A CASE STUDY

TRANSPORT PERFUSION FLUID

Daniel Weiand, Consultant Microbiologist and Educational Lead, reflects on the role of abdominal organ transport perfusion fluid culture.

A male in his 30s, with background of end-stage renal failure (ESRF) secondary to chronic glomerulonephritis (GN), underwent uneventful kidney transplantation in autumn 2016.

Seventy days post-operatively, he was readmitted with acute graft dysfunction, fevers, rigors and neutropenia. Ultrasound showed reduced renal perfusion, and a CT scan demonstrated a probable arterial pseudoaneurym.

He was taken back to theatre. Intra-operative findings included a completely thrombosed renal vein and iliac artery pseudoaneurysm.

The decision was made to perform graft nephrectomy and use a saphenous vein graft to mend the iliac artery.

In terms of relevant laboratory results, transport perfusion fluid (TPF) collected at the time of transplant (Day 0) led to isolation of *Candida albicans* (susceptible in vitro to fluconazole). Tissue from the iliac artery pseudoaneurysm (Day +70) also led to isolation of *C. albicans* (susceptible to fluconazole).

Fungal typing performed in Aberdeen demonstrated an identical multi-locus sequence typing (MLST) pattern for both isolates. Specimens sent to the histopathology laboratory demonstrated an abscess within the kidney (PAS stain, fig 1), as well as fungal spores and hyphae within the iliac artery (Grocott stain, fig 2).

Background

Infectious complications are among the major causes of morbidity and mortality in patients undergoing solid organ transplantation. However, the original source of such infections is often unknown. Proven donor-derived transmission of infection is an infrequent event.

What is transport perfusion fluid?

TPF mimics, in a simple fashion, the intracellular electrolyte balance of mammalian cells. A number of cell impermeant agents in the TPF prevent the cells from swelling during cold ischemic storage.

Different types of TPF are available for purchase from multiple manufacturers. For example, Soltran® is used for kidney transplants, and has a advertised (unopened) shelf-life of 15 months.

TPF is used in the process of transporting harvested abdominal organs from the donor hospital to the recipient hospital, where the transplant will take place.

The liver, pancreas, and kidney can be successfully preserved, by flushing the organs with TPF and storing them at hypothermia, to allow tissue matching and sharing of organs between transplant centres.

In line with European practice, all organs should be stored in three bags. In the inner-most bag, the individual organ is submerged in sufficient cold preservation solution. The bagged organ is then placed in a special transport box and covered with melting ice.

Specimen processing

Historically, clinical staff at most transplant centres, including The Newcastle upon Tyne Hospitals NHS Foundation Trust, have not sent TPF for culture from abdominal organs.

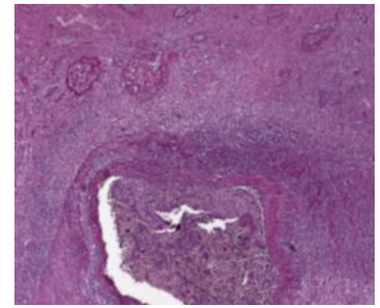

Fig 1. Abscess within the kidney (PAS stain)

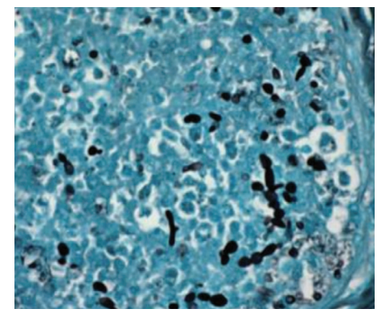

Fig 2. Fungal spores and hyphae within the iliac artery (Grocott stain)

In August 2016, NHS Blood and Transplant (NHSBT) requested that a specimen of TPF be collected for culture from every transplanted abdominal organ (i.e. liver, kidney and pancreas transplants).

In practice, organs arrive triple-bagged, and the outer-most bag is opened by a non-sterile assistant. The inner two bags plus organ are removed to the sterile perfusion tray. TPF is then sampled from the inner-most bag, and sent for culture.

There remains little guidance on how best to process TPF samples, nor how to manage positive cultures. In January 2018, NHSBT issued a statement acknowledging that "the process for reporting and receiving reports of transport fluid results has led to significant workload and confusion within centres".

> *"Almost a quarter of laboratories recommended against routinely culturing TPF because of concerns relating to the low positive predictive value of results"*

User surveys

In 2017, NHSBT conducted a survey of 25 microbiology laboratories servicing abdominal organ transplant programs. Responses were received from 14 out of 25 (56%) microbiology laboratories.

Almost a quarter of laboratories recommended against routinely culturing TPF because of concerns relating to the low positive predictive value of results. There was general consensus that a list of reportable organisms should be agreed, with most laboratories expressing an interest in isolation of yeasts from TPF.

In 2018, nephrology colleagues at the Newcastle upon Tyne Hospitals NHS Foundation Trust contacted all UK renal transplant units, focussing on "*Candida* positive-TPF" (CP-TPF).

Responses were received from six transplant units. Rates of isolation of *Candida* spp. from TPF varied from 2-10%, and treatment of organ recipients differed substantially. Some units were not routinely treating *Candida* spp. isolated from TPF, whilst others reported a "case-by-case" decision-making process, and one centre recommended 6 weeks' antifungal therapy for all cases of CP-TPF.

Local practice

At Newcastle upon Tyne Hospitals NHS Foundation Trust, between September 2016 and December 2017, 129 deceased donor kidney transplants were performed. An organism was isolated in 38 out of 129 (29%) cases, and *Candida* spp. were isolated from 14 out of 129 (11 %) cases.

All *Candida* spp. were reported as fluconazole-susceptible. Twelve out of 14 patients were treated with four weeks' oral fluconazole. Only one of the recipients with bacteria (rather than fungi) isolated from TPF was initiated on antibiotic therapy (Linezolid targeting MRSA isolated from TPF).

The road ahead

Candida spp. are isolated from TPF more commonly than thought, and are often pathogenic. The range and severity of complications in the recipients remains varied, suggesting recipient factors are most important.

Our unit now prescribes four weeks' appropriate antifungal therapy when *Candida* spp. are isolated from TPF. Defending our previous policy of no treatment is difficult because of the risk of serious infectious complications. However, the clinical significance of non-fungal isolates from TPF remains debatable.

A UK Standards of Microbiology Investigations (SMI) is needed to standardise and unify our TPF-related clinical and laboratory practice. Wide variation exists with regards to the pre-analytical, analytical, and post-analytical phases of specimen processing and reporting. A consultation process completed over the summer for a UK SMI for Abdominal Organ Transport Fluid testing. BMS

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