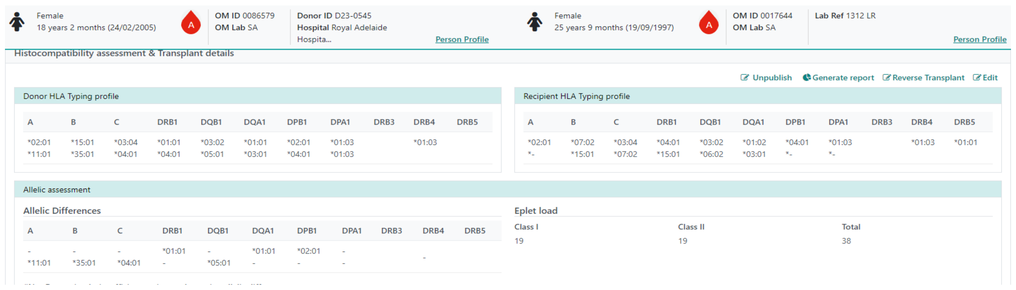
Differential adsorption of HLA and non-HLA antibodies following combined liver and kidney tranplantation

Authors LAKE M[1], EMERY T[1], LEAHY R[1], TSIOPELAS E[1], MCDONALD K[1], SULLIVAN H[1], MUNASINGHE W[1], DEAYTON S[1], GALEA J[1], BILOGREVIC F[1], FLEET A[1], SULLIVAN L[1], CARROLL R[1,]

[1]South Australian Transplantation and Immunogenetics Service, Australian Red Cross Lifeblood

Introduction: A 26-year-old female with primary hyperoxaluria had previously received 2 liver transplants (Tx). The first in 2015 was complicated by hepatic artery thrombosis and the second in 2021 complicated by chronic rejection and chronic renal failure, she was relisted in 2023 for combined kidney liver transplant. cPRA 99%, with very high titre of antibodies (Ab) to AT1R (>400 U/ml). A deceased donor match was received, which involved crossing a strong donor specific antibody (DSA) to HLA-A*11 (MFI 15000, 10/05/2023, Figure 1) and a DSA to DRB1*01 (MFI 1500). Flow cytometry crossmatch (FXM) was a positive T-cell and positive B cell FXM. The patient received peri operative plasma exchange (PLEX) and low dose candesartan.



Methods: AT1R antibodies were tested using a sandwich ELISA, neat and 1:10 dilution (Cell Trend GmbH, Germany, now One Lambda Canoga Park, CA). Serum for HLA antibody detection were treated with EDTA & tested using Luminex Single Antigen assay (LABScreen™ Single Antigen, One Lambda, Canoga Park, CA). Other non HLA antibodies were tested using Luminex Autoantibody assay (LABScreen™ Autoantibody, One Lambda, Canoga Park, CA)

Result: There was a minor reduction in A*11 antibody MFI with pre operative PLEX but a profound reduction 2-4 hours post liver perfusion (See Figure 1) and the FXM become weak positive and AXE protocol revealed similar results to the FXM. Two more post operative PLEX sessions were performed as per the local AT1R Ab management protocol for kidney allografts. Initially there was good urine output and creatinine fell. However subsequently the patient develop bleeding diathesis and PLEX could not be continued. After the sessions of PLEX were stopped the patient developed new liver and renal graft dysfunction lasting 6 weeks. Biopsies were consistently negative for C4d, however all showed severe acute tubular necrosis (ATN) . The HLA DSA deceased in strength at 6-weeks post-Tx (HLA-A*11 MFI 5000, DQB1*05 MFI 1000), whereas the AT1R Ab levels remained at >400 U/ml. Liver and kidney function normalised at 3-months post-transplant. At 15 months post transplant HLA DSA were undetectable, AT1R levels remain high. Over the same time period non HLA autoantibodies were investigated (Figure 2a,2b,2c,2d). Those targets with a previous publication of risk of graft loss/dysfunction (1,2) – together with those with significant changes are shown. There was a decrease after PLEX and transplant with a subsequent rebound of antibodies to PTPRN and HNRNPK.

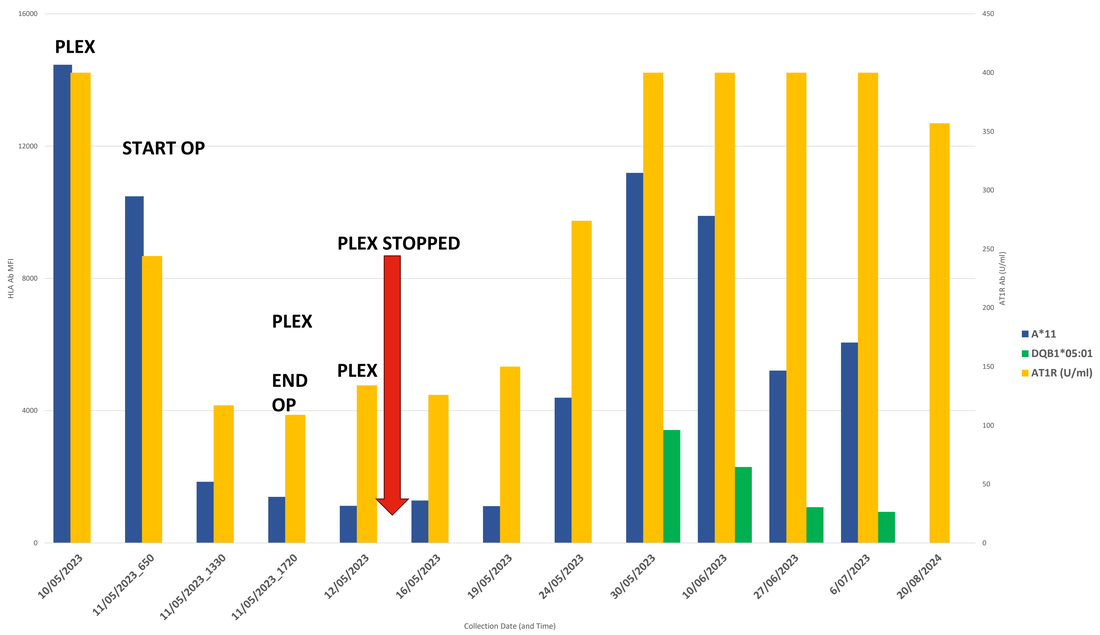


Figure 1: Temporal changes in HLA Ab (HLA-A*11 (blue) and HLA-DQB1*05:01 (green)) and AT1R Ab (yellow) following combined liver/kidney transplantation. Transplantation was performed on 11/05/2023.

Figure 2a, 2b, 2c, 2d: Temporal changes in group 1 non HLA Auto Antibodies following combined liver/kidney transplantation. Line shows 95% threshold for healthy controls

Conclusion: Liver-kidney transplantation is associated with adsorption of both HLA and non HLA DSA including AT1Ab. In this case the recurrence of very high levels of AT1Rab was associated with severe ATN and prolonged graft dysfunction. AT1Rab have been shown to be associated with prolonged ATN (3). Antibodies to HNPRK and PTPRN both showed major reduction after liver transplantation and these antibodies have been associated with rejection. The only other antibodies to show significant changes were PRKCH and CHA1B.

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