The Royal College of Pathologists
Pathology: the science behind the cure

PATIENT SAFETY
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HLA typing – a cautionary tale

Human leucocyte antigen (HLA) typing of a potential deceased donor performed on call by polymerase chain reaction (PCR), using commercially available typing kits, generated an ambiguous result at the HLA-A locus. The result could either have been homozygous (only one antigen present) or heterozygous (two antigens present). The laboratory chose to report the heterozygous result, as it was considered clinically safer to do so. The liver and both kidneys from the donor were allocated and transplanted.

The laboratory subsequently performed next generation sequencing (NGS), which revealed the true result to be homozygous. A revised HLA type was issued and recipient centres were notified. The recipients of the organs were not affected by the revision to the HLA type.

A CAPA (corrective action, preventative action) was raised in the laboratory and a root cause analysis performed. The findings were shared with all staff who perform the technique. An example of a true heterozygous result was obtained for comparison with the result obtained on call, to aid future interpretations.

The incident was reported on the organisation's internal risk management system as a near miss. It was also reported to the Organ Donation and Transplantation (ODT) service's incident reporting system and to the HLA typing kit manufacturer, with a request for the kit to include further assays to help improve discrimination.

The recipient centres later raised concerns that the revised report was confusing and lacked sufficient explanation.

Patient safety issues

1. Laboratory error

HLA typing has always been plagued by difficulties in discriminating similar HLA results and it is difficult to completely mitigate the risk of a similar situation occurring in the future. The clinical impact of reporting HLA results must always be considered. Despite this incident, this laboratory cannot justify the expense and resources necessary to sustain a back-up rapid HLA typing method for the exceptionally rare instances where it would be beneficial. In this case, repeat testing using the same technology would not have resolved the ambiguity. Given that the majority of laboratories nationally are currently using the same kit, referring the sample to a second laboratory for testing would also not have resolved the ambiguity.

2. Communication of amended report

The recipient centres were confused by the revised report as the nature of the revision had not been described. The HLA typing laboratory could have been clearer that a high-level revision had taken place. In addition, ODT did not forward the explanatory message provided by the laboratory when forwarding the report.

Opportunities for shared learning

Other laboratory tests have similar challenges with insufficient discriminatory accuracy. This case highlights how high the stakes are when rapid turnaround is required, back-up testing is not immediately available and errors may have serious or life-threatening consequences to patients.

In the case of our scenario, helpful actions included: supplying a 'true positive' for staff to refer to when ambiguous results are generated; raising awareness of the issues with laboratory staff, ODT and front-line clinical teams; and suggesting a potential solution to the kit manufacturer.

The unclear revised report and the ODT's failure to forward the explanation are noteworthy. No harm ensued but this was another near miss. Failures in communication or follow-up of critical or unexpected findings is a nationally recognised patient safety risk. And risk is compounded when initial reports are subsequently amended.

A recent Health Safety Investigation Branch (HSIB) report has looked at factors influencing the communication of test results as well as opportunities to mitigate risk of occurrence.[1] HSIB's focus is unexpected significant findings in x-rays, but its recommendations are relevant to all diagnostics. These include the requirement for agreed thresholds for alerting front-line teams of critical or unexpected results, notification of patients after an agreed timeframe, and monitored test result acknowledgement systems.

[1] Healthcare Safety Investigation Branch. Failures in Communication or Follow-up of Unexpected Significant Radiological Findings. July 2019. www.hsib.org.uk/documents/135/hsib_report_failures_communication_follow_up_unexpected_significant_radiological_findi.pdf