Organ Donation and Transplantation from Patients with COVID-19 Vaccine Induced Thrombosis with Thrombocytopenia Syndrome (TTS)

Thrombosis with thrombocytopenia syndrome (TTS)[a], is a rare complication of the AstraZeneca and Janssen (Johnson and Johnson) COVID-19 vaccines, that can result in life threatening thrombocytopenia and venous and arterial thromboses. The exact pathophysiology of TTS is still unknown, though the majority of cases are associated with the presence of pathological antibodies against platelet factor 4 (PF4). It has similar features to heparin-induced thrombocytopenia (HIT).

The AstraZeneca COVID-19 vaccine is available in Australia and has resulted in TTS in a small number of individuals. Deceased organ donation for transplantation may be a consideration when this condition leads to death, particularly following cerebral thrombosis and/or haemorrhage. Current guidance is that donation and transplantation is generally not recommended in proven or suspected TTS, and should only be considered after careful risk-benefit assessment (see below).

Potential donors recently vaccinated with the COVID-19 AstraZeneca vaccine who have died from other causes and with no features of TTS can proceed to donation as per usual processes.

Clinical criteria for TTS include:
- Onset of symptoms 4 to 42 days after receiving the AstraZeneca COVID-19 vaccine
- Thrombosis – cerebral venous sinuses, splanchnic vein, limb deep venous thrombosis, pulmonary embolism, arterial thrombosis (e.g. limb, myocardial ischaemia)
- Thrombocytopenia (platelet count < 150 x 10^9/L)[b]
- High d-dimer (typically > 5 x upper limit of normal)

Suspected TTS is confirmed with a positive PF4 antibody test in the presence of these clinical features. These antibodies are only detectable by specific ELISA methods in specialized laboratories.

There is limited experience about the suitability for organ donation of patients dying with TTS. The largest published experience is from the UK.[1] Of 13 consented deceased organ donors who presented with clinical and laboratory features of TTS, 10 proceeded to donate organs to 26 recipients (15 kidneys, 7 livers, 1 heart, 1 bilateral lung, 1 simultaneous pancreas-kidney, 1 pancreas islet). Median follow-up at publication was 19 days. Three recipients developed early allograft failure requiring explantation (two livers and one kidney), 2 kidney recipients had impaired graft function requiring haemodialysis, and one recipient died within a day of transplantation from a presumed cardiac event. There were seven major thrombotic or haemorrhagic postoperative complications (3 bleeds and 4 venous or arterial allograft thromboses) in 6 recipients, resulting in the loss of 3 transplants as described above; these events occurred within 9 days of transplantation. Three liver recipients developed detectable anti-PF4 antibodies between 3 and 22 days post-transplant; 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 has since undertaken further transplants from donors with TTS with updated summary information and accompanying guidance available.[2]

<u>Recommendations for donor suitability:</u>

The main risks to consider in relation to proceeding with organ donation for transplantation in potential donors with TTS include:

[a] Also known as vaccine-induced immune thrombotic thrombocytopenia syndrome (VITT), vaccine-induced pro-thrombotic immune thrombocytopenia (VIPIT), vaccine-associated immune thrombotic thrombocytopenia (VATT)
[b] Platelet count may be normal at presentation in >5% of TTS cases. Not all thrombocytopenia following COVID-19 vaccination is TTS – immune thrombocytopenia has been seen following the Pfizer-BioNTech, Moderna and the AstraZeneca COVID-19 vaccines.

1) Thrombosis or bleeding that may impair donor organ function and suitability
2) Possibility of pre-existing haemostatic and endothelial dysfunction in the organ that may result in early thrombosis or bleeding in the graft post transplantation
3) Possible transmission of pathogenic lymphocytes producing anti-PF4 that could trigger a similar auto-immune phenomenon in the recipient resulting in the development of thrombosis and thrombocytopenia. This risk is theoretically greater when utilising organs with high passenger leucocyte burden (e.g., liver, lung, small bowel and pancreas).

Australian experience with TTS is limited and suitability for organ donation has been assessed in only a few patients. Current guidance is that donation and transplantation is generally not recommended in proven or suspected TTS, and should only be considered after careful risk-benefit assessment and with specific consent from the intended recipient or their surrogate decision maker.

Donor investigations:

Standard investigations to diagnose and monitor TTS should be undertaken, according to guidance from the Thrombosis and Haemostasis Society of Australia and New Zealand (THANZ)[3]

Suitable functional and imaging investigations may be required to assess organ suitability and to exclude significant thrombosis and/or bleeding.

Donor management:

Donors should be managed according to THANZ guidelines for vaccine-induced TTS[3]. Platelet transfusions and heparin administration should be avoided as they may exacerbate this syndrome.

Treatment should be provided to counter the development of thrombosis and other manifestations of TTS that may compromise organ suitability for transplantation. This includes intravenous immunoglobulin (IVIg) and non-heparin anticoagulation. Preferred agents include bivalirudin and argatroban, with the alternatives of danaparoid and fondaparinux being less suitable due to having longer half-lives (same non-heparin protocols as used in HIT).[4]

Care of the recipient:

Recipients should be counselled about the uncertainties of donation from a donor with TTS and the possibility of serious consequences. Recipients of organs from donors with TTS should have additional monitoring that includes regular platelet count, d-dimer and PF4 antibodies.[2] If development of TTS is suspected, it should be appropriately investigated, platelet transfusions and all forms of heparin avoided, and prompt expert haematology advice sought.

References:

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2. NHSBT Organ Donation and Transplantation from Patients with Vaccine Induced Thrombosis and Thrombocytopenia (VITT). Available at: https://www.odt.nhs.uk/covid-19-advice-for-clinicians/ Accessed 26-7-2021.
3. Thrombosis & Haemostasis society of Australia New Zealand (THANZ) Multidisciplinary VITT Guideline for Doctors 7/7/2021. Available at: https://www.thanz.org.au/resources/covid-19 Accessed 26-7-2021.
4. Joseph J, Rabbolini D, Enjeti AK, et al. Diagnosis and management of heparin-induced thrombocytopenia: a consensus statement from the Thrombosis and Haemostasis Society of Australia and New Zealand HIT Writing Group. Med J Aust. 2019 Jun;210(11):509-516. doi: 10.5694/mja2.50213. Epub 2019 Jun 2.