The clinical relevance of non-HLA antibodies in antibody-mediated rejection in a single centre kidney transplant patient cohort

BACKGROUND

It has been well established that anti-HLA donor-specific antibodies (DSAs) are the main cause of antibody-mediated rejection (AMR). There is anecdotal evidence, however, that non-HLA antibodies might be involved in AMR episodes after solid organ transplantation with an increasing number of patients presenting with pathological features of AMR in the absence of anti-HLA DSAs. Furthermore, AMR has been seen in recipients following transplantation from a HLA identical sibling. Whilst there is evidence that AMR can be caused by non-HLA donor-specific antibodies, this area has not been investigated extensively and there is uncertainty surrounding the circumstances in which these antibodies are generated and the development of their pathogenic potential.

RESULTS

Of the 60 non-HLA markers, a significant difference (p < 0.05) in pre- and post-transplant mean fluorescence intensity (MFI) values was seen in 15 markers. Lower MFI values were seen post-transplant for all 15 statistically significant markers. Of these, 5 markers met the suggested cut-off value to be classed as positive – Actin (p = 0.03), Collagen II (p = 0.004), Collagen III (p = 0.02), HARS (p = 0.02) and LGALS3 (p = 0.0006).

DISCUSSION

A significant difference in pre- and post-transplant MFI values was seen in 25% of the non-HLA markers tested. Interestingly, significantly lower MFI values were seen post-transplant across all of these markers. However, it was expected that non-HLA antibody MFI values would have been higher post-transplant as this would suggest a potential role for these antibodies in patients with suspected AMR but no anti-HLA DSA. Lower non-HLA antibody MFI values post-transplant could be explained by the effects of immunosuppressive drugs given to patients following transplantation. All 23 patients had antibodies against at least one non-HLA antigen. This suggests that these antibodies might be autoimmune in nature.

CONCLUSIONS

Graft rejection is multifaceted and the potential effects of non-HLA antibodies in graft rejection are poorly understood. There also may be other factors that influence the pathogenicity of non-HLA antibodies on allografts. Further research is required in this area. In particular, larger, collaborative studies could aid in establishing the clinical relevance of non-HLA antibodies in solid organ transplantation. Further research could also include an investigation of the relevance of non-HLA antibodies in patients with AMR in the presence HLA DSA.

REFERENCES


METHODS

• 10μl patient serum added to 40μl non-HLA beads. Incubate at 22°C for 30 mins in the dark on a rotating platform
• 3 washes with 250μl wash buffer
• 50μl conjugate added (1 in 10 dilution). Incubate at 22°C for 30 mins in the dark on a rotating platform
• 150μl wash buffer added to each well and plate run on either Luminex® LABScan3D™ or Luminex® 200™ platform

Assays are performed in 96 well filter plates. Supernatants were discarded using a vacuum manifold.