CASE REPORT

Case of Suspected SARS-CoV-2 Vaccine-induced Immune Thrombotic Thrombocytopenia: Dilemma for Organ Donation

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Abstract

Several vaccines were developed and rolled out at an unprecedented rate in response to the coronavirus disease-2019 (COVID-19) pandemic. Most vaccines approved globally by WHO for emergency use to combat the pandemic were deemed remarkably effective and safe. Despite the safety, rare incidences of vaccine-induced thrombosis and thrombocytopenia (VITT), sometimes known as vaccine-induced prothrombotic thrombocytopenia (VIPIT), have been reported. We report a case of young female with prothrombotic conditions and suspected VITT who developed catastrophic cerebral venous sinus thrombosis (CVST) and progressed to brain death. We highlight hurdles of organ retrieval from a brain-dead patient with suspected SARS-CoV-2 vaccine-induced immune thrombotic thrombocytopenia. There is limited data and lack of substantial evidence regarding transplantation of organs from brain-dead patients with suspected VITT.

Keywords: Cerebral venous sinus thrombosis, COVID vaccine, Organ donation, PF4 antibody, Thrombocytopenia, Vaccine-induced prothrombotic immune thrombocytopenia (VIPIT), Vaccine-induced thrombotic thrombocytopenia (VITT).

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Introduction

Vaccines have been implicated in the development of autoimmune effects. Cases with arthritis, vasculitis, Guillain–Barre syndrome, and thrombocytopenia have been reported.[1]

Amidst global vaccination drive to contain the pandemic of coronavirus disease-2019 (COVID-19), there have been few case reports of thrombosis at unusual sites and thrombocytopenia. Clinical sequelae have been reported in a few patients and typically occur between 4 and 28 days after vaccination with the ChAdOx1 nCoV-19 vaccine.[2]

Shortly after the injection of the AstraZeneca (ChAdOx1 nCov19) COVID-19 vaccine, very rare episodes of thrombosis at uncommon sites, primarily cerebral or sinus vein thrombosis (CVT), accompanying thrombocytopenia have been described.[3]

This rare disorder resembles heparin-induced thrombocytopenia (HIT) with production of autoantibody against platelet factor 4 (PF4).[4]

We report a case of suspected SARS-CoV-2 vaccine-induced immune thrombotic thrombocytopenia (VITT) with catastrophic cortical venous sinus thrombosis 18 days after the first dose of COVID AstraZeneca vaccine. The patient deteriorated neurologically despite intensive care management and progressed to brain death. Legal authorized relative of patient wished and consented for organ donation. Patient was maintained in neurocritical care, and multidisciplinary opinion was sought to prepare the patient as deceased organ donor. There is scarcity of data and consensus regarding safety of organ donation from deceased donor with suspected VITT. We contacted Regional Organ and Tissue Transplant Organization (ROTTO) regarding organ retrieval before initiating organ transplant. Organ retrieval was differed. However, we took the kidney and liver biopsy from deceased donor. Follow-up liver and kidney biopsy report did not show lymphocyte burden. Suitability standards for organ donation change over time and are influenced by the receiver's circumstances.[5]

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Our finding implies denying patient with suspected VITT may have a negative impact on lifesaving procedures like organ transplantation. Evidence-based medicine (EBM) is designed to assist doctors in providing the best possible treatment to their patients.[6] Present case highlights the need for new local and national clear guidelines to be set for transplantation of organs from brain-dead patients with suspected VITT.

Case Description

A 24-year-old young female presented to the emergency department with a history of headache, nausea, and vomiting followed by one episode of seizure. She had a past drug history of regular intake of oral contraceptive pills for menstrual irregularities. She underwent basic blood investigations and underwent computed tomography (CT) brain venography after stabilization

and airway management. Clinical and abnormal laboratory parameters were noted as shown in Table 1.

Patient was observed in the neurointensive care and treated conservatively. Patient also gave pertinent history of vaccination by AstraZeneca (Covishield vaccination) 18 days prior. Hematologist opinion was sought, and antiplatelet factor 4 (PF4) antibody was sent in view of suspicion of VITT. She was treated with IVIG 70 g on day 3 of admission due to persistent thrombocytopenia (Fig. 1).

