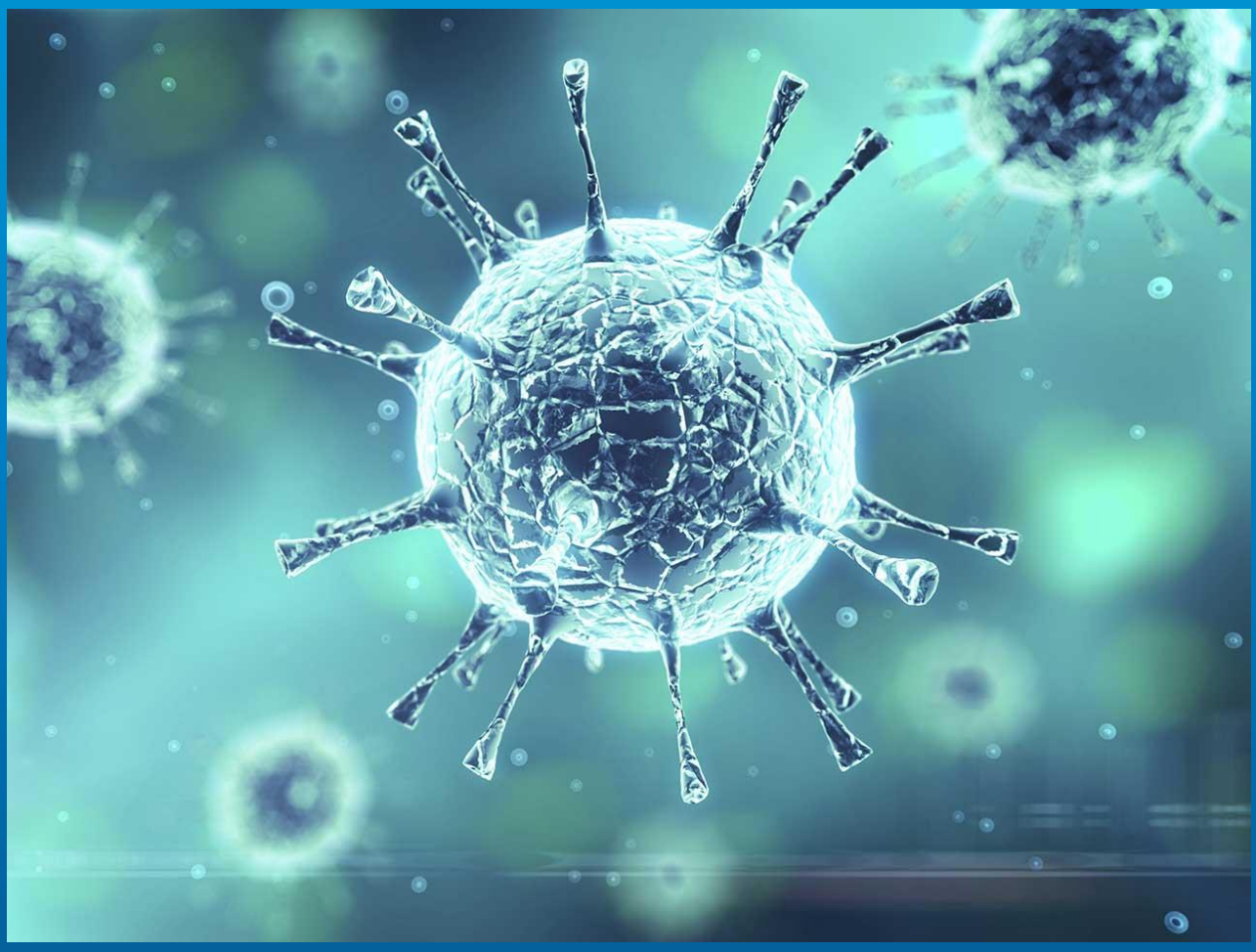
NHS
Blood and Transplant



Events investigated for possible donor-derived transmission of infections, malignancies, and other cases of interest

April 2019 - March 2020

Preface

This report has been produced by Clinical Governance, Organ Donation and Tissue and Transplantation Directorate (OTDT), NHS Blood and Transplant.

All figures quoted in this report are events as reported to NHSBT between 1 April 2019 and 31 March 2020. The purpose of this report is to share information with clinical teams working in organ donation, organ retrieval and transplantation about cases reported and investigated for this timeframe.

