Hitching a ride: a case of passenger lymphocyte syndrome with donor-derived HLA-specific antibodies in solid organ transplantation

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Introduction

Passenger lymphocyte syndrome (PLS) occurs when donor immune cells (memory B cells, plasma cells) are transferred with an allograft and result in the production of donor-derived antibodies. PLS is most associated with ABO-mismatched transplants, where donor-derived ABO antibodies target recipient blood cells leading to hemolysis. PLS is often in grafts rich in lymphoid tissue, such as lung and liver, and is typically self-limiting. Here, we report two novel cases of donor-derived HLA specific antibodies identified in previously unsensitized recipients following transplantation.

Cases:

Case 1 (Figures 1 & 2)

- A 63-year-old woman underwent simultaneous liver-kidney transplantation from a deceased donor with an 8/10 HLA antigen mismatch.
- Despite a pre-transplant cPRA of 0%, single antigen bead (SAB) testing 3 weeks post-transplant demonstrated a cPRA of 85%. New antibodies were not donor specific, and that recipient had not received blood products.
- Testing of pre-transplant donor serum revealed a nearly identical HLA antibody profile, indicating that newly detected antibodies were likely donor-derived.
- Some antibodies present in the donor were absent from the recipient post-transplant. These antibodies may have been absorbed by recipient tissues as recipient-specific antibodies, particularly those targeting recipient HLA-B51.
- **Eplet analysis** identified the shared eplet 80I+69TNT on recipient HLA-B51 and B49 B52 B53 B59 B77. These antigens were present in the donor profile but were absent in the recipient serum, supporting absorption by HLA-B51 positive recipient tissues.
- Consistent with the expected course of PLS, donor–derived HLA antibody levels were transient and declined post-transplant at a rate consistent with antibody half-life.

Case 2 (Figures 3)

- A 61-year-old man underwent liver transplantation from a deceased donor and is currently awaiting a kidney transplant.
- Despite a pre-transplant cPRA of 0%, SAB testing 2 weeks post-transplant revealed a cPRA of 99%. New HLA class I antibody reactivity was not donor-specific.
- Testing of pre-transplant donor serum revealed a similar antibody profile; however, antibody reactivity in the recipient was stronger, suggesting reactivation of donor memory B cells.
- Comparison of donor antibody profile with the recipient's 2-week post-transplant serum diluted 1:64 and 4-month post-transplant sample demonstrated a nearly identical reactivity pattern.
- Consistent with the expected course of PLS, donor–derived HLA antibody levels were transient and have continued to decline post-transplant.

Case 1:

No HLA antibodies were identified in the recipient pre-transplant.

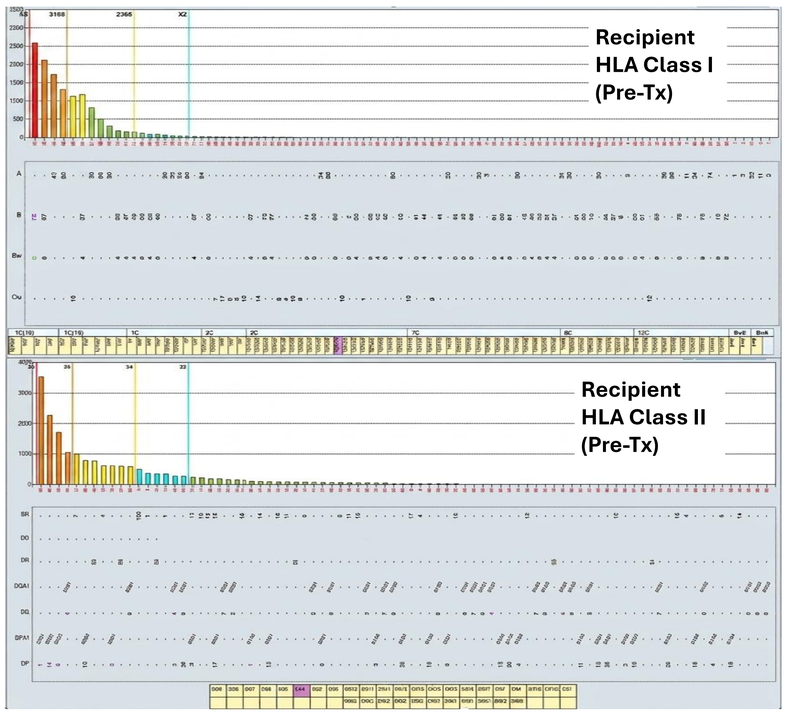


Figure1: Recipient pre-transplant HLA antibody profile. Testing of pre-transplant recipient serum using the Rapid Optimized single antigen Bead assay (ROB) assay demonstrated no HLA specific Class I (top panel) or Class II (bottom panel) antibody reactivity.

Comparison of recipient and donor HLA antibody profiles demonstrating shared donor-derived reactivities and a recipient-specific eplet.

