THE DIFFERENTIAL IMPACT OF IMMUNOSUPPRESSANT WITHDRAWAL AFTER GRAFT FAILURE ON *DE NOVO* CLASS I AND II ANTIBODY DEVELOPMENT

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INTRODUCTION

A 62-year-old Filipino female who lost her first kidney graft due to chronic allograft nephropathy 21 years post-transplant was listed for evaluation for a second kidney transplant. The patient was withdrawn from immunosuppressants (IS) at the time of relisting; the patient did not receive a nephrectomy. The patient had been at 0% cPRA at the time of transplant and remained so over the life of the graft.

METHODS

The donor HLA typing was performed at the time of transplant in 2001 using Terasaki HLA Tissue Typing Trays and Lambda Monoclonal Trays (One Lambda). The recipient HLA typing was performed upon relisting using LinkSeq PCR Typing (One Lambda).

Recipient anti-HLA antibody testing was performed prior to transplant using Lambda Cell Trays (One Lambda). Prior to and after relisting, the recipient's anti-HLA antibody testing was performed using LABScreen PRA and Single Antigen kits (One Lambda).

RESULTS

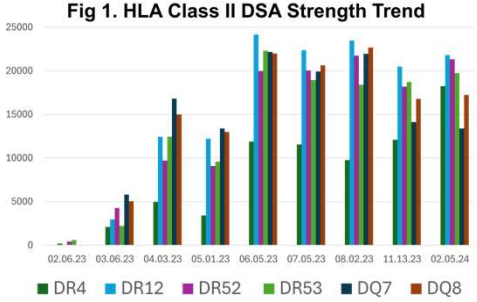
Table 1. Patient and Donor HLA (Mis)Matching

	A	*B*	*C*	*DRB1*	*DRB 3,4,5*	*DQA1*	*DQB1*	*DPA1*	*DPB1*
Patient	34	61	7	15	51	01	5	02	01:01
	34	61	7	15	51	01	5	02	01:01
Donor	24	35	NT	4	53	03*	8*	NT	NT
	31	39	NT	12	52	05/06*	7*	NT	NT

The donor's HLA-C, -DQ, and –DP loci were not tested (NT) at the time of transplant in 2001. HLA-DQA1 and -DQB1 typing (*) was imputed using the Haplostat Asian Pacific Islander dataset. Donor HLA mismatches are indicated in red.

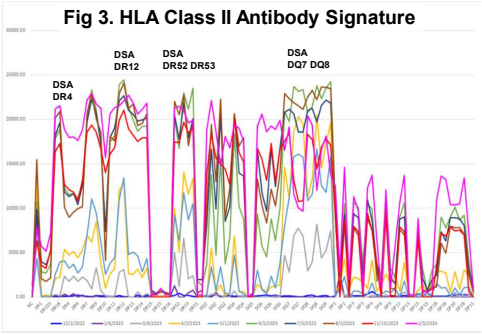
RESULTS

Fig 1. HLA Class II DSA Strength Trend



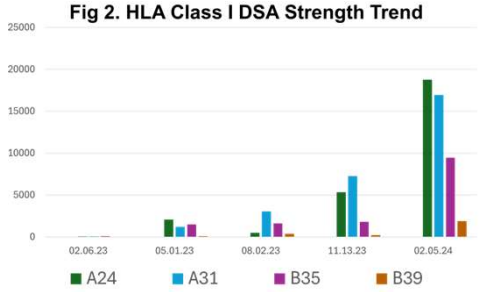
Two months after IS withdrawal (ISW), the patient's cPRA remained 0%. Three months post ISW, her cPRA increased to 91%. De novo Class II DSAs were detected with MFIs ranging from 2000-7000. The strength and breadth of Class II antibodies continued to increase. Five months post ISW, the HLA-DR and -DQ DSA strengths plateaued, and the cPRA reached 100%. Six months post ISW, intermediate level HLA-DP antibodies were detected, with MFIs ranging from 7000-9000.

Fig 3. HLA Class II Antibody Signature



RESULTS

Fig 2. HLA Class I DSA Strength Trend



Eight months post ISW, two weak Class I DSAs A31 (MFI 2,500) and B35 (MFI 1,420) were detected. Eleven months post ISW, Class I DSAs strength reached intermediate levels. At that time, -C antibodies were first detected (MFI 5000-10000). Only after 14 months post ISW did B35 DSA and most -C antibodies reach levels equivalent to the -DP antibodies 6 months post-ISW. Only one mismatched HLA, B39, remained negative.

CONCLUSIONS

Optimizing the HLA match, with an emphasis on -DR and -DQ, remains an important factor to decrease the alloreactivity between donor and recipient and the chance of *de novo* DSA development.

The complete HLA mismatch between the recipient and the donor in this case is likely significant to the breadth of sensitization that developed. All of the developed antibodies shared epitopes or cross-reacted with the immunizing epitopes of the failed graft.

HLA-DQ and -DR DSAs developed months earlier compared to Class I DSAs, with about ten times the strength of the Class I DSAs. HLA-C and -DP antibodies were the last *de novo* antibodies to develop and the weakest developed antibodies, likely due to cell surface expression.