Despite treatment, the patient's clinical condition deteriorated with a drop in GCS and seizure episode. She needed intubation and ventilation. Repeat CT scan brain showed hemorrhagic transformation (Fig. 2).

Emergent DSA with mechanical thrombectomy was attempted with no clinical and neurological improvement. Catastrophic hemorrhagic transformation in the frontal area led to progressive brain death with absent brainstem reflexes and a positive apnea test.

Patient was maintained in neurocritical care, and multidisciplinary opinion was sought to prepare the patient as a deceased organ donor after consent and wish of legally authorized relatives. Organ donation was differed as per advised by the ROTTO in the best interest of recipient safety. We took the tissue biopsy from solid organs liver and kidney in view of suspicion of VITT.

Table 1: Patient characteristics and abnormal laboratory parameters

Age (year)	24	
Sex	Female	
Preexisting condition	None	
Medication on admission	Contraceptive pills for menstrual disorder	
Symptoms	Seizure	
Time from vaccination to admission	18 days	
Finding of CT venography on admission	Cortical venous sinus thrombosis and cerebral edema	
Location of thrombosis found	Cortical venous sinus thrombosis and portal vein thrombosis on USG Doppler	
Platelet count—nadir	22×10^3/µL	Ref range ($150–450 \times 10^3$/µL)
D-dimer peak	924 ng/mL	up to 243 ng/mL
INR peak	1.48	1–1.5
aPTT	33.2 seconds	25–36′ seconds
Fibrinogen nadir	72 mg/dL	150–450
Collagen vascular workup	n/RNP/Sm positive	
ELISA PF4 antibody test	Negative	
Anticoagulation treatment	LMWH (low-molecular weight heparin)	
Other treatment	DSA with thrombus extraction	
Liver and kidney biopsy report	Normal (no lymphocyte burden)	
Outcome	Fatal	

Discussion

Cortical venous sinus thrombosis is often the cause of stroke in age-group 20–50 year. It is more common in women than men.[7]

Prevalence of CVT is 54% in patient with oral contraceptive and 1% in patient with systemic lupus erythematosus (SLE) as a risk factor.[8]

Apart from the presence of above risk factors, the young female reported in present case had additional history of vaccination with AstraZeneca (ChAdOx1 nCov19). Pathogenic mechanisms of CVT after vaccination against SARS-CoV-2 related to other associated risk factors/associated conditions (e.g., contraceptives, genetic or acquired thrombophilia, ear/sinus infections, cancer, Behçet's disease).[9]

Vaccination-induced immune thrombotic thrombocytopenia (VITT) with cases of atypical thrombosis and thrombocytopenia may occur after immunization with the adenoviral vector-based COVID-19 vaccine. Although the reported incidence is still very low, the absolute risk of CVT was estimated to be low (5 per million vaccinated individuals) and has no bearing on the overall benefit of vaccination. VITT can be debilitating or even fatal if left untreated.

Patient in the present case was vaccinated 18 days prior to admission in the intensive care unit. She had thrombocytopenia (platelet count—22×10^3) and seizures with brain imaging findings suggestive of cortical venous sinus thrombosis. The rare adverse event of VITT is suspected with history of symptoms of thrombosis and bleeding inclusive of but not limited to persistent and severe headache, focal neurological symptoms, seizures seen in present case with time period of onset between 4 and 28 days of