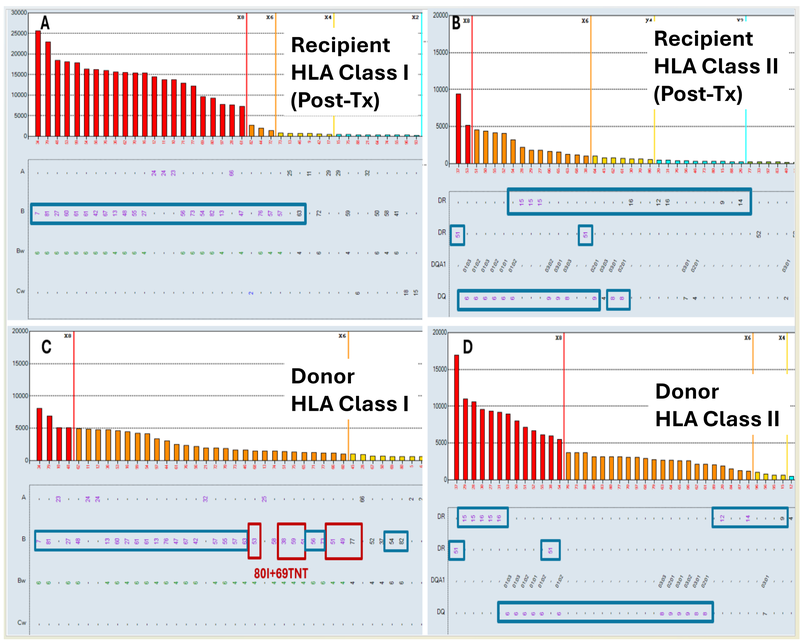


Figure 2: Single antigen bead assay results demonstrating the HLA antibody profile of the recipient serum 2 weeks post-transplant (A,B) and donor (C,D). HLA antibody reactivities shared between the donor and recipient are highlighted in blue boxes. Eplet 80I+69TNT which is shared by recipient antigen HLA-B51 and B49, B52, B53, B59, B77 is highlighted in red boxes and only present in the donor profile.

Case 2:

Donor-derived HLA class I antibodies in recipient serum demonstrate transient persistence following liver transplantation.

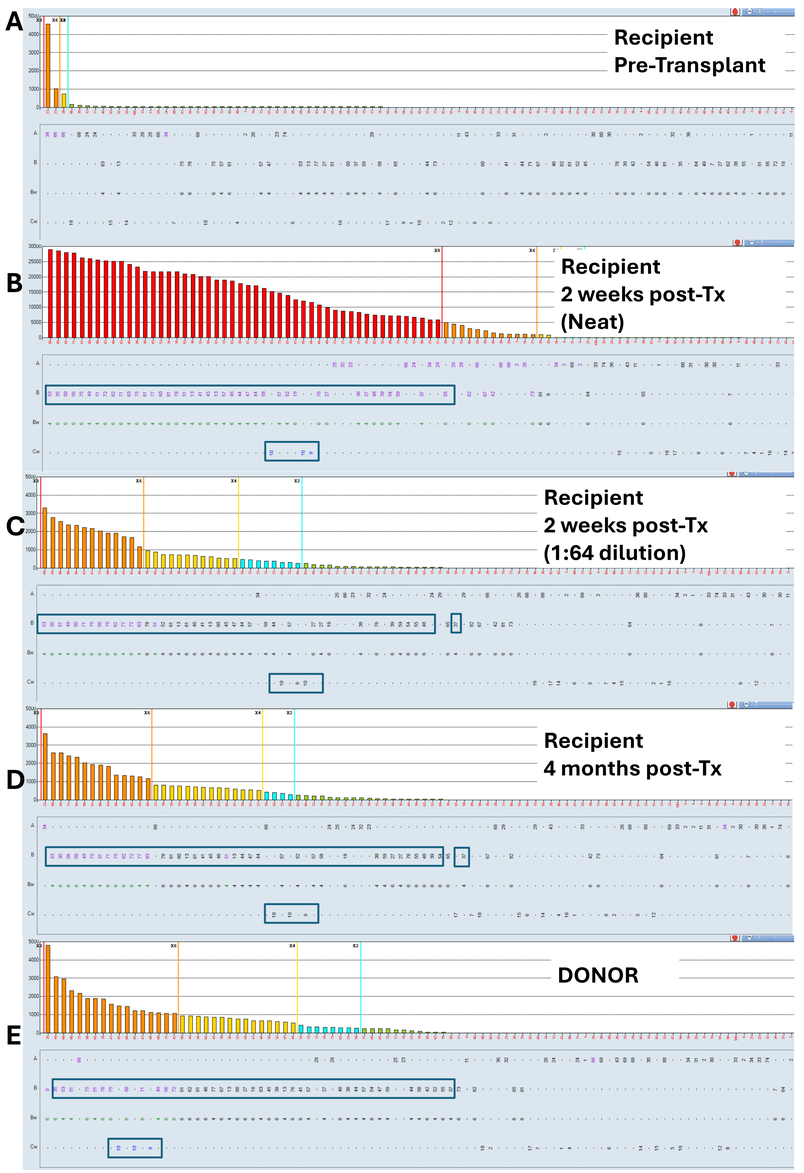


Figure 3: Comparison of HLA class I histograms for recipient serum obtained pre-transplant (A), 2 weeks post-transplant (B), 2 weeks post-transplant following 1:64 dilution (C), and 4 months post-transplant (D), along with donor serum (E). The recipient's post-transplant antibody profile closely reflects that of the donor, consistent with passenger lymphocyte syndrome. Similar reactivity levels observed in the 1:64 diluted 2-week and 4-month post-transplant sera further support the transient nature of the donor-derived antibodies and are consistent with the expected ~ 3-week half-life of IgG.

Conclusions

We describe 2 cases in which recipients developed de novo HLA antibodies early post-transplant. New HLA antibodies were not donor specific and antibody profiles were nearly identical to those detected in donor sera, consistent with passenger lymphocyte syndrome. In one case, a recipient specific antibody was identified in the donor but not the recipient, likely due to absorption by recipient tissues. Donor-derived antibodies were transient and declined over time. These cases highlight the importance of recognizing PLS as a possible source of de novo post-transplant HLA antibodies. Caution is warranted when assigning unacceptable antigens based on donor-derived reactivity, particularly in liver recipients awaiting kidney transplantation, as these antibodies can markedly increase cPRA.