Case report

Intracerebral haemorrhage due to vaccine-induced immune thrombocytopenia and thrombosis

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Introduction

Vaccine-induced Immune thrombocytopenia and thrombosis (VITT) is a rare complication following vaccination with the ChAdOx1 nCov-19 [recombinant adenoviral vector encoding the spike protein antigen of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)]. VITT has been reported in several countries and there are no published reports of this entity from Sri Lanka[1]. We report a case of VITT causing fatal intra-cerebral haemorrhage (ICH) following ChAdOx1 nCov-19 vaccination.

Case report

A 61-year-old housewife with a history of type 2 diabetes mellitus and dyslipidaemia presented with right face, arm and leg weakness and slurred speech on waking up from bed. She was last known to be well 6 hours ago. She was administered SARS-CoV-2 adenoviral vector vaccine two weeks ago after which she developed mild fever and headache which resolved in four days.

On examination she was conscious and rational, pulse 88 per minute and regular, blood pressure 160/95 and had right hemiparesis and dysarthria. Non-contrast CT brain done on admission was normal (Figure 1). She was not thrombolysed as the time of onset of stroke was uncertain. Antiplatelets and statin therapy was initiated.

Twelve hours following the admission she developed generalized tonic-clonic seizures and the Glasgow coma scale (GCS) dropped to 8/15. Non contrast CT brain was repeated following seizures and revealed left intra-cerebral and intraventricular haemorrhage (Figure 2). Laboratory investigations are summarized in Table 1.

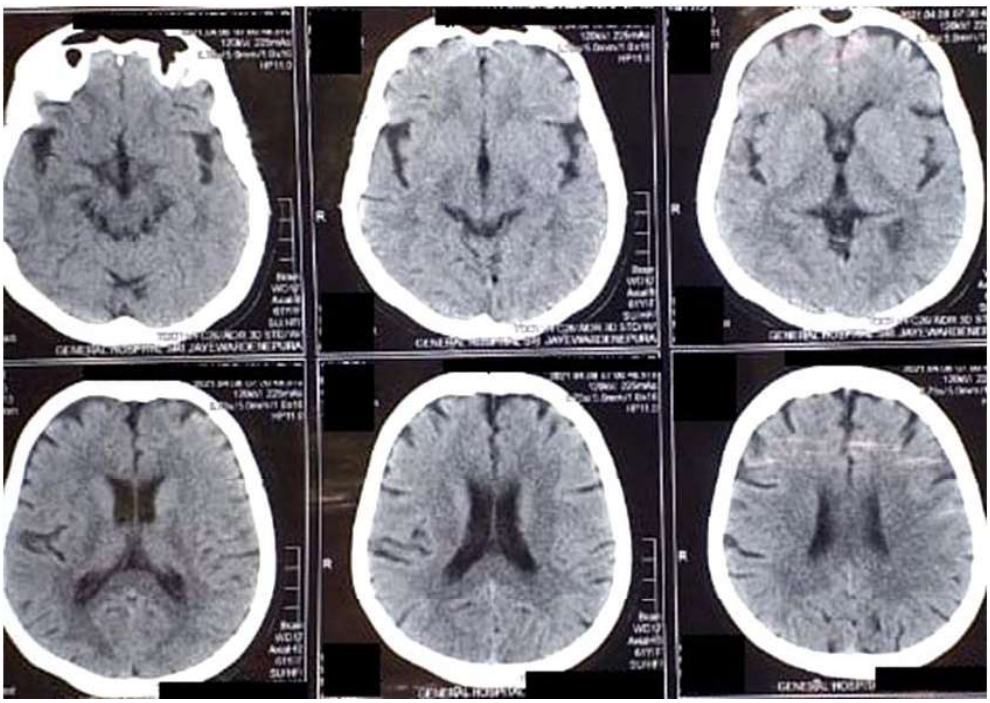

Figure 1. Normal non-contrast CT of brain on admission.

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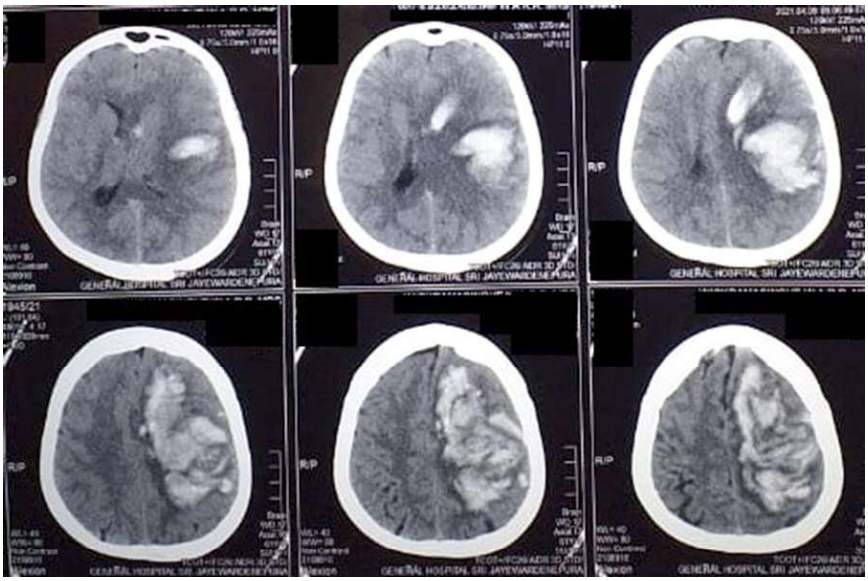

