Case Report

A case of ischemic stroke and transient thrombocytopenia in a young female following adenoviral vector-based COVID-19 vaccination: Was the association incidental or causal?

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Abstract

Since March 2021, cases with unusual clots, particularly cerebral venous sinus thrombosis and splanchnic vein thrombosis, have been reported worldwide following adenoviral vector-based coronavirus disease 2019 (COVID-19) vaccination. This entity has been termed vaccine-induced thrombotic thrombocytopenia (VITT). We report a 23-year-old healthy female who developed seizures, altered sensorium, and left hemiparesis, 20 days after receiving the first dose of adenoviral vector-based COVID-19 vaccine "Covishield™." The patient had transient thrombocytopenia. The D-dimer level was 2460 ng/mL. Magnetic resonance imaging (MRI) demonstrated occlusion of M2 segment of the middle cerebral artery and cerebral infarction. Platelet factor-4 antibodies level was normal. Treatment with aspirin and antiepileptic drugs resulted in a remarkable recovery. This is the first Indian case report of ischemic stroke and transient thrombocytopenia following SARS-CoV-2 ChAdOx1 nCoV-19 vaccination. Our case had clinical features consistent with the diagnosis of probable VITT. Familiarity with VITT is crucial because timely treatment with non-heparin anticoagulants and intravenous immunoglobulin improves the outcome.

Keywords: Cerebral Infarction, cerebral venous thrombosis, platelet factor-4, vaccine-induced thrombotic thrombocytopenia

Introduction

In January, India granted restricted emergency approval for two coronavirus disease 2019 (COVID-19) virus vaccines. These vaccines include the recombinant chimpanzee adenovirus vector vaccine (Covishield) encoding the severe acute respiratory syndrome corona-virus 2 (SARS-CoV-2) spike (S) glycoprotein manufactured by the Serum Institute of India, Pune, and the whole-virion inactivated coronavirus vaccine (Covaxin) developed by the Indian Council of Medical Research and Bharat Biotech. In India, up to February 25, 2022, a total of 10,407,359,583 vaccine doses have been administered.[1]

Since March 2021, cases with unusual clots, particularly cases of cerebral venous sinus thrombosis and splanchnic vein thrombosis were recorded. The European Medicines Agency expert group reviewed 62 cases of cerebral venous sinus thrombosis and 24 cases of splanchnic vein thrombosis, which were reported in EudraVigilance (the European Union drug safety database). Eighteen of these cases succumbed to death.[2] Similar cases were also observed in the USA following another adenovector-based

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vaccine, "The Janssen Ad26.COV2.S COVID-19 vaccine." The US Food and Drug Administration temporarily suspended the use of the Janssen vaccine after reports of six cases of cerebral venous thrombosis with thrombocytopenia.[3] The Adverse Event Following the Immunization committee of the Government of India reported 26 cases of thromboembolic events, all following administration of the Covishield vaccine. The report recognized that there is a very minuscule, but definitive risk of thromboembolic events following Covishield vaccination.[4]

Venous thrombosis and thrombocytopenia following COVID-19 vaccination are recognized as vaccine-induced thrombotic thrombocytopenia (VITT). VITT is an autoimmune disorder that resembles heparin-induced thrombocytopenia in patients who have never been exposed to heparin. VITT has been reported following ChAdOx1 nCoV-19 (Oxford–AstraZeneca) recombinant adenoviral vector vaccine administration.[5] Adenoviral vector vaccines generate an immunological reaction against the vector component of the vaccine, resulting in heparin-induced thrombocytopenia syndrome. Adenoviral vector vaccine incites the production of autoantibodies against the platelet factor 4 (PF4) complex. Antibodies against PF4, in turn, trigger platelets to aggregate and subsequently form blood clots.[6] VITT is generally characterized by cerebral or systemic venous events. A current estimate indicates that about 1 in 50,000 persons below 50 years of age who receive the Oxford–AstraZeneca vaccine are likely to develop VITT.[7]

Cerebral venous thrombosis is a well-recognized manifestation of VITT; however, arterial involvement has infrequently been described. Here, we are reporting an Indian patient who had a major arterial event and had probable VITT.

