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Title

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

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Abbreviations

PF4	Platelet factor 4
UK	United Kingdom
VITT	Vaccine-induced thrombosis and thrombocytopenia

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supplied follow-up information required for this study. Lastly, and most of all, we thank all deceased donors and their families.

Vaccine-induced thrombosis and thrombocytopenia (VITT) may follow immunisation 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 haemorrhage and laboratory features consistent with VITT,[4] between 28th January and 9th April 2021. All had received their first dose of ChAdOx1 nCoV-19 vaccine before admission (see Table). 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, one kidney); two transplanted kidneys have impaired allograft function, currently requiring haemodialysis; and one recipient died within a day of transplantation from a presumed cardiac event. There were seven major thrombotic or haemorrhagic post-operative 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 nine 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 transplantation. Two of the three patients with bleeding had pre-existing risk factors for hemorrhage (dual anti-platelet agent therapy, anticoagulation for metallic cardiac valve); none of the patients with thromboses had significant pre-existing pro-coagulant tendencies.

So far, three liver recipients had detectable anti-PF4 antibodies between three and 22 days post-transplantation; one of these recipients experienced a thrombotic complication without allograft loss and the other two had uncomplicated post-operative courses. Ten recipients (six kidneys, 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 two-fold. First, early major thrombosis or clinically significant bleeding, which may result from pre-existing haemostatic 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 heparinisation 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 are 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.

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Table. Deceased donors with VITT and the recipients of their organs

Characteristic	Value
Consented deceased donors [a]	**13** [b]
Age (years)	34 (21 – 63)
Female	11 (85%)
Donation after brain death	13 (100%)
Time from vaccine administration to hospital admission (days)	10 (7 – 18)
Clinical features [c]	
Intracranial haemorrhage	12 (92%)
Cerebral venous sinus thrombosis	7 (54%)
Extra-cranial thrombosis [d]	6 (46%)
Platelet count ($x10^9$/L)	
On admission to hospital	26 (3 – 61)
Lowest value prior to donation	7 (2 – 50)
Fibrinogen (g/L, NR 2 – 4) [e]	1.0 (<0.3 to 4.5)
D-dimer (ng/mL, NR <500) [f]	41,000 (6,500 to >80,000)
Anti-PF4 antibodies (OD, assay cut-off 0.4) [g]	2.7 (1.4 – 3.2)
Transplant recipients	**26**
Age (years)	40 (2 – 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 post-operative 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 post-operative platelet count ($x10^9$/L) [k]	124 (32 – 267)
Anti-PF4 antibodies [g]	
Positive	3
Negative	10
Result pending	2
Not tested	11

Numbers are n (%) or median (range). 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 haemorrhage only. [d] Portal vein (2), pulmonary embolus (1), splenic vein (1), mesenteric vein (1), aorta (1). [e] Lowest result reported by donor centre. [f] Highest result reported by donor centre. [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 haemodialysis/haemofiltration in the first seven post-operative 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. Does not include graft failure/explant. [k] In the first two weeks after transplantation.