Check for updates

DOI: 10.1111/ajt.16735

LETTER TO THE EDITOR

Organ transplantation from deceased donors with vaccine-induced thrombosis and thrombocytopenia

To the Editor:

Vaccine-induced thrombosis and thrombocytopenia (VITT) may follow immunization with the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2.[1,2] Autoantibodies to platelet factor 4 (PF4) may mediate VITT through antibody-dependent platelet activation, though the underlying etiology is uncertain.[3] Anti-PF4 antibodies are also seen in heparin-induced thrombocytopenia, though most cases of VITT do not have prior heparin exposure. More than 20 million people in the United Kingdom (UK) have received the ChAdOx1 nCoV-19 vaccine. We carried out an early analysis of organ donation and transplantation from UK donors with VITT, to understand the implications of this emerging syndrome. Articles 6(1)(e) and 9(2)(h) and (i) of the General Data Protection Regulations provide the basis for NHSBT to use patient identifiable data without prior consent, for the purposes of monitoring the safety of the national transplant program.

We identified 13 consented deceased organ donors, who presented with thrombosis and/or hemorrhage and laboratory features consistent with VITT,[4] between 28 January and 9 April 2021. All had received their first dose of ChAdOx1 nCoV-19 vaccine before admission (see Table 1). Ten donors proceeded to donate 27 allografts to 26 recipients. After a median follow-up of 19 days, 21 of 27 (78%) allografts have satisfactory function. Three recipients developed early allograft failure requiring explantation (two livers and one kidney); two transplanted kidneys have impaired allograft function, currently requiring hemodialysis; and one recipient died within a day of transplantation from a presumed cardiac event. There were seven major thrombotic or hemorrhagic postoperative complications (three bleeds and four venous or arterial allograft thromboses) in six recipients, resulting in the loss of three transplants as described above; these events occurred within 9 days of transplantation. Of the six recipients with bleeding or thrombotic events, two had received their second dose of ChAdOx1 nCoV-19 vaccine within 30 days before transplantation; neither patient had features suggestive of VITT at the time of transplantation. Two of the three patients with bleeding had preexisting risk factors for hemorrhage (dual antiplatelet agent therapy, anticoagulation for metallic cardiac valve); none of the patients with thromboses had significant preexisting procoagulant tendencies.

So far, three liver recipients had detectable anti-PF4 antibodies between 3 and 22 days posttransplant; one of these recipients experienced a thrombotic complication without allograft loss and the other two had uncomplicated postoperative courses. Ten recipients (six kidneys and four livers) tested negative for anti-PF4 antibodies.

The UK experience to date suggests that the potential risks of transplanting organs from donors with VITT are twofold. First, early major thrombosis or clinically significant bleeding, which may result from preexisting hemostatic and endothelial dysfunction in the allograft. Second, possible transmission of pathogenic lymphocytes producing anti-PF4. The clinical significance of this is unclear; further follow-up will determine whether this portends development of VITT in the recipient.

UK guidance has been drawn up for the selection, recovery, and transplantation of organs from donors with VITT, as well as recipient monitoring.[5] We suggest that liver, lung, pancreas, and small bowel transplants from donors with VITT should only proceed in urgent situations, as these organs contain high numbers of "passenger" donor lymphocytes. Since anti-PF4 antibodies can provoke platelet activation and thromboses, platelet transfusion should be avoided during organ recovery and transplantation processes where possible. The contribution of systemic heparinization during organ recovery to thrombosis within the allograft is uncertain, and argatroban is an alternative anticoagulant.[5] Current UK guidance recommends that heparin can be used as per standard practice in the recipient unless features of VITT develop.[5] For recipients of organs from VITT donors, monitoring of the platelet count, fibrinogen, D-dimers, and anti-PF4 antibodies is essential.[5]

Further experience of organ transplantation from donors with VITT and longer term recipient follow-up will help guide clinical decision-making. In the meantime, transplantation of organs from these donors should only proceed after careful consideration of the methods for organ recovery and of the risks and benefits for a potential recipient, and an appropriate consent discussion.