Case Report

A 23-year-old healthy female had fever, lethargy, and headache along with pain at the injection site after having received the first dose of the adenoviral vector-based COVID-19 vaccine "Covishield™." Twenty days post-vaccination, she had multiple episodes of left focal seizures. The patient failed to respond to oral antiepileptic drugs and was subsequently referred to our Neurology Emergency. At admission, she was unconscious. Glasgow coma scale score was 10 (E2, V3, M5). Her blood pressure was 130/82 mmHg, and her pulse rate was 86 per minute. Cranial nerves and fundus examination were normal. Motor examination revealed left hemiparesis (motor power 3/5 on the medical research council (MRC) scale). The left plantar reflex was extensor. Cardiac evaluation, including electrocardiogram and echocardiogram, did not reveal any abnormality. Her hematological evaluation, done before emergency admission, revealed hemoglobin of 11.3 g/dL, a total leukocyte count of 14,300 per mm^3, and a platelet count of 2.39 lakh per mm^3. Serum electrolytes and C-reactive protein level along with liver and kidney function tests all were normal. Computed tomography (CT) scan head did not show any abnormality. Repeat hematological evaluation revealed a platelet count of 10,000 per mm^3. Her C-reactive protein was 34.34 mg/L and D-dimer level was 2460 ng/mL. Serum lipid profile, random blood sugar, thyroid function test, and serum homocysteine were within the normal range. Serum antinuclear antibody was positive. The cerebrospinal fluid examination did not reveal any abnormality (four mononuclear cells per mm^3, protein 36 mg/dL, and sugar 57 mg/dL). Cerebrospinal fluid evaluation for herpes simplex, varicella, measles, and mumps viruses was negative. Magnetic resonance imaging (MRI) of the brain revealed T2/ fluid-attenuated inversion recovery (FLAIR) hyperintense signal changes in the right frontotemporoparietal region with restriction of diffusion in the same region on diffusion-weighted images (DWI) and corresponding hypointense signal change on apparent diffusion coefficient (ADC) image, suggesting right middle cerebral artery territory infarction. Magnetic resonance angiogram (MRA) revelated attenuation of the right middle cerebral artery, M2 segment, along with paucity of the distal vasculature [Figure 1].

She was immediately treated with intravenous lacosamide. Her seizures were controlled, and she regained consciousness. She also received aspirin of 150 mg/day. The patient recovered remarkably, and she was independent with all her daily activities. Repeat MRI brain done after 6 weeks revealed the evolution of infarction in the right middle cerebral artery territory to the subacute–chronic stage. MRA and magnetic resonance venogram (MRV) were unremarkable [Figure 2]. D-dimer was reduced to 220 ng/mL. PF4 antibodies level measured at the sixth week of illness was normal.

Discussion

This is the first Indian case report of ischemic stroke and transient thrombocytopenia following ChAdOx1 nCoV-19

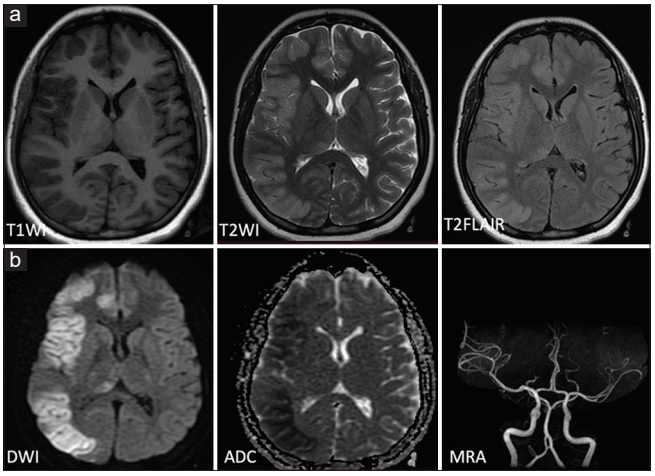

Figure 1: Brain imaging at 1 week. (a) Magnetic resonance axial T1W image shows hypointensity and effacement of sulci in the right cerebral hemisphere. T2W and T2 FLAIR images show hyperintensity in the right cerebral hemisphere. (b) DWI shows hyperintensity in the right cerebral hemisphere, with corresponding hypointensity in the ADC image, suggesting acute infract. MRA shows narrowing right middle cerebral artery M2 segment and paucity of peripheral vasculature. ADC = apparent diffusion coefficient, DWI = diffusion-weighted image, MRA = magnetic resonance angiogram, T1W = T1 weighted, T2W = T2 weighted