Acknowledgement

NHS Blood and Transplant Clinical Governance would like to thank all colleagues in the organ donation, organ retrieval and transplant community responsible for reporting clinical incidents and events to us. We are grateful to all clinical colleagues for providing the information required to investigate each case. Without the in-depth investigations and help from colleagues this report would not be possible. Thanks also to pathology and microbiology colleagues UK wide and all who have provided their expertise during the investigations

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Executive Summary

Organ Donation and Transplantation in the United Kingdom (UK) is an NHS success story. The last decade has seen a huge increase in the number of deceased donors and lifesaving or life transforming transplants. However, last financial year and this one has been different. Until February 2020, we were confident that we would once again see a UK record number of organ donors and transplants. Then the global COVID-19 pandemic hit in March and the impact was felt across the whole of the NHS. In March 2020 we witnessed a sharp reduction in activity with a decline in deceased donors as well as the number of transplants.

We observed a fall in the overall number of deceased organ donors - 1,580 compared to 1,600 the previous year. The impact of course was that the number of patients who received a deceased organ donor transplant fell from 3,952 during 2018/19 to 3,760.

Despite these challenges and even during the worst days of the pandemic during the first wave, we saw incredible family support for organ donation. We are grateful to all colleagues who have worked tirelessly to maintain organ donation, organ retrieval and transplantation throughout.

This report is intended to provide a resumé of cases where infection and cancers of possible donor origin have been investigated. It is a representation of what was reported to OTDT. Some additional cases of interest are also described.

During 1 April 2019 to 31 March 2020, 820 incidents were reported to OTDT. When incidents are reported to OTDT, they are classified under 6 main categories for investigation purposes and are outlined below:

- Donation (206)
- Organ Retrieval (182)
- Transplantation (185)
- Transplant Support Services (Organ offering and allocation) (106)
- Living Donation (12)
- Quality Assurance (129)

The number in brackets represents the number of reported incidents for that category.

Infection

The underlying principle remains that the risk of an infection being passed on through transplanted organs and tissues must be kept to an acceptable minimum. What constitutes an acceptable minimum is dependent on the balance of risk and benefit for the potential intended recipient in terms of either receiving that transplant or waiting until the next suitable organ offer. In some super-urgent and urgent situations, a higher risk of infection may be acceptable. The reports below reflect clinical incidents that have been reported or have come to the attention of OTDT, investigated and lessons shared.

Bacterial, parasitic, and fungal infections

ODT INC – *Leishmania donovani*

A liver recipient was reported to have been diagnosed with visceral leishmaniasis (VL) 4 months post-transplant. They were successfully treated with liposomal amphotericin B. Retrospective testing of the donor demonstrated serological evidence of prior exposure to Leishmania. The donor had been to India, an endemic area for Leishmania, in the previous 12 months .

Donor-derived infection was a plausible explanation; There were no alternative epidemiological links for the recipient other than having received an organ from a donor with proven Leishmania infection.

This was a liver only donor, hence there were no other recipients involved.

Leishmania infection is common in endemic areas of the world and there are no other reports of transmission via solid organ transplantation in non-endemic areas. Most infections are asymptomatic but untreated VL is often fatal. Imported infection is rare in non-endemic areas hence there is no screening during donor characterisation. Where donor or recipient epidemiological and clinical history is suggestive, VL should be considered in the diagnostic differential of compatible clinical presentation such as unexplained fever and pancytopenia.

ODT INC – *Escherichia coli*

E. coli was isolated from the liver transport fluid . The liver recipient had become septic within 24 hours from transplant, with E*.coli* isolated from blood cultures. Transplant centre microbiology confirmed that the same organism with similar antimicrobial sensitivities had been isolated from both organ transport fluid and recipient's blood cultures, supporting but by no means proving a possible common origin of infection.

The donor had a complex medical history which included diabetes (type 1), polycystic kidneys, previous pericardial effusions, lung sepsis and renal failure requiring haemodialysis. They also had a previous infection from a peritoneal dialysis site. Bacterial translocation in the donor remained as a possibility.

ODT INC – *Mycobacterium tuberculosis*

Two months' post lung transplant a recipient was readmitted into hospital, with possible sepsis. Following investigation, the recipient was found to be positive for *Mycobacterium tuberculosis* (MTB). They responded to quadruple anti-tuberculous treatment.

The donor was known to have come from an area where MTB is endemic but were not known to have tuberculosis. Routine pre-retrieval donor bronchial tissue and bronchoalveolar lavage samples tested negative for MTB. Following review of the donor and recipient history, it is possible that the donor had latent MTB with reactivation in the lung recipient due to immunosuppression. The strain was characterised and not found to be

associated with any clusters, outbreaks or cases reported in the UK, supporting but not proving an infection of donor origin. A different source of infection could not be ruled out.

The liver and kidney recipients tested negative for TB; the liver recipient received anti-tuberculous prophylaxis.

Viruses

ODT INC – Herpes Simplex Virus (HSV)-2

Liver recipient started to show signs of graft dysfunction at the end of the first week post-transplant. HSV-2 driven sub-acute liver failure was subsequently diagnosed: recipient was commenced on anti-viral treatment, to which they responded. The recipient was negative for HSV-2 antibody pre-transplant, confirming this to be a primary infection and not a reactivation of a pre-existing infection. Retrospective testing of donor serum showed that they were positive for HSV-2 antibody and DNA at the time of donation.

