Achieving Successful Transplantation Despite Positive Virtual Crossmatches

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Introduction

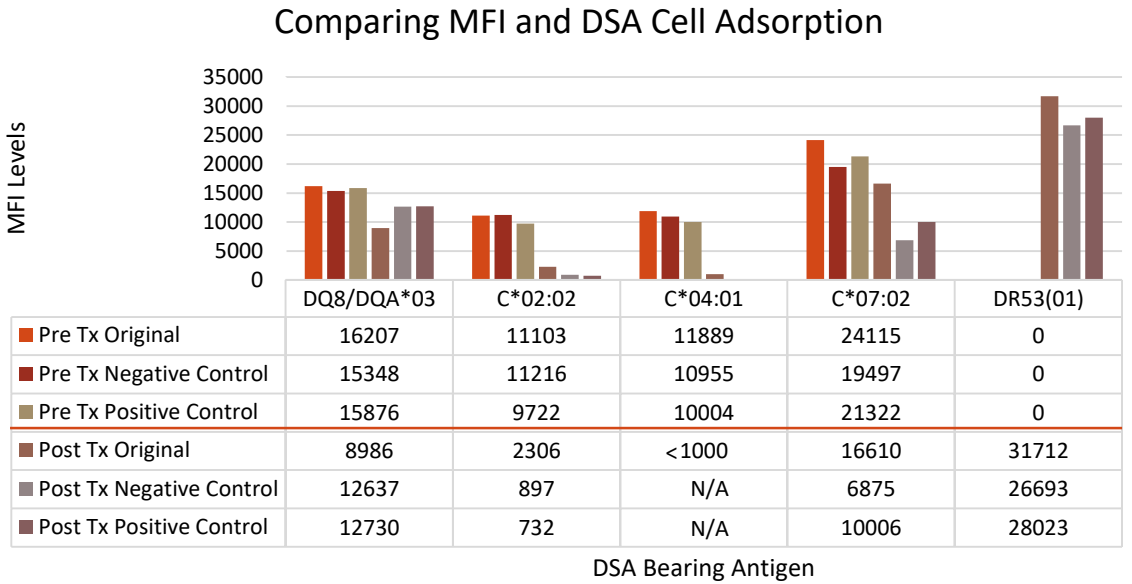
- Identifying clinically appropriate HLA antibodies is crucial for determining suitable donor-recipient matches for virtual crossmatches and post-transplant monitoring.
- Patients with high CPRA have fewer compatible donors, limiting potential matches for allocation.
- Donor specific antibodies (DSA) was evaluated in four successful transplants that previously had a positive virtual with MFI greater than 4000 for the ability to bind to selected surrogate donor cells by adsorption that bear relevant DSA antigens.
- An additional case was evaluated with DSA that developed 2 years post transplantation
- MFI of the DSA were compared with original and adsorbed sera of pre and post transplants.
- The results showed that the DSA did not bind to the cells, indicated they were biologically irrelevant for transplantation.

Materials and Methods

- 5 cases are presented.
- HLA typing was performed by NGS and SSO.
- Identification of HLA antibodies utilized single antigen bead (SAB) and C1q assays by One Lambda.
- Non-HLA antibody was detected by One Lambda AT1R ELISA assay.
- Physical crossmatch was performed by flow cytometry.
- Patient's sera were adsorbed with donor's blood that contained pertinent DSA bearing antigens (positive control) and with donors that did not contain DSA (negative control).

	cPRA	C1q	AT1R Pre-Tx (U/mL)	AT1R Post-Tx (U/mL)	Pre-Tx DSA
Case 1	56%	<1000	6.79	7.42	DQ8/DQA*03
Case 2	79%	<500	8.90	8.74	C*02:02
Case 3	63%	<500	9.04	7.03	C*04:01
Case 4	99%	<500	5.64	10.86	C*07:02
Case 5	0%	Not Tested	18.7	16.3	Post-Tx: DR53(01)

Figure 1: Cases 1-3 are Heart Tx and 4-5 are Renal Tx . CPRA, C1q, and AT1R testing were performed. Cases 1-4 had antibodies prior to organ transplant. Case 5 was the only recipient that developed de-novo DSA as pre-TX was negative.



	DQ8/DQA*03	C*02:02	C*04:01	C*07:02	DR53(01)
Pre Tx Original	16207	11103	11889	24115	0
Pre Tx Negative Control	15348	11216	10955	19497	0
Pre Tx Positive Control	15876	9722	10004	21322	0
Post Tx Original	8986	2306	<1000	16610	31712
Post Tx Negative Control	12637	897	N/A	6875	26693
Post Tx Positive Control	12730	732	N/A	10006	28023

Figure 2: Pre-transplant and post-transplant serums were adsorbed with surrogate donor cells that contained pertinent pre-transplant DSA for cases 1-4. Case 5 was adsorbed with donor cells bearing post-transplant DSA. The adsorbed serums were also compared against patient's original serum. MFI levels were used to compared these serums.

Results and Discussion

- Four cases had a positive virtual, but negative physical crossmatches.
- Cases 1-4 had negative C1q testing, indicating antibodies detected prior to transplant were clinically irrelevant.
- In addition, case 5 with de-novo DSA against DR53 is shown to demonstrate recipients that developed DSA without AMR and possible false positive reactivity of some antibodies.
- There were no significant changes from pre- and post-transplant AT1R levels.
- After adsorption of patient's sera with lymphocytes from surrogate donor that carried pertinent DSA, the DSA was still detected and could not be removed by adsorption.
- These findings are important as it challenge the traditional understanding of the implications of a positive virtual crossmatch.
- Patients may safely receive solid organ transplantation with clinically insignificant HLA antibodies and high MFI values, provided that the physical crossmatch is negative.
- All five cases continued to do well without any allograft dysfunction or signs of rejection for up to four years.
- This study demonstrate that transplant may be possible despite a positive virtual for highly sensitized patients is . Many of these patients face challenges of a limited organ donor pool.