Strategies to Circumvent Discrepancies in Pre-Transplant Donor Specific Antibodies Workup

Dear Editor,

Accurate assessment of donor-specific antibodies (DSAs) plays a pivotal role in pre-transplant evaluation to mitigate the risk of graft rejection.[1] However, a challenging dilemma arises when DSA-SAB results show positive results, but other assays, such as complement-dependent cytotoxic crossmatch (CDC-XM) and flow crossmatch (FC-XM) provide negative results.

We present two cases to illustrate the diagnostic challenges encountered during the pre-transplant workup:

Case 1: A 31-year-old man underwent a pre-transplant evaluation including CDC-XM, FC-XM, panel reactive antibody (PRA) testing, and DSA-SAB assay with his father as a donor. Despite negative results in CDC-XM and FC-XM, the DSA-SAB assay revealed unexpected weak-to-moderate positivity (MFI range = 1000-5000) against a wide range of HLA class I and class II antigens [Figure 1a and 1b]. PRA testing showed no-HLA sensitization [Figure 1c and 1d], but the test negative control (CON) values were high, indicating the nonspecific

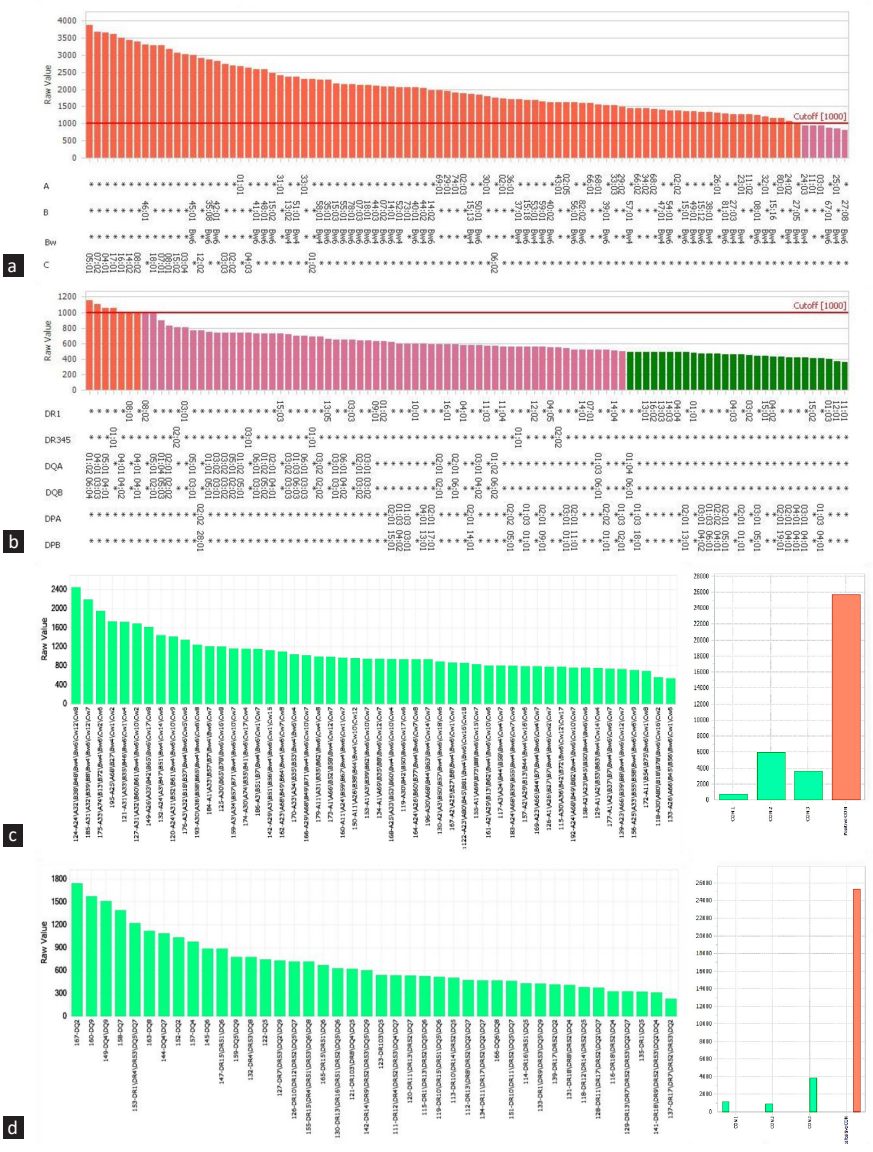

Figure 1: Assessment of true or false anti-HLA antibodies: a case. Figure showing broad reactivity to (a) HLA-class I single antigen beads profile; (b) HLA-class II single antigen beads profile; (c) HLA-class I PRA beads profile; (d) HLA-class II PRA beads profile. Colored rectangles indicate the MFI of antibodies for corresponding HLA antigens. (a and b): Red color indicates MFI ≥ 1000, purple indicates MFI ≤ 1000 and dark green indicates MFI ≤ 500. (c and d): Green color indicates negative bead reactions for a particular HLA antigen, and orange indicates positive bead reactions. (Y-axis: MFI values, X-axis: SAB HLA specificity) HLA: human leukocyte antigen. PRA: panel reactive antibody

binding, which leads to false-positive tests. In such a scenario, PRA testing alongside DSA-SAB helps.[2]

Case 2: A 33-year-old man was planned for transplant with his sister as a donor. Patient exhibited HLA class II positivity for self-antigen DRB1*13:01, in DSA-SAB testing (Immucor). However, CDC-XM and FC-XM were negative. Repeat testing with another kit from a different vendor (One Lambda, Inc.) showed the absence of antibodies for self-antigen DRB1*13:01. Reported false positivity may occur due to the presence of antibodies to denatured antigens.[2,3]

We propose stepwise strategies to address these diagnostic challenges:

1. Patient history should be assessed thoroughly for sensitization events.
2. Conduct high-resolution typing and utilize multiple assays to determine true antibodies, including different platforms, solid-phase assays and kits from other vendors.
3. Perform epitope analysis to decipher antibody specificities.[4]

This letter emphasizes the importance of quality control, technical validation, and personalized patient-focused assessments in pre-kidney transplant evaluations.

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Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent.

Conflicts of interest
There are no conflicts of interest.

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