It is highly probable that the HSV-2 in the liver recipient was a donor-transmitted HSV-2 infection. Comparative molecular analysis of the strains was not possible. There was no evidence of HSV-2 infection in any of the 3 other organ recipients, possibly due to the fact that they were on prophylactic treatment for CMV; additionally, one recipient had serological evidence of pre-existing HSV infection.

The next two cases are related to Human Herpes Virus 8 (HHV-8) infection. HHV-8 testing is not required as part of organ donor characterisation.

ODT INC – HHV-8, liver transplantation

A liver recipient died of Kaposi sarcoma 6 months post transplantation.

Retrospective testing was performed on donor and recipient sera. This revealed that the recipient did not have detectable antibodies to HHV8 pre-transplantation, indicating a newly acquired, primary infection. Donor tested positive for HHV-8 antibody and DNA at the point of organ donation.

There were 3 other recipients. No evidence of HHV8 infection was demonstrated in the heart and one of the kidney recipients.

The other kidney recipient had evidence of seroconversion to HHV8 post-transplantation. They remain asymptomatic as regards to the HHV8 infection.

ODT INC – HHV-8, liver transplantation

A liver recipient transplanted nine years previously, developed Kaposi Sarcoma two years' post-transplant the donor was a liver only donor.

Search for donor and recipient archived samples was unsuccessful so no testing could be carried out. Review of cases did not reveal risk factors associated with HHV8 infection in the recipient, whereas potential risk factors were identified in the donor. There was insufficient evidence to assign imputability.

2.0 Malignancy

ODT INC – Papillary renal carcinoma

A papillary renal carcinoma was found on a deceased donor kidney; confirmed post-transplant. During retrieval, a lung nodule and kidney nodule were found and sent for frozen section histopathology.

The interim histopathology report detailed that the lung nodule could not be examined as calcified but did not appear malignant and the kidney nodule was a solid cyst and no malignancy identified. Two weeks later, tumour cells were identified on the kidney nodule following further immunochemistry testing. The final report was received and detailed a “Papillary Renal Carcinoma”. Centres informed and recipients will be monitored.

ODT INC – Hepatocellular Carcinoma

It was identified post transplantation, following discussion with the donor’s General Practitioner (GP), that the donor had a newly diagnosed hepatocellular carcinoma. This was not known prior to donation and transplantation. The donor had had a recent hospital admission but medical notes from that admission were not available. Despite numerous attempts, the GP was not contactable prior to donation, therefore this diagnosis was unknown prior to the donation. One kidney transplanted, centre informed.

ODT INC – Clear Cell Carcinoma

Excision of a lesion on a right kidney prior to implantation at transplant centre. The lesion was small and thought to be non-suspicious. The result was not followed up at the centre. 12 months later an internal audit took place that highlighted the result; clear cell carcinoma in the donated kidney. Recipient centres informed that a biopsy was done and the result circa a year post transplant.

Cases for Interest

ODT INC – Cytomegalovirus (CMV)

Two transplant recipients at the same centre were incidentally found to have detectable CMV viraemia around 7 weeks post-transplant. They were confirmed to be CMV antibody negative pre-transplant; due to lack of samples, it was not possible to ascertain when they had first become viraemic. Donor was CMV IgG , IgM and DNA negative at the time of donation.

This was a DCD donor who had received 4 units of RBC and was exposed to 7 units of RBC during A-NRP. All archives of these donations were tested and were negative for CMV DNA.

There was no evidence linking these infections with the transplanted organs or blood components.

ODT INC – Strongyloides

A post-mortem diagnosis of disseminated strongyloidiasis was made in a renal transplant recipient. Retrospective testing of donor and recipient sera demonstrated that the former was negative, and the latter was positive for strongyloides antibodies before the transplant. The recipient was from an endemic area and suffered reactivation of a pre-existing infection.

Conclusion

The benefit of reporting concerns post-transplant cannot be over-estimated. Timely reporting of incidents is important as it may affect the health of another transplant recipient and may inform clinical management of patients.

We would like to acknowledge all centres that continue to report to us but also encourage everyone to report rare, unusual and/or unsuspected findings post-transplant.

We would advise that any cancer diagnosed post-transplant is reported to OTDT.

In relation to infection, we would again advise that any unusual infection, unexpected occurrence, or something that may impact the health of another recipient is reported.

Please continue to do so via the link below:

https://www.odt.nhs.uk/odt-structures-and-standards/governance-and-quality/tell-us-about-an-incident/

Thank you to everyone involved in the organ donation, organ retrieval and transplant pathway for their continued help and support, and above all for reporting to us and assisting OTDT with our investigations.