cases of CVST following immunization with the First dose of adenovirus-vector vaccines ChAdOx1 nCoV-

19 (Oxford-AstraZeneca) and Ad26.COV2.S (Janssen/J&J) has been reported globally (Wise et al., 2021).

Only 1 report to date documents possible VITT after the second dose of the mRNA-1273 vaccine globally (Sangli et al., 2021). Herein, we report a case of CVST following immunization with a second dose of ChAdOx1 nCov-19 vaccine in an Indian male without any pre-existing comorbidities. This is arguably the first report of such kind from India.

Conclusions

The report presents a rare occurrence of thrombotic thrombocytopenia after the second dose of the covid-19 vaccine. We attribute this thrombotic condition to the vaccine due to the remarkable temporal relationship. The proposed mechanism of VITT is the production of rogue antibodies against platelet factor-4 resulting in massive platelet aggregation and clotting. The case should alert healthcare providers to the possibility of such precipitously fatal complications while vaccine recipients should be warned about the symptoms of VITT.

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None

Conflict of interest

None

Ethical approval

Not Applicable

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