Clinical Relevance of Human Leukocyte Antigen (HLA) Antibodies

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Introduction

- Accurate HLA antibody detection is critical for the allocation and exclusion of donors, virtual crossmatch, and post-transplant monitoring for DSA and AMR.
- Laboratories have encountered difficulty with non-specific binding and, thus, detection of clinically irrelevant HLA antibodies with SAB testing.
- The summarized cases show that transplants may be performed across clinically irrelevant antibodies. These findings may affect the proper allocation of organs to patients while preventing AMR.

Materials and Methods

- 5 patients are presented.
- HLA antibodies were tested by SAB and C1q.
- Crossmatch was performed by flow cytometry.
- HLA typing was performed by NGS and SSO.

Results

- Clinically irrelevant HLA antibodies in class I may include A2, A11, A23-24, A34, A80, B8, B13, B44-45, B67, B76, B82, C07, C12, and C17.
- Clinically irrelevant HLA antibodies in class II may include DR1, DR4, DR9-10, DR51-53, DQ2 (DQB1*02:01 / DQA1*05:01), and DQA1 pattern with DQB1*4, 5, 6 or 7, 8, 9.

Heart Transplants

- Patient 1 was transplanted with DSA against DQ8 (MFI 16,207). The pattern looked more like DQA1 antibodies.
- Patient 2 was transplanted with DSA against C*02:02 (MFI 11,103).
- Patient 3 was transplanted with DSA against C*04:01 (MFI 11,889).
- All 3 patients' DSA were negative by C1q and flow crossmatch.
- All 3 continue to do well without any allograft dysfunction or signs of rejection.

Renal Transplants

- Patient 1 had a high PRA of 99.87 and DSA against a potential donor (C*07:02; MFI 24,115).
- Patient was transplanted with negative crossmatch and desensitization treatment.
- Patient had no complication of AMR.
- Patient 2 had weak DSA against A*02:01 (MFI 1,695).
- The patient received a transplant and continues to do well without any allograft dysfunction or signs of rejection.

Discussion

- As demonstrated for the first time, patients may safely receive solid organ transplantation with either weak or clinically irrelevant HLA antibodies and high MFI values but a negative crossmatch.
- All patients had negative C1q testing by SAB, which also indicated that these antibodies were weak or clinically irrelevant.
- All patients have had good graft survival for up to two years.
- These findings are critical for properly allocating organs for highly sensitized patients. Many of these patients had high CPRA, meaning they faced the challenges of a small UNOS donor pool.
- By eliminating one of the hurdles they face with clinically irrelevant HLA antibodies, these patients will have a better chance of receiving a transplant while also avoiding AMR.

Heart Tx	CPRA	Pre-Transplant DSA	Pre-Transplant MFI	C1q	1 month post	6 months post	1 year post	1.5 year post	2 years post
Patient 1	56%	DQ8 / DQA1*03	16,207	<1000	16,610	18,102	9,891	8,232	13,286
Patient 2	79%	C*02:02	11,103	<500	3,149	1,892		Not tested	Not tested
Patient 3	63%	C*04:01	11, 889	<500	35	0	271		

Renal Tx	CPRA	Pre-Transplant DSA	Pre-Transplant MFI	C1q	1 month post	6 months post	8 months post	1 year post	1.5 year post
Patient 1	99%	C*07:02	24,115	<500	16,610	5,115	5,154	9,260	3,822
Patient 2	45%	A*02:01	1,695	Not tested	Not tested	Not tested	4,397	Not tested	Not tested