Figure 2. Non-contrast CT of brain at 12 hours after admission showing large intra-cerebral and intraventricular haemorrhage on the left side.

Table 1. Summary of laboratory investigations on day 1 and day 2 after admission

Laboratory Analysis	*Reference value*	*Day 1*	*Day 2*
Haemoglobin (g/dl)	11.0-16.0	13.4	7.7
Platelet count (10^3/ul)	150-400	55	27
Leucocytes (10^3/ul)	4.00-11.00	10.2	15.4
APTT(s)	22-36	26	39.9
PT(s)	12-15	11.5	17.3
TT(s)	15-21	18.8	26.5
D-Dimer (ng/ml)	<550	>10,000	N/A
Creatinine (umol/l)	51-106	72	93
CRP (mg/dl)	<6	18	26
Dengue Antigen		Negative	N/A
Dengue Antibodies		IgM negative	
IgG positive	N/A		

Antiplatelet therapy was withheld and urgent neurosurgical referral was done. She was transferred to neurosurgical intensive care unit where she was intubated and ventilated. Craniotomy was not performed due to severe coagulopathy. An external ventricular drain was placed after correction of coagulopathy with cryoprecipitate and fresh frozen plasma. It was planned to initiate intravenous immunoglobulin. However, her GCS dropped to 3/15 with haemodynamic instability and died on 2nd day of admission.

Table 2. Diagnostic criteria for VITT (2)

Type of VITT	*Description*
Definite VITT	All five of the following criteria. 1. Onset of symptoms 5-30 days after vaccination against SARS-CoV-2 2. Presence of thrombosis 3. Thrombocytopaenia (platelet count <150,000/mm^3) 4. D-dimer level >4000 FEU 5. Positive anti-PF4 antibodies on ELISA
Probable VITT	D-dimer level > 4000 FEU but one criterion not met (timing, thrombosis, thrombocytopaenia or anti-PF4 antibodies)
Possible VITT	D-dimer level unknown or 2000-4000 FEU with one other criterion not met or two criteria not met.

(FEU = Fibrinogen equivalent units)

Discussion

VITT is an immune thrombocytopaenia and thrombosis mediated by platelet activating antibodies against platelet factor – 4 (PF-4) and presents 5-30 days after vaccination[2]. Diagnostic criteria of VITT are given in table 2. This patient fulfilled the diagnostic criteria for probable VITT. VITT commonly causes intracranial or extracranial venous thrombosis. In one of the largest case series studied, 42 out of 220 patients had intracranial haemorrhage secondary to venous thrombosis[2]. Intracerebral haemorrhage in this patient was most likely secondary to cerebral vein thrombosis (resulting in 18-fold rise in d-dimer level) coupled with severe thrombocytopaenia. Antiplatelet therapy at admission would have contributed.

Treatment of VITT remains uncertain. Use of IV Immunoglobulin 1g/kg for 2 days has been used to raise the platelet count and reduce hypercoagulability (2-4). Heparin-based anticoagulants and warfarin should be avoided. Direct oral Xa inhibitors, and direct thrombin inhibitors can be used in the absence of bleeding. Platelet transfusions should be avoided except in the presence of major bleeding. The mortality is higher among patients with a platelet count of <30,000 per cubic millimeter, cerebral venous sinus thrombosis and intracranial haemorrhage. Plasma exchange can be used in patients with platelet count of <30,000 per cubic millimeter and intracranial haemorrhage. Overall case-fatality rate was 22% which increases to 73% in patients with a platelet count less than 30,000/mm^3 and intracranial haemorrhage.

Key Points

- VITT is a rare but a serious complication of ChAdOx1 nCov-19 vaccination.
- VITT is an immune thrombocytopaenia and thrombosis mediated by anti-PF-4 antibodies.
- VITT should be suspected in any patient with symptoms of a stroke presenting 5-30 days after vaccination for COVID-19.
- Antiplatelet drugs, warfarin and heparin-based anticoagulants should be avoided if VITT is suspected and until a diagnosis of VITT is safely excluded.
- Treatment of VITT remains uncertain.

References

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