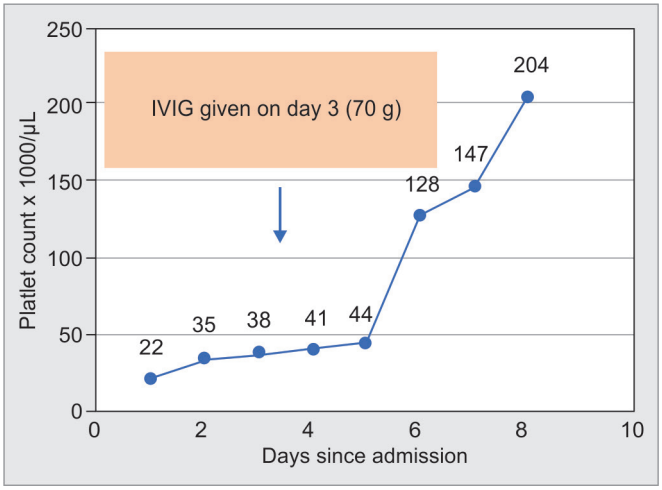


Fig. 1: Platelet trends since admission

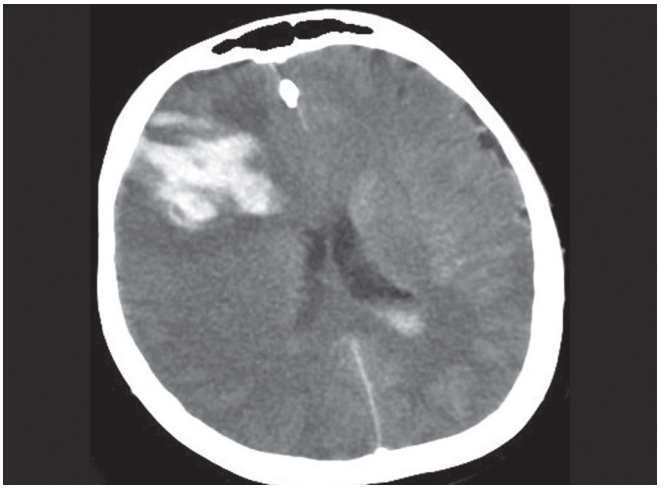
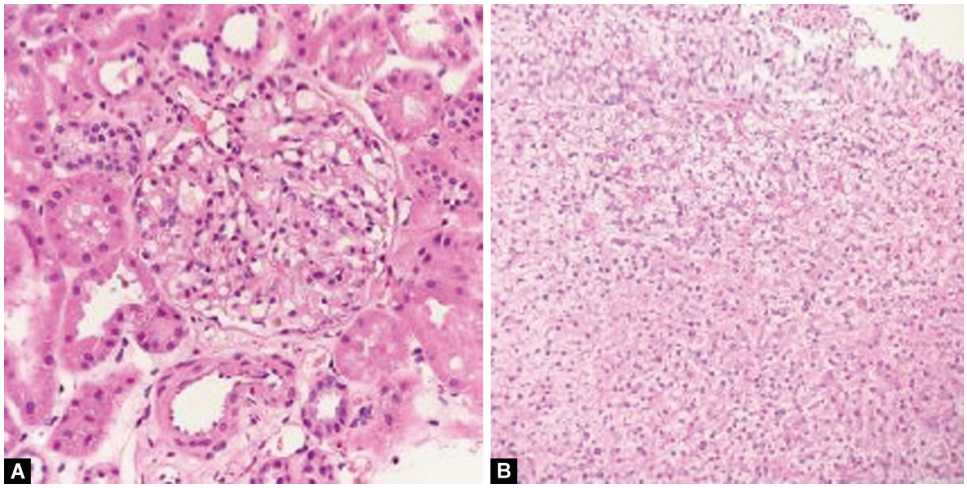


Fig. 2: Follow-up CT scan—brain



Figs 3A and B: Tissue biopsy—liver and kidney

vaccination, low platelet count on initial CBC, and imaging finding of blood clot.[10]

On the basis of both clinical and serologic evidence, VITT closely resembles autoimmune heparin-induced thrombocytopenia (HIT).[10]

Hematologist consultation is advocated/was sought, and PF4 antibody (ELISA) was sent in present case.

Case fatality rate in reported case of CVT with VITT is more than mortality reported in patient with CVT from pre-COVID era.[11]

To the best of our knowledge, till date, other than the UK experience of organ donation following possible VITT diagnosis, there are no other published case reports or case series describing such outcomes.[12]

VITT is caused by an autoimmune reaction that might cause a comparable reaction in a naïve receiver. We differed organ donation in patient reported after sharing case information and suspicion of VITT with ROTTO. Our patient liver and kidney biopsy reports were normal (Fig. 3).

