Cerebral venous thrombosis after vaccination against COVID-19 in the UK: a multicentre cohort study

Richard J Perry, Arina Tamborska, Bhagteshwar Singh, Brian Craven, Richard Marigold, Peter Arthur-Farraj, Jing Ming Yeo, Liqun Zhang, Ghaniah Hassan-Smith, Matthew Jones, Christopher Hutchcroft, Esther Hobson, Dana Warcel, Daniel White, Phillip Ferdinand, Alastair Webb, Tom Solomon, Marie Scully, David J Werring, Christine Roffe*, on behalf of the CVT After Immunisation Against COVID-19 (CAIAC) collaborators†*

Summary

Background A new syndrome of vaccine-induced immune thrombotic thrombocytopenia (VITT) has emerged as a rare side-effect of vaccination against COVID-19. Cerebral venous thrombosis is the most common manifestation of this syndrome but, to our knowledge, has not previously been described in detail. We aimed to document the features of post-vaccination cerebral venous thrombosis with and without VITT and to assess whether VITT is associated with poorer outcomes.

Methods For this multicentre cohort study, clinicians were asked to submit all cases in which COVID-19 vaccination preceded the onset of cerebral venous thrombosis, regardless of the type of vaccine, interval between vaccine and onset of cerebral venous thrombosis symptoms, or blood test results. We collected clinical characteristics, laboratory results (including the results of tests for anti-platelet factor 4 antibodies where available), and radiological features at hospital admission of patients with cerebral venous thrombosis after vaccination against COVID-19, with no exclusion criteria. We defined cerebral venous thrombosis cases as VITT-associated if the lowest platelet count recorded during admission was below 150×10^9 per L and, if the D-dimer was measured, the highest value recorded was greater than 2000 µg/L. We compared the VITT and non-VITT groups for the proportion of patients who had died or were dependent on others to help them with their activities of daily living (modified Rankin score 3–6) at the end of hospital admission (the primary outcome of the study). The VITT group were also compared with a large cohort of patients with cerebral venous thrombosis described in the International Study on Cerebral Vein and Dural Sinus Thrombosis.

Findings Between April 1 and May 20, 2021, we received data on 99 patients from collaborators in 43 hospitals across the UK. Four patients were excluded because they did not have definitive evidence of cerebral venous thrombosis on imaging. Of the remaining 95 patients, 70 had VITT and 25 did not. The median age of the VITT group (47 years, IQR 32–55) was lower than in the non-VITT group (57 years; 41–62; p=0·0045). Patients with VITT-associated cerebral venous thrombosis had more intracranial veins thrombosed (median three, IQR 2–4) than non-VITT patients (two, 2–3; p=0·041) and more frequently had extracranial thrombosis (31 [44%] of 70 patients) compared with non-VITT patients (one [4%] of 25 patients; p=0·0003). The primary outcome of death or dependency occurred more frequently in patients with VITT-associated cerebral venous thrombosis (33 [47%] of 70 patients) compared with the non-VITT control group (four [16%] of 25 patients; p=0·0061). This adverse outcome was less frequent in patients with VITT who received non-heparin anticoagulants (18 [36%] of 50 patients) compared with those who did not (15 [75%] of 20 patients; p=0·0031), and in those who received intravenous immunoglobulin (22 [40%] of 55 patients) compared with those who did not (11 [73%] of 15 patients; p=0·022).

Interpretation Cerebral venous thrombosis is more severe in the context of VITT. Non-heparin anticoagulants and immunoglobulin treatment might improve outcomes of VITT-associated cerebral venous thrombosis. Since existing criteria excluded some patients with otherwise typical VITT-associated cerebral venous thrombosis, we propose new diagnostic criteria that are more appropriate.

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Introduction

Globally, more than 4·1 million people have died from COVID-19.[1] In response to this public health emergency, several vaccines against COVID-19 have been developed, with more than 3·7 billion doses administered worldwide.[2] After the introduction of the adenovirus vector vaccine ChAdOx1 (Oxford–AstraZeneca), five cases of severe venous thrombosis with thrombocytopenia were reported in Norway, each starting 7–10 days after administration of the first vaccine dose. Four of these cases had cerebral venous sinus thrombosis.[3] This syndrome has since been termed vaccine-induced immune thrombotic thrombocytopenia (VITT).[3–5] A similar condition has been described with another adenovirus vector vaccine, Ad26.COV2.S (Johnson & Johnson).[6,7] There are also case reports in which two

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*Contributed equally

†A complete list of the collaborators is given in the appendix (p 1)

Comprehensive Stroke Service, National Hospital for Neurology and Neurosurgery (R J Perry PhD, Prof D J Werring PhD) **and Department of Haematology** (B Craven MBBCh, D Warcel MBBS, Prof M Scully MD), **UCL Hospitals NHS Foundation Trust, London, UK; Stroke Research Centre, UCL Queen Square Institute of Neurology, London, UK** (R J Perry, Prof D J Werring); **National Institute for Health Research Health Protection Research Unit in Emerging and Zoonotic Infections, Institute of Infection, Veterinary and Ecological Sciences, University of Liverpool, Liverpool, UK** (A Tamborska MBChB, B Singh MRCP, Prof T Solomon FMedSci); **Tropical and Infectious Diseases Unit, Royal Liverpool University Hospital, Liverpool, UK** (B Singh); **Department of Stroke Medicine, University Hospital Southampton NHS Foundation Trust, Southampton UK** (R Marigold FRCP); **John van Geest Centre for Brain Repair, Department of Clinical Neurosciences, Cambridge, UK** (P Arthur-Farraj PhD); **Queen's Medical Centre, Nottingham University Hospitals NHS Trust, Nottingham, UK** (J M Yeo MRCP); **Department of Neurology, St George's University Hospital NHS Foundation Trust, London, UK** (L Zhang PhD); **Department of Neurology, Queen Elizabeth Hospital Birmingham,**