False Cw Antibody Reactivity Detected By Solid Phase Antibody Testing Unecessarily Restricts Donor Availability for Two Solid Organ Recipients

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BACKGROUND

As the field shifts to greater reliance on virtual crossmatches, accurately assessing a patient's HLA sensitization is more important than ever. We present two cases where sole reliance on single antigen bead testing would have restricted donor offers. Patient 1 is a 70-year-old male evaluated for a bilateral lung transplant. Initial single antigen bead (SAB) testing showed reactivity to all Cw antigens except for self C*15, suggesting an antibody targeting the 65QKR eplet. Avoiding this eplet would equate to a 99% CPRA and likely result in denial by the transplant program due to the patient's rapidly worsening condition and reduced likelihood of identifying a compatible donor in time. Patient 2 is a 47-year-old male listed for a kidney transplant. Initial SAB testing showed reactivity to all Cw antigens except for Cw7, suggesting an antibody targeting the 184H eplet. Avoiding this eplet and the patient's Class II antibodies would result in a 98% CPRA. Initial investigations aimed to identify which Cw antigens could be safely crossed for each patient to improve their chances of transplant.

Results

Patient 1

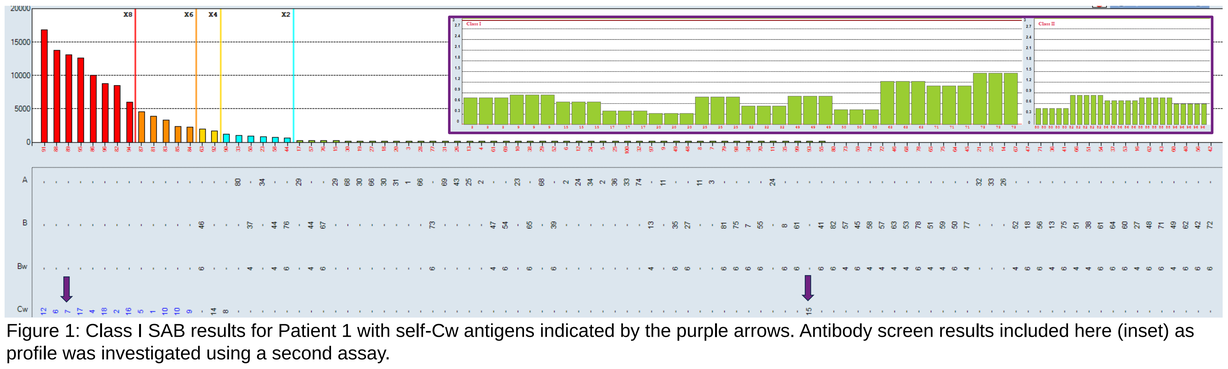

Figure 1: Class I SAB results for Patient 1 with self-Cw antigens indicated by the purple arrows. Antibody screen results included here (inset) as profile was investigated using a second assay.

DSA	Crossmatch Results	
	T cell	B cell
Cw4 at 10271 MFI, Cw7 at 12791 MFI	Negative	Negative
Cw2 at 8249 MFI, Cw8 at 979 MFI	Negative	Negative
Cw10 at 2889 MFI, C*16 at 5297 MFI	Negative	Negative
Cw5 at 4172 MFI	Negative	Negative

Table 1: Summary of surrogate crossmatch testing results for Patient 1. Surrogate crossmatches against donors with differing Cw antigens were all T and B cell negative, despite apparent cumulative DSA targeting Cw antigens ranging between ~4,000 and 23,000 MFI.

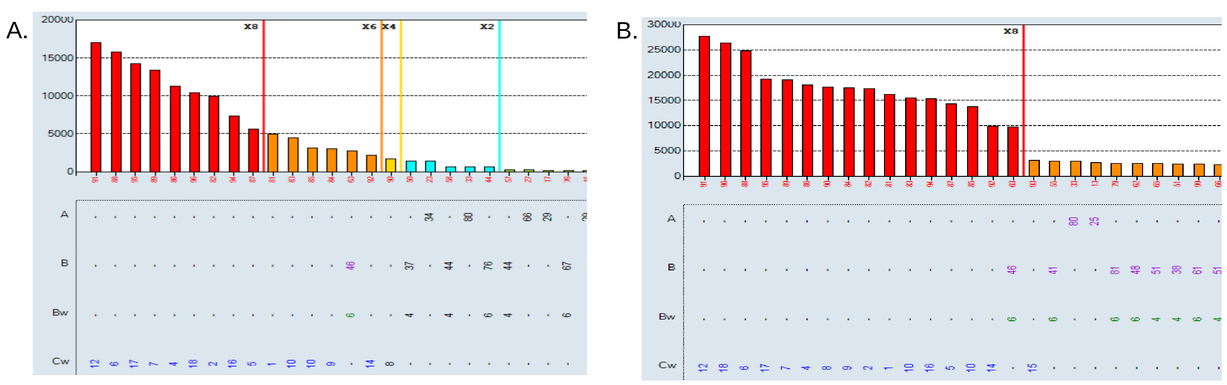

Figure 2: Class I SAB results for Patient 1 using (A) untreated or (B) acid treated beads.

