Brain, Behavior, and Immunity 95 (2021) 514–517

Contents lists available at ScienceDirect

Brain Behavior and Immunity

journal homepage: www.elsevier.com/locate/ybrbi

Short Communication

Cerebral venous sinus thrombosis and thrombocytopenia after COVID-19 vaccination – A report of two UK cases

Puja R. Mehta [a,b,1,*], Sean Apap Mangion [a,1], Matthew Benger [c], Biba R. Stanton [a], Julia Czuprynska [d], Roopen Arya [d], Laszlo K. Sztriha [a]

[a] Department of Neurology, King's College Hospital NHS Foundation Trust, London, UK
[b] Maurice Wohl Clinical Neuroscience Institute, King's College London, Department of Basic and Clinical Neuroscience, London, UK
[c] Department of Neuroradiology, King's College Hospital NHS Foundation Trust, London, UK
[d] King's Thrombosis Centre, Department of Haematological Medicine, King's College Hospital NHS Foundation Trust, London, UK

ARTICLE INFO

Keywords:
Neurology
Stroke
Cerebrovascular disease
COVID-19
Vaccine
Cerebral venous sinus thrombosis
Thrombocytopenia
Immunology

ABSTRACT

Recent reports have highlighted rare, and sometimes fatal, cases of cerebral venous sinus thrombosis (CVST) and thrombocytopenia following the Vaxzevria vaccine. An underlying immunological mechanism similar to that of spontaneous heparin-induced thrombocytopenia (HIT) is suspected, with the identification of antibodies to platelet factor-4 (PF4), but without previous heparin exposure. This unusual mechanism has significant implications for the management approach used, which differs from usual treatment of CVST. We describe the cases of two young males, who developed severe thrombocytopenia and fatal CVST following the first dose of Vaxzevria. Both presented with a headache, with subsequent rapid neurological deterioration. One patient underwent PF4 antibody testing, which was positive. A rapid vaccination programme is essential in helping to control the COVID-19 pandemic. Hence, it is vital that such COVID-19 vaccine-associated events, which at this stage appear to be very rare, are viewed through this lens. However, some cases have proved fatal. It is critical that clinicians are alerted to the emergence of such events to facilitate appropriate management. Patients presenting with CVST features and thrombocytopenia post-vaccination should undergo PF4 antibody testing and be managed in a similar fashion to HIT, in particular avoiding heparin and platelet transfusions.

1. Introduction

Recent data published by the European Medicines Agency have highlighted 18 cases of cerebral venous sinus thrombosis (CVST), the majority (67%) of which had associated thrombocytopenia, following vaccination with Vaxzevria (previously named COVID-19 Vaccine AstraZeneca), amongst over 20 million recipients of this vaccine (European Medicines Agency, 2021). More recently, the Medicines and Healthcare products Regulatory Agency (MHRA) have reported 22 cases of CVST with associated thrombocytopenia following vaccination with Vaxzevria, amongst 18.1 million recipients in the UK (Medicines and Healthcare Products Regulatory Agency, 2021).

The majority of the cases reported thus far have involved female patients under the age of 55 and occurred between 4 and 16 days after vaccination. Because it is a rare event and data are still being collected, it is currently not certain if the rate of CVST associated with the COVID-19 vaccine is higher than the background rate, which is 1.32–1.57/100,000/year (Coutinho et al., 2012; Devasagayam et al., 2016). The mortality from vaccine-associated CVST appears higher than expected at 29–33% (European Medicines Agency, 2021; Medicines and Healthcare Products Regulatory Agency, 2021; Paul-Ehrlich-Institut, 2021), as opposed to the usual mortality of approximately 4.4% (Haghighi et al., 2012).

Typical laboratory features include a platelet count < 100 x10^9/L, raised D-dimers, and an inappropriately low fibrinogen. A causal link has not been proven, but there is a growing consensus amongst thrombosis experts that the underpinning pathophysiological mechanism is similar to that of spontaneous heparin-induced thrombocytopenia (HIT), in which, in the absence of recent heparin exposure, antibodies target a complex of platelet factor-4 (PF4) and heparin, and activate cellular FcγIIA receptors on platelets, inducing a prothrombotic cascade together with thrombocytopenia (Greinacher et al., 2021; British Society for

* Corresponding author.
E-mail addresses: puja.mehta@kcl.ac.uk (P.R. Mehta), laszlo.sztriha@kcl.ac.uk (L.K. Sztriha).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.bbi.2021.04.006
Received 31 March 2021; Received in revised form 5 April 2021; Accepted 8 April 2021
Available online 20 April 2021