The appropriateness of tissue biopsy to stratify risk and graft survival in recipient is not documented in suspected cases of VITT as deceased donor. Organs from case of VITT present with high passenger lymphocyte burden. Transplant of such organs (e.g., liver, lung, small bowel, and pancreas) has a potential of transmitting immune cells that could trigger a similar autoimmune phenomenon in naive recipient passenger lymphocyte syndrome (PLS), so safety of organ donation from deceased donor with VITT is not established.[13]

We conclude that in view of lack of substantial evidence, brain-death patient with suspected VITT adds hurdle to the organ donation program. It may have a negative impact on lifesaving program like organ transplantation. We infer that new local and national guideline to be set as per emerging data before denying using these organs. Thorough review with (multidisciplinary team) judgment on risks versus benefits, as well as detailed informed patient (recipient) consent and follow-up, is suggested to prevent its impact on already scared national organ donation drive.

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References

1. Bereau M. Vaccination and induction of autoimmune diseases. Inflamm Allergy Drug Targets 2015;14(2):94–98. DOI: 10.2174/1871528114666160105113046.
2. Chen PW, Tsai ZY, Chao TH, Li YH, Hou CJ, Liu PY. Addressing vaccine-induced immune thrombotic thrombocytopenia (VITT) following COVID-19 vaccination: a mini-review of practical strategies. Acta Cardiol Sin 2021;37(4):355. DOI: 10.6515/ACS.202107_37(4).20210628A.
3. Franchini M, Liumbruno GM, Pezzo M. COVID-19 vaccine-associated immune thrombosis and thrombocytopenia (VITT): diagnostic and therapeutic recommendations for a new syndrome. Eur J Haematol 2021;107(2):173–180. DOI: 10.1111/ejh.13665.
4. Dotan A, Shoenfeld Y. Perspectives on vaccine induced thrombotic thrombocytopenia. J Autoimmun 2021;121:102663. DOI: 10.1016/j.jaut.2021.102663.
5. Pandit RA, Zirpe KG, Gurav SK, Kulkarni AP, Karnath S, Govil D, et al. Management of potential organ donor: Indian Society of Critical Care Medicine: position statement. Indian J Crit Care Med 2017;21(5):303–316. DOI: 10.4103/ijccm.IJCCM_160_17.
6. Kulkarni AP. Let there be guidance!!! Indian J Crit Care Med 2020;24(Suppl 1):S1. DOI: 10.5005/jp-journals-10071-G23181.
7. Silvis SM, De Sousa DA, Ferro JM, Coutinho JM. Cerebral venous thrombosis. Nat Rev Neurol 2017;13(9):555–565. DOI: 10.1038/nrneurol.2017.104.
8. Ferro JM, Canhão P, Stam J, Bousser MG, Barinagarrementeria F. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). Stroke 2004;35(3):664–670. DOI: 10.1161/01.STR.0000117571.76197.26.
9. Ferro JM, Sousa DA, Coutinho JM, Martinelli I. European stroke organization interim expert opinion on cerebral venous thrombosis occurring after SARS-CoV-2 vaccination. Eur Stroke J 2021:23969873211030842. DOI: 10.1177/23969873211030842.
10. Pai M, Chan B, Stall NM, Grill A, Ivers N, Maltsev A, et al. Vaccine-induced immune thrombotic thrombocytopenia (VITT) following adenovirus vector COVID-19 vaccination. Science Briefs of the Ontario COVID-19 Science Advisory Table. Infect Dis Clin Care 2021;2(17):1–7. DOI: 10.47326/ocsat.2021.02.17.2.0.
11. Duman T, Uluduz D, Midi I, Bektas H, Kablan Y, Goksel BK, et al. A multicenter study of 1144 patients with cerebral venous thrombosis: the VENOST study. J Stroke Cerebrovasc Dis 2017;26(8):1848–1857. DOI: 10.1016/j.jstrokecerebrovasdis.2017.04.020.

12. UK Donor VITT Transplant Study Group, Greenhall GHB, Ushiro-Lumb I, Pavord S, Currie I, Perera MTPR, et al. Organ transplantation from deceased donors with vaccine-induced thrombosis and thrombocytopenia. Am J Transplant 2021:10.1111/ajt.16735. DOI: 10.1111/ajt.16735.

13. Greenhall GH, Ushiro-Lumb I, Pavord S, Currie I, Perera MT, Hartog H, et al. Organ transplantation from deceased donors with vaccine-induced thrombosis and thrombocytopenia. Am J Transplant 2021. DOI: 10.1111/ajt.16735.