Patient 2

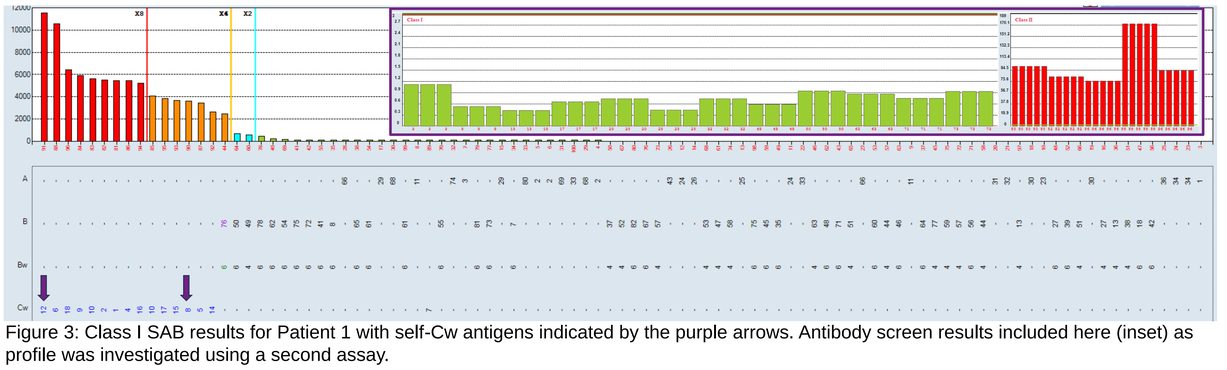

Figure 3: Class I SAB results for Patient 1 with self-Cw antigens indicated by the purple arrows. Antibody screen results included here (inset) as profile was investigated using a second assay.

DSA	Crossmatch Results	
	T cell	B cell
Cw8 at 3594 MFI	Negative	Negative
Cw5 at 3457 MFI	Negative	Negative
Cw9 at 2562 MFI, C*12 at 5456 MFI	Negative	Negative
Cw10 at 4057 MFI, DQ2 at 28314 MFI	Negative	Positive

Table 2: Summary of surrogate crossmatch testing results for Patient 1. Surrogate crossmatches against donors with differing Cw antigens were all T and B cell negative, despite apparent cumulative DSA targeting Cw antigens ranging between ~3,000 and 8,000 MFI.

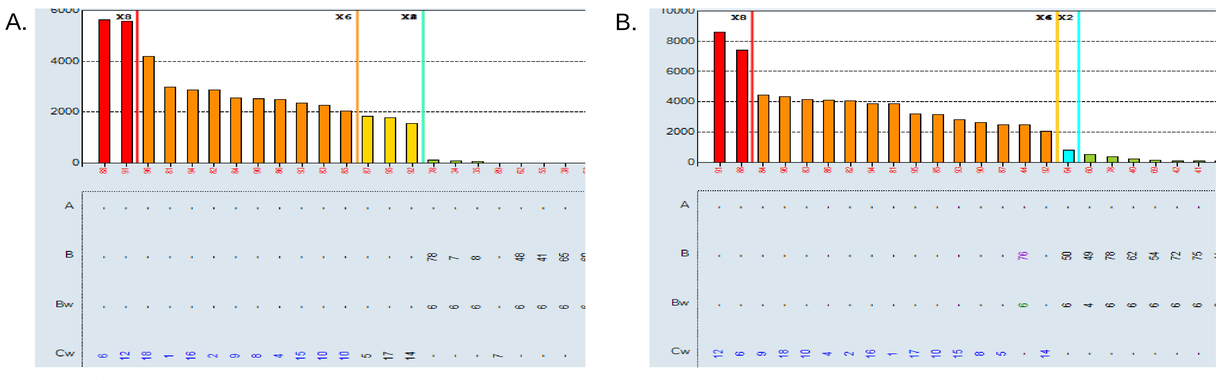

Figure 4: Class I SAB results for Patient 1 using (A) untreated or (B) acid treated beads.

DISCUSSION

Here we describe two patient cases whose antibody profiles were complicated by false Cw reactivity as detected by SAB. Additional investigation by antibody screens, surrogate crossmatching, and acid treatment of beads confirmed the false positive antibody detection. This additional investigation allowed for Patient 1 to be listed with no avoids in UNET and they quickly received a lung transplant from a Cw5 homozygous donor with a subsequent T and B cell negative retrospective crossmatch. This experience prompted additional investigation when patient's 2 profile was discovered, and similar results were obtained demonstrating false Cw antibody reactivity. Patient 2 has seen an increase in donor opportunities since the Cw antigens have been removed as avoids in UNET.

In addition to the two patients described above, our lab has identified two additional patients where similar patterns of Cw reactivity have appeared. Interestingly, the broad Cw reactivity only first appeared several months after transplant for both these patients. While the SAB testing shows significant de novo Cw DSA in both cases, investigative testing supports that these new reactivity patterns are false.

Conclusions

These patterns of false reactivity significantly hinder the HLA laboratory's ability to provide accurate clinical information to the transplant programs we support. These cases illustrate the importance of a thorough, multi-platform evaluation of a patient's HLA antibody profile, particularly for highly sensitized individuals, in order to provide the best data for patient care. The HLA lab must be cognizant that overcalling unacceptable antigens or DSA can be as detrimental to a patient as missing an eplet targeting antibody. These cases also illustrate the continued utility of physical crossmatch testing in cases where there is a lack of concordance between the results of different antibody testing platforms.