*Joint first author.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.
© 2021 The Authors. *American Journal of Transplantation* published by Wiley Periodicals LLC on behalf of The American Society of Transplantation and the American Society of Transplant Surgeons

TABLE 1 Deceased donors with VITT and the recipients of their organs

Characteristic	Value
Consented deceased donors[a]	13[b]
Age (years)	34 (21 to 63)
Female	11 (85%)
Donation after brain death	13 (100%)
Time from vaccine administration to hospital admission (days)	10 (7 to 18)
Clinical features[c]	
Intracranial hemorrhage	12 (92%)
Cerebral venous sinus thrombosis	7 (54%)
Extra-cranial thrombosis[d]	6 (46%)
Platelet count ($\times 10^9$/L)	
On admission to hospital	26 (3 to 61)
Lowest value prior to donation	7 (2 to 50)
Fibrinogen (g/L, NR 2 to 4)[e]	1.0 (<0.3 to 4.5)
D-dimer (ng/ml, NR < 500)[f]	41 000 (6500 to >80 000)
Anti-PF4 antibodies (OD, assay cut-off 0.4)[g]	2.7 (1.4 to 3.2)
Transplant recipients	26
Age (years)	40 (2 to 63)
Female	12 (46%)
Transplant type	
Kidney-only	15
Liver[h]	7
Heart	1
Bilateral lung	1
Simultaneous pancreas and kidney (SPK)	1
Pancreatic islet	1
Major postoperative complications[i]	7
Liver recipients	
Major hemorrhage	0
Thrombosis/thromboembolism	3
Kidney/SPK/islet recipients	
Major hemorrhage	3
Thrombosis/thromboembolism	1
Heart/lung recipients	
Major hemorrhage	0
Thrombosis/thromboembolism	0
Patient and allograft outcomes	
Delayed graft function/early graft dysfunction[j]	4
Graft explant	3
Death	1
Lowest postoperative platelet count ($\times 10^9$/L)[k]	124 (32 to 267)
Anti-PF4 antibodies[g]	
Positive	3
Negative	10
Result pending	2
Not tested	11

Note: Numbers are *n* (%) or median (range).

Abbreviations: VITT, vaccine-induced thrombosis and thrombocytopenia; NR, normal range; PF4, platelet factor 4; OD, optical density units.

[a]Individuals in whom consent for organ donation has been granted.

[b]All organ offers from one donor were declined, so no organs were retrieved. Two donors had organs retrieved that were not eventually transplanted. Ten donors donated at least one organ that was transplanted.

[c]Clinical features are not exclusive; six donors presented with intracranial hemorrhage only.

[d]Portal vein (2), pulmonary embolus (1), splenic vein (1), mesenteric vein (1), aorta (1).

[e]Lowest result reported by donor center.

[f]Highest result reported by donor center.

[g]Donor serum samples from all probable cases were centrally tested by NHSBT for anti-PF4 antibodies, using the Lifecodes PF4 IgG enzyme-linked immunosorbent assay (ELISA, Immucor).

[h]Includes two split liver transplants from one donor.

[i]Numbers represent events; some recipients experienced more than one complication. Excludes death.

[j]Defined as at least one session of hemodialysis/hemofiltration in the first 7 postoperative days in kidney recipients, any need for ongoing extracorporeal membrane oxygenation in heart/lung recipients, or super-urgent listing for re-do transplantation in liver recipients. Excludes graft failure/explant.

[k]In the first 2 weeks after transplantation.

KEYWORDS

autoantibody, clinical research/practice, coagulation and hemostasis, donors and donation: donor follow-up, infection and infectious agents – viral: influenza, kidney transplantation/nephrology, liver transplantation/hepatology

ACKNOWLEDGMENTS

The authors are grateful to the organ donation teams, specialist nurses in organ donation, National Organ Retrieval Service teams, and the staff of the platelet immunology laboratory at NHSBT Filton who assisted with aspects of donor characterization. They also thank the recipient transplant coordinators, and other members of the transplant teams caring for the transplant recipients, who supplied follow-up information required for this study. Lastly, and most of all, they thank all deceased donors and their families.

DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

UK Donor VITT Transplant Study Group

George H. B. Greenhall[1*]

Ines Ushiro-Lumb[2*]

Sue Pavord[3]

16006143, 2021, 12, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/ajt.16735 by Cochrane Germany, Wiley Online Library on [07/12/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Ian Currie[1]
M. Thamara P. R. Perera[4]
Hermien Hartog[4]
Quentin A. Hill[5]
Ismail Mohamed[6]
Muhammad A. Khurram[6]
Reza Motallebzadeh[7]
Gareth Jones[7]
Aileen Marshall[7]
Joerg-Matthias Pollok[7]
Nicholas Torpey[8]
Gavin J. Pettigrew[8]
Sanjay Mehra[9]
Hemant Sharma[9]
Francis Calder[10]
Nicos Kessaris[10]
Jay Nath[11]
Debabrata Roy[12]
Gabriel C. Oniscu[13]
Marc Clancy[14]
Karthik Santhanakrishnan[15]
Jorge Mascaro[4]
Sern Lim[4]
Marius Berman[16]
Sue Madden[1]
Lisa Mumford[1]
Darius Mirza[4]
Chris Watson[8]
Olive McGowan[1]
Douglas Thorburn[7]
Rommel Ravanan[1]
Beverley J. Hunt[10]
Chris J. Callaghan[1]
David J. Roberts[17]
John Forsythe[1]

[1]*NHS Blood and Transplant, Bristol, UK*
Email: george.greenhall@nhsbt.nhs.uk
[2]*NHS Blood and Transplant, London, UK*
[3]*Oxford University Hospitals, Oxford, UK*
[4]*Queen Elizabeth Hospital, Birmingham, UK*
[5]*St James's University Hospital, Leeds, UK*
[6]*Royal London Hospital, London, UK*
[7]*Royal Free Hospital, London, UK*
[8]*Addenbrooke's Hospital, Cambridge, UK*
[9]*Royal Liverpool University Hospital, Liverpool, UK*
[10]*Guy's Hospital, London, UK*
[11]*Southmead Hospital, Bristol, UK*
[12]*University Hospital, Coventry, UK*
[13]*Royal Infirmary of Edinburgh, Edinburgh, UK*
[14]*Queen Elizabeth University Hospital, Glasgow, UK*
[15]*Wythenshawe Hospital, Manchester, UK*
[16]*Royal Papworth Hospital, Cambridge, UK*
[17]*NHS Blood and Transplant, Oxford, UK*

ORCID

George H. B. Greenhall https://orcid.org/0000-0002-4816-1474
Ines Ushiro-Lumb https://orcid.org/0000-0003-0989-8091
Ian Currie https://orcid.org/0000-0003-1636-6130
Muhammad A. Khurram https://orcid.org/0000-0002-3555-0374
Nicos Kessaris https://orcid.org/0000-0002-4067-7003
Gabriel C. Oniscu https://orcid.org/0000-0003-1714-920X
Chris Watson https://orcid.org/0000-0002-0590-4901
Rommel Ravanan https://orcid.org/0000-0003-3324-9024
Chris J. Callaghan https://orcid.org/0000-0003-3334-4152

REFERENCES

1. Greinacher A, Thiele T, Warkentin TE, Weisser K, Kyrle PA, Eichinger S. Thrombotic thrombocytopenia after ChAdOx1 nCov-19 vaccination. *N Engl J Med*. 2021;384(22):2092-2101.
2. Schultz NH, Sørvoll IH, Michelsen AE, et al. Thrombosis and thrombocytopenia after ChAdOx1 nCoV-19 vaccination. *N Engl J Med*. 2021;384(22):2124-2130.
3. Scully M, Singh D, Lown R, et al. Pathologic antibodies to platelet factor 4 after ChAdOx1 nCoV-19 vaccination. *N Engl J Med*. 2021;384(23):2202-2211.
4. British Society for Haematology. Guidance produced from the Expert Haematology Panel (EHP) focussed on Covid-19 Vaccine induced Thrombosis and Thrombocytopenia (VITT). 2021(v1.3). https://b-s-h.org.uk/about-us/news/guidance-produced-by-the-expert-haematology-panel-ehp-focussed-on-vaccine-induced-thrombosis-and-thrombocytopenia-vitt/. Accessed May 14, 2021.
5. NHS Blood and Transplant. Organ Donation and Transplantation from Patients with Vaccine Induced Thrombosis and Thrombocytopenia (VITT) (INF1569/2). https://www.odt.nhs.uk/covid-19-advice-for-clinicians/. Accessed May 16, 2021.

16006143, 2021, 12, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/ajt.16735 by Cochrane Germany, Wiley Online Library on [07/12/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License