Version of Record: https://www.sciencedirect.com/science/article/pii/S1052305721003451
Manuscript_4866d3f5792699968ad5340f51efd5ce

Case Report:

Acute ischemic stroke revealing ChAdOx1 nCov-19 vaccine-induced immune thrombotic thrombocytopenia: impact on recanalization strategy

Guillaume Costentin, MD[1], Ozlem Ozkul-Wermester, MD[1], Aude Triquenot[1], MD, Véronique Le Cam-Duchez, MD, PhD[2], Nathalie Massy, MD[3] , Ygal Benhamou, MD, PhD[4], Evelyne Massardier, MD[1]

[1]*Department of Neurology, Rouen University Hospital, F-76000 Rouen, France*
[2]*Rouen University Hospital, Vascular Hemostasis Unit, F 76031, Rouen, France ; Normandie Univ, UNIROUEN, INSERM U1096, Rouen, France*
[3] *Department of Pharmacovigilance, Rouen University Hospital, F-76000 Rouen, France*
[4] *Department of Internal Medicine, Rouen University Hospital, F-76000 Rouen, France*

Guillaume Costentin, MD.
Rouen University Hospital
Department of Neurology
F-76000 Rouen, France
Tel.: +(33) 2 32 88 33 47; Fax: + (33) 2 32 88 84 22
E-Mail: guillaume.costentin@chu-rouen.fr

Ozlem Ozkul-Wermester, MD.
Rouen University Hospital
Department of Neurology
F-76000 Rouen, France
Tel.: +(33) 2 32 88 67 86; Fax: + (33) 2 32 88 84 22
E-Mail: ozlem.ozkul-wermester@chu-rouen.fr

Aude Triquenot, MD.
Rouen University Hospital
Department of Neurology
F-76000 Rouen, France
Tel.: +(33) 2 32 88 67 86; Fax: + (33) 2 32 88 84 22
E-Mail: aude.triquenot@chu-rouen.fr

Véronique Le Cam-Duchez, MD., PhD
Rouen University Hospital
Vascular Hemostasis Unit
F-76000 Rouen, France
Tel.: +(33) 2 32 88 67 86; Fax: + (33) 2 32 88 84 22
E-Mail: veronique.le-cam@chu-rouen.fr

Nathalie Massy, MD.
Rouen University Hospital
Department of Pharmacovigilance
F-76000 Rouen, France
Tel.: +(33) 2 32 88 67 86; Fax: + (33) 2 32 88 84 22
E-Mail: nathalie.massy@chu-rouen.fr

Ygal Benhamou, MD., PhD
Rouen University Hospital
Department of Internal Medicine
F-76000 Rouen, France
Tel.: +(33) 2 32 88 67 86; Fax: + (33) 2 32 88 84 22
E-Mail: ygal.benhamou@chu-rouen.fr

Evelyne Massardier, MD.
Rouen University Hospital
Department of Neurology
F-76000 Rouen, France
Tel.: +(33) 2 32 88 67 86; Fax: + (33) 2 32 88 84 22
E-Mail: evelyne.massardier@chu-rouen.fr

Department and institution where work was performed:
Rouen University Hospital
Department of Neurology
F-76000 Rouen, France

Grant support: none

Corresponding Author:
Guillaume Costentin, MD.
Rouen University Hospital
Department of Neurology
F-76000 Rouen, France
Tel.: +(33) 2 32 88 33 47; Fax: + (33) 2 32 88 84 22
E-Mail: guillaume.costentin@chu-rouen.fr

Running title: stroke due to vaccine-induced thrombocytopenia

Keywords: nCov-19 vaccination; thrombocytopenia; stroke; thrombectomy; intravenous thombolysis

Declarations of interest: none.

Abstract

Vaccine-induced immune thrombotic thrombocytopenia is a rare syndrome following the ChAdOx1 nCov-19 or Ad26.COV2.S vaccine. Reported patients developed mainly venous thrombosis. We describe a case of a young healthy women suffering from acute ischemic stroke due to large vessel occlusion without cerebral venous thrombosis 8 days after vaccination and its consequences on recanalization strategy.

Considering the thrombocytopenia, intravenous thrombolysis was contraindicated. She underwent mechanical thrombectomy with complete recanalization and dramatically improved clinically. Positive detection of anti-PF4-heparin-antibodies confirmed vaccine-induced immune thrombotic thrombocytopenia diagnosis.

