A problem of complexity could do with a simple solution

What happened and what were the issues/implications?

Human leukocyte antigen (HLA) typing – the determination of allelic variants of loci of the exceptionally polymorphic major histocompatibility complex – is used in organ transplantation to avoid antibody incompatibilities and minimise the risk of rejection (antibody and T-cell dependent).

While variations in most HLA loci (A, B, C, DR, DQ) were initially defined by serological methods, providing a minimum level of resolution still used today as the basis for organ allocation in the UK, HLA-DPB1 alleles have only been defined by DNA-based techniques. This means resolving the sequence of the cis-arranged variation in DPB1 exons, which requires a higher level of typing resolution.

Deceased donor typing must be ready within 4 hours of receiving the donor material, but full-length gene sequencing time currently exceeds this. Instead, rapid, lower resolution PCR-based methods have to be used. Occasionally, a donor carries a DBP1 allele that cannot be identified by such methods.

In the UK, about 1,500 deceased organ donors are referred for pretransplant HLA typing each year, typically outside of routine working hours. Complete HLA DPB1 types cannot be assigned in about 0.4% of these using the current, rapid techniques. For example:

The on-call tissue typist was unable to report DPB1 for a deceased donor because the result produced a rare HLA type which did not give assurance in the potential assigned type.

When this happens and a potential organ recipient is carrying HLA DPB1-specific antibodies, compatibility cannot be predicted. In these cases, a pretransplant crossmatch (donor cells + recipient serum) can be performed. This can delay the transplant decision

and increase the cold ischaemia time of the retrieved organs. Where such testing is impractical, because of a time limit for decision making, the donor offer may be declined.

What actions were taken?

In the above case, the available typing results were reported to NHS Blood and Transplant (NHSBT) Organ and Tissue Donation and Transplantation (OTDT) to allow the process of organ offering and allocation. In addition, the HLA laboratory provided the raw output DPB1 results produced by the analyser. Although this does not include a definitive result, it does contain information on the possible DPB1 alleles, plus a translation into the serological epitopes carried by the donor (even though these collectively could not be interpreted as a definitive DPB1 type). All the available information was then sent to the local H&I laboratories serving their respective receiving transplant centres. In some cases, the partial type, together with the raw data for DPB1, can be sufficient to allow a compatibility assessment to be safely made.

DNA sequence-based typing was completed over the following normal working days, after all transplants were undertaken and a correct HLA DPB1 type was determined.

In response to further, similar events, a survey was sent to H&I laboratories to understand the actual impact when their centre receives an offer of a donor that lacks completed HLA DPB1 typing.

What did you learn?

The currently available methods for pre-allocation deceased donor HLA typing are not capable of assuring that a full type can be achieved in all cases. There are possible workarounds, such as using all the data that are available.

The probable consequences of not having a complete donor HLA type vary between transplant types if the potential recipient carries antibodies corresponding to the missing HLA. For kidneys, the majority of centres indicated that a wet crossmatch would most likely be performed. This could add delays to the process leading to transplantation plus additional costs. For cardiothoracic transplantation, declining the offer was a likely consequence.

Because of the nature of deceased donor organ allocation, where donor testing is performed in 1 centre with transplantation at multiple centres, this issue is common to all H&I laboratories. Sharing experiences and workarounds certainly helps, but the root cause, a matter of complexity, requires a technical solution. In simple terms, we need to be able to sequence the full length of DPB1 genes (and the rest) precisely and within around 4 hours from sample to reporting, day or night.

How was the learning shared?

The lack of a full HLA type for a deceased donor is considered a quality incident, which is reviewed locally and by NHSBT-OTDT.

The UK-wide survey replies were compiled and presented at an annual conference of the British Society for Histocompatibility and Immunogenetics.

All HLA typing quality events relating to deceased donor HLA typing are presented at an annual workshop hosted by H&I NEQAS.

Submit a case study of your own and claim CPD credits

(Please ensure a word count of 700 words or less.)

Help the College's patient safety work by sharing your knowledge and experiences with colleagues.

Reflect on something that impacted or may have impacted on patient safety. The case study should describe care that went well or not so well and why.

We would also like to hear:

- how this was approached and resolved, either on an individual or team basis and/or by the wider system
- what was learned
- how this was shared.

Reflection is a valuable learning tool and constitutes high quality CPD. If you send us your own case study, you may claim 1 CPD credit per case study and enter this in your online CPD portfolio.

Please submit your own case study to cpd@rcpath.org using the template provided and enter this in your online CPD portfolio. You may claim 1 CPD credit per case.

The best case studies will be published in future Patient Safety Bulletins.

Please ensure that your employing organisation is aware of the incident.