Impact of donor Ublituximab-treatment on crossmatch results

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Introduction

Interfering drugs in patient serum can cause false reactions in Flow crossmatch. Here we report a case where treatment of donor resulted in interference in crossmatch by eliminating B-cells

Method

This case utilizes the HLA typing and Flow crossmatch method. For allo-crossmatch, donor lymphocytes are mixed with patient serum and patient antibodies which are bound to donor cells are detected by anti-human IgG antibody attached to FITC. Florescence is a readout for recipient antibodies bound to donor lymphocytes. Comparison with a negative control serum devoid of antibodies provides a fluorescence channel shift. At our center, a shift of 100 is considered positive for both T cell and B cell flow crossmatch. In contrast, an auto-crossmatch, mixes recipient lymphocytes with recipient serum to detect recipient antibodies bound to their own cells. Virtual crossmatch is interpreted by comparing donor HLA typing with recipient antibody profiles.

HLA	A	B	C	DRB1	DRB 3/4/5	DQB1	DQA1	DPB1	DPA1
Recipient	30:02	42:01	17:01	03:02	3*01:01	04:02	04:01	01:01	02:02
	23:01	07:06	07:02	11:01	3*02:02	06:02	01:02	17:01	02:01
Donor	02	51	14	14	5*01	05:03	01	04:02	01:03
	32:01	51	16:02	15	3*02	06:02	01	04:01	02:01

Figure 1. HLA Typing of donor and recipient.

Conflict of interest

Authors have no conflict of interest.

Results

Serum Date	Serum #	CSN	Component	Rpt Interpretation
10/01/2025	S-216568		Potential dHLA	A2 A32; B51 B51; Bw4 Bw4; Cw14 Cw16; DR14 DR15; DR52 DR51; DQA01 DQA01 DQ5 DQ6 DPA01:03 DPA02:01 DPB04:01 DPB04:02
10/01/2025	S-216568		DSA and MFI	NO DSA
10/01/2025	S-216568		Virtual XM Result	CURRENT NEGATIVE
06/28/2021	S-160247		Potential dHLA	A2 A32; B51 B51; Bw4 Bw4; Cw14 Cw16; DR14 DR15; DR52 DR51; DQA01 DQA01 DQ5 DQ6 DPA01:03 DPA02:01 DPB04:01 DPB04:02
06/28/2021	S-160247		DSA and MFI	ANTI HLA DPB1*04:01 (MFI 2717)
06/28/2021	S-160247		Virtual XM Result	HISTORIC NEGATIVE

Figure 2. Virtual crossmatch result. There was no DSA in the current sample.

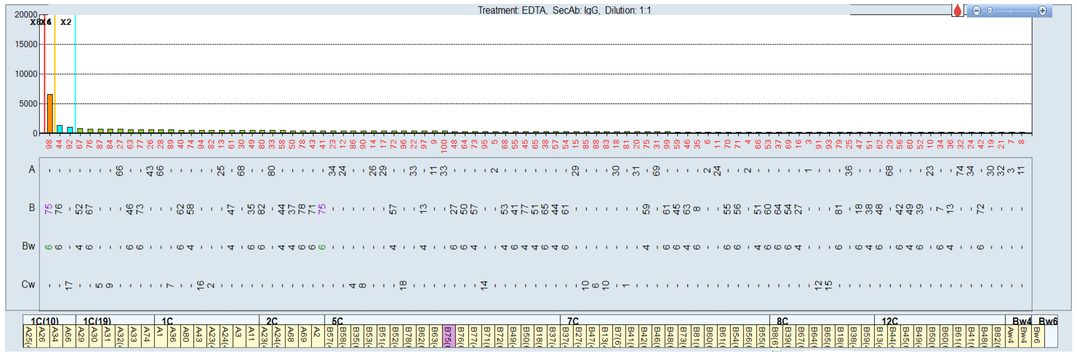
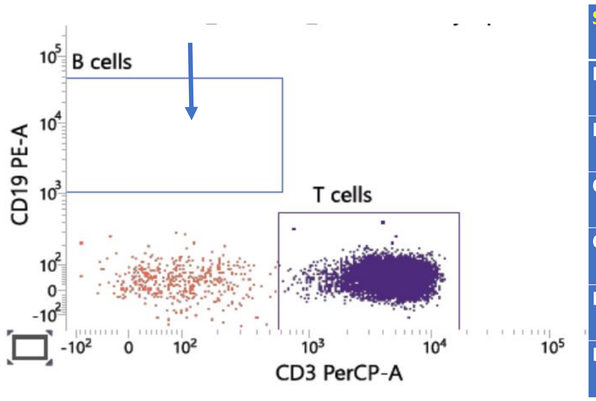


Figure 3. Antibody ID. There was no DSA in the current sample. Class II PRA was 0%. Therefore, AB ID was not run for class II

A

B-cells not detected



B

Samples	Result
Historical T-cell	Negative
Historical B-cell	Invalid. No B-cell signal
Current T-cell	Negative
Current B-cell	Invalid. No B-cell signal
Pre-transplant T-cell	Negative
Pre-transplant B-cell	Invalid. No B-cell signal

Figure 4. No detection of B-cells A. Absence of CD19 positive B-cells in donor sample. B. Flow crossmatch result

Discussion

Here we report a case in which a new class of drug treatment received by donor caused interference in flow crossmatch. For a 42 year old male patient, kidney from a 35 year old female with KDPI (Kidney donor profile index) of 28% became available. A virtual crossmatch (VXM) was negative for the current and historical samples. In physical crossmatch, we detect T-lymphocytes with anti-CD3 and B-lymphocytes using anti-CD19. However, after Flow crossmatch, there was no signal for B-cells indicating that there were no B-cells in donor sample. Donor medical history showed that donor had MOGAD (Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease) vs RRMS (Relapsing-Remitting Multiple Sclerosis) which are autoimmune diseases and was treated with monoclonal antibody drug Briumvi. Briumvi or Ublituximab is a monoclonal antibody and targets CD20 of B-cells. Ublituximab targets the CD20 amino acid residues 155-159 and 168-171 which are present on extracellular loop of CD20. Ublituximab is IgG kappa monoclonal antibody and has glycoengineered fragment crystallizable (Fc) segment which has been modified to increase binding affinity to FCγRIIIa receptors. Thus, Ublituximab can preferentially enhance Antibody dependent cytotoxicity over complement dependent cytotoxicity (CDC). When we observed that B-cells are depleted without affecting T-cells, we resulted B-cell crossmatch as invalid. Clinicians asked about path forward because kidney quality and other compatibility was suitable. There was no DSA in most recent sample for which AB ID had been done and one DPB1*04:01 DSA (MFI 2717) was in historical sample. DP expression is less on cell surface and usually only very high-level DSAs can cause positive crossmatch and MFI 2717 was unlikely to cause positive B-cell crossmatch. PRA for most recent sample was 0,0. Thus patients was not sensitized. Taking into account these factors, we advised clinicians that there is low-risk in accepting the offer. Kidney offer was accepted and kidney was transplanted. Post-transplant, there is no DSA and PRA is 0,0.

Conclusion

We present a case in which a new class of glycoengineered monoclonal antibody drug which is highly effective in depleting donor B-cells caused invalid B-cell crossmatchIt may be important to balance need for virtual and physical crossmatch.

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