In case of acute ischemic stroke after recent ChAdOx1 nCov-19 or Ad26.COV2.S vaccine, platelet count should be systematically checked before giving thrombolysis, and direct mechanical thrombectomy should be proposed in patients with large vessel occlusion.

Introduction

Vaccine-induced immune thrombotic thrombocytopenia (VITT) is a rare syndrome which results in unusual blood clots with high levels of antibodies to platelet factor 4, mainly affecting healthy young individuals after vaccination with the ChAdOx1 nCov-19 or Ad26.COV2.S vaccine (1-4). VITT resembles autoimmune heparin-induced thrombocytopenia (aHIT), with a disseminated intravascular coagulation-like state (DIC) (1). While thrombosis events mostly involve cerebral venous sinuses or splanchnic-vein, rare cases of acute ischemic stroke (AIS) are reported, without description of revascularization strategy (1,5,6). We describe a case of an AIS with large vessel occlusion (LVO) revealing VITT and consequences on recanalization strategy.

Case report

A 26-year-old healthy women, using oestroprogestative contraceptive, developed flu-like syndrome including nausea, muscle and body aches, fatigue and bilateral progressive headache 3 days after first vaccination with ChAdOx1 nCov-19. Headache intensity was initially moderate, worsening over days and getting drug-resistant. She did not have history of migraine. She presented to a local hospital emergency department 7 days after vaccination, clinical examination was normal without meningeal syndrome. RT-PCR assay for SARS-CoV-2 was negative. Platelet count was 57,000/mm3. The following day, she suddenly had right hemiplegia and aphasia, NIHSS was 15. Brain MRI revealed left middle cerebral artery AIS with M1-segment occlusion, and ruled out cerebral venous thrombosis. Considering the thrombocytopenia, intravenous thrombolysis with recombinant tissue plasminogen activator (IV rtPA) was contraindicated. She was transferred to our stroke center where mechanical thrombectomy (MT) was performed with recanalization (TICI 2c) 3.5 hours after symptoms onset. NIHSS at 24 hours was 5 and CT scan showed hemorrhagic

infarction type 2. Cervical CT angiography was normal. There were no procedure-related complications. Platelet count decreased to 17,000/mm3, fibrinogen level was 89 mg/dl, suggesting a DIC state. Thrombophilia screening and antiphospholipid testing were negative. Thoraco-abdominopelvic CT revealed asymptomatic pulmonary embolism and portal vein thrombosis. Cardiac monitoring and transesophageal echocardiography were normal, ruling out paradoxical embolism. Strongly positive detection of anti-PF4-heparin-antibodies confirmed VITT diagnosis.

Discussion

Special attention should be paid in patients presenting with AIS within three weeks following Covid-19 vaccination. Given the importance of time delays in managing the hyperacute phase, identifying a possible VITT is essential to determine the best recanalization strategy. In patients without predisposing factors, guidelines recommend not to delay IV rtPA treatment for AIS while waiting for coagulation testing (7). Since patients with VITT have severe thrombocytopenia with often a DIC–like state, IV rtPA, resulting in fibrinogen level decrease, may be associated with higher incidence of intracerebral haemorrhage and mortality. Moreover, various bleeding complications of VITT were reported (1-6).We conclude that suspicion of VITT is a contraindication to IV rtPA for AIS. Platelet count should be systematically checked before giving IV rtPA, and for patients with LVO, direct MT should be proposed.

REFERENCES

1. Greinacher A, Thiele T, Warkentin TE, et al Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination. N Engl J Med. 2021;21:04840.

2. Schultz NH, Sørvoll IH, Michelsen AE, et al. Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination. N Engl J Med. 2021;21:04882.

3. Muir KL, Kallam A, Koepsell SA, et al. Thrombotic Thrombocytopenia after Ad26.COV2.S Vaccination. N Engl J Med. 2021;21:05869

4. See I, Su JR, Lale A, et al. US Case Reports of Cerebral Venous Sinus Thrombosis With Thrombocytopenia After Ad26.COV2.S Vaccination. JAMA. Published online April 30, 2021.

5. Scully M, Singh D, Lown R, et al. Pathologic Antibodies to Platelet Factor 4 after ChAdOx1 nCoV-19 Vaccination. N Engl J Med. 2021;21:05385.

6. Al-Mayhani T, Saber S, Stubbs MJ, et al. Ischaemic stroke as a presenting feature of ChAdOx1 nCoV-19 vaccine-induced immune thrombotic thrombocytopaenia. J Neurol Neurosurg Psychiatry. Published online May 25, 2021.

7. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2019; 50:344-e418.