vaccination. Our case had many features consistent with the diagnosis of definite VITT[8] [Table 1]. There is no published report of VITT from India so far. However, Dutta *et al.* described a 51-year-old man, who presented with severe headache 6 days after administration of the first dose of Covishield. In addition to headache, the patient had vomiting, bilateral lateral rectus palsy, and papilledema. Magnetic resonance venography revealed thrombosis in the superior sagittal sinus and transverse sinus, along with extensive venous collaterals. The patient did not have thrombocytopenia. PF4 antibodies were negative.[9]

VITT should always be suspected if patients develop severe and persistent headaches, focal neurological deficits, visual changes, seizures, and encephalopathy following vaccination with ChAdOx1 nCov-19 adenovector-based vaccine. VITT generally develops within 6 weeks following vaccination.[10] VITT should also be suspected in patients with acute ischemic stroke after adenovector-based vaccination and thrombocytopenia.[8] Platelet transfusion in these patients is generally avoided, as it may enhance the possibility of thrombotic events. However, our patient received platelets in the emergency department, and this possibly helped in normalizing the platelet counts.

Table 1: Diagnostic criteria of definite vaccine-induced immune thrombotic thrombocytopenia (given by Pavord *et al.*[8])

Onset 5-30 days after vaccination
Evidence of thrombosis
Thrombocytopenia (<150,000 mm^3)
Elevated D-dimer level (>4000 ng/mL)
Demonstrable platelet factor-4 antibodies in blood

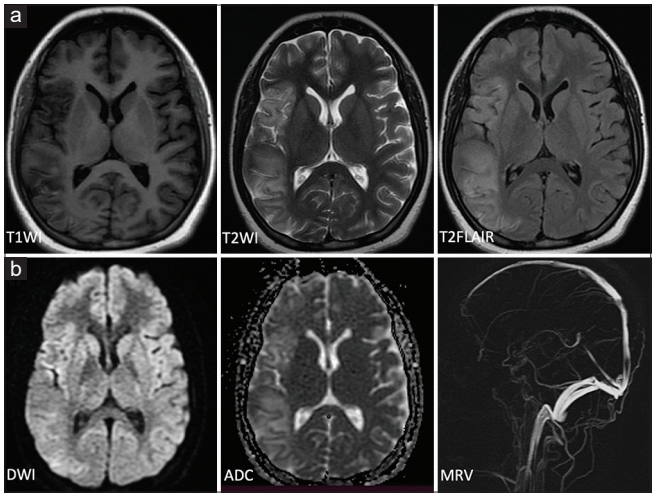

Figure 2: Follow-up brain imaging at 6 weeks. (a) Magnetic resonance axial T1W image shows effacement of sulci in the right cerebral hemisphere with hyperintense signal changes along the gyri. T2W and FLAIR images show hyperintensity in the right cerebral hemisphere. (b) DWI shows no restriction and ADC image shows hyperintensity in the right cerebral hemisphere (subacute–chronic infarct). Magnetic resonance venogram shows normal flow in the venous sinuses. ADC = apparent diffusion coefficient, DWI = diffusion-weighted image, T1W = T1 weighted, T2W = T2 weighted

In conclusion, major cerebral artery occlusion following ChAdOx1 nCov-19 adenovector vaccination can be an unusual manifestation of VITT. Familiarity with VITT is crucial because timely treatment with non-heparin anticoagulants and intravenous immunoglobulin may improve the outcome.

Key points for primary care physicians

VITT is an uncommon complication of the ChAdOx1 nCoV-19 vaccination. Cerebral venous thrombosis is a common manifestation of VITT. Large-vessel occlusion following the ChAdOx1 nCoV-19 vaccination should be promptly investigated for VITT. Prompt diagnosis and treatment of VITT with intravenous immunoglobulin is generally life-saving.

Patient consent

Consent for publication was obtained from the patient.

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Conflicts of interest

There are no conflicts of interest.

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