Organ donation and transplantation from patients with thrombosis and thrombocytopenia occurring after coronavirus vaccination

1.0: Introduction

Vaccine associated thrombocytopenia and thrombosis (VATTs), also termed vaccine induced prothrombotic thrombocytopenia (VIPIT) is a rare syndrome of:

- thrombosis (most frequently cerebral venous sinus thrombosis but venous or arterial thrombosis may occur at any site)
- thrombocytopenia (platelet count of < 150 x 10^9/l)
- high levels of D-dimer (usually >4000 µg/L), often with low fibrinogen levels
- testing for antibodies to Platelet Factor 4 (PF4) (heparin induced thrombocytopenia; HIT test) by ELISA will give a positive result, despite the absence of prior exposure to heparin treatment .

VATTs may be associated with unfavourable outcomes. In the currently available German series, 4/9 patients died (https://www.researchsquare.com/article/rs-362354/v1). A link to current guidance on the care of patients with VATTs can be found here: https://b-s-h.org.uk/about-us/news/a-message-from-bsh-president-professor-adele-fielding-march-2021/)

2.0 Safety of organ donation from deceased donors with VATTs:

- VATTs is thought to be driven by an auto-antibody that leads to platelet activation. In conditions with an auto-immune patho-physiological basis, current NHSBT guidance recommends caution when utilising organs with high passenger leucocyte burden (e.g. liver, lung & small bowel) due to the potential of transmitting immune cells that could trigger a similar auto-immune phenomenon in the naive recipient (passenger lymphocyte syndrome; PLS).
- To date other than the UK experience of organ donation following possible VATTs diagnosis there are no other published case reports or case series describing such outcomes.
- UK patients have received kidney, liver, lung, islet, and heart transplants from deceased donors with possible or probable VATTs. Recipient outcomes are being carefully monitored.

3.0 Guidance

3.1 Donor organ selection

- Although all organs can be used after evaluation of risks vs benefits to individually matched recipients, there is potential for VATTs in the organ recipient. This risk is likely to be higher in liver, lung, pancreas, and small bowel transplants. Risk might also be associated with a recipient developing VATTs themselves after exposure to coronavirus vaccination in the preceding 28 days prior to transplantation. Hence a careful review and MDT decision on risks vs benefits and detailed informed patient consent is recommended before utilisation of these organs. At the present time it is felt that accepting liver, lung, pancreas & islet, or small bowel transplantation should only happen in the most urgent situations and with clear documentation of the MDT discussion and the consent processes.
- Organs may bear petechiae in many donors who have very low platelet counts. This should not deter use of the organ unless it is extensive.

3.2 Organ retrieval

- Care of the donor in the immediate pre-retrieval phase and during retrieval including the use of systemic anticoagulants and platelet transfusions
    - Although it is unknown whether platelet transfusion could exacerbate VATTs, platelet transfusion should be avoided where possible e.g. pre or during retrieval, during the use of NRP or other types of machine perfusion or bypass procedures and during transplantation to the recipient. However, this is a caution, and necessary peri-operative platelet transfusion is not contra-indicated
    - Heparin may be used as a systemic anticoagulation agent in the donor at time of retrieval (eg: cold perfusion or NRP). At this stage it is not known if use of Unfractionated Heparin (UFH) in the donor at time of retrieval would contribute to intravascular thrombosis in the organ. Alternative regimens using argatroban as a replacement for UFH in the organ retrieval process are being derived and update will be issued at the earliest opportunity.
    - The retrieval team should be prepared to convert to rapid retrieval protocol (eg: DCD like manner with cold flush) in the event of significant bleeding during the retrieval process.

3.3 Care of recipient

- Care of recipient post-transplant
    - In most respects, care will be as per standard protocols. Thromboprophylaxis can be given in the normal way unless VATTs is suspected. It is safe to use Heparin as part of cardio-pulmonary bypass when using hearts from donors with suspected/confirmed VATTs.
    - The potential for VATTs is likely to be in the first 10-20 days post-transplant. If VATTs is suspected, it is recommended to stop any form of UFH or Low Molecular Weight Heparin (LMWH) and using intermittent pneumatic compression or fondaparinux
    - Recommended additional monitoring: daily FBC and D-dimer on post-operative days; POD 0-7, and then three/week for the subsequent 2 weeks. Test for PF4 antibodies POD 7 & 14. Low threshold for investigating for venous or arterial thrombosis (including graft vasculature) by appropriate imaging
- When to suspect VATTs in a recipient post-transplant
    - On serial monitoring, a rise in D-dimer levels of >20% or fall in platelet counts of >20% should trigger closer surveillance, including testing for PF4 antibodies.
    - Consider with any new thrombosis POD 0-21 associated with thrombocytopenia and a high D-dimer. It should also be considered if no thrombosis but a thrombocytopenia with a platelet count lower than expected (it is accepted that thrombocytopenia is common after some organ transplants) with a raised D-dimer (usually >4000 µg/L) and a low Claus fibrinogen.
- What to do if VATTs is suspected
    - Consider other causes of thrombocytopenia (e.g. immunosuppression, sepsis)
    - Avoid platelet transfusions and all forms of heparin including heparin-based flushes
    - Test for PF4 antibodies

- Seek expert advice on an urgent basis. Urgent treatment such as intravenous immunoglobulins may be required. Contact the regional haemostasis and thrombosis team on-call out of hours, and an expert haematology panel can also be contacted via the regional ODT manager on-call for case discussion and support.

This guidance will be updated with emerging evidence in consultation with relevant specialist societies and experts.