Acute Heart Transplant Rejection in the Presence of Apparently Weak, Non-Complement-Fixing Donor-Specific Antibodies Detected at the Time of Transplant

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ABSTRACT

Aim: A 66 year old female with an end-stage NYHA class IV inotrope-dependent, ischemic cardiomyopathy received a heart transplant on 9-12-09 from a donor having antigens B13 and DR7. Pre-transplant antibody testing indicated only weakly positive, non-complement-fixing donor-specific antibodies. The patient suffered a cardiac arrest on POD#6 and was resuscitated. She was in cardiogenic shock from allograft failure and subsequently expired on POD#9 of multiorgan failure due to “acute humoral rejection”. These antibodies were investigated further.

Methods: Antibodies were evaluated using Labscreen PRA (One Lambda), Labscreen Single Antigen (One Lambda) beads, and C1q Single Antigen (One Lambda) beads, and crossmatching was performed using standard T and B cell CDC and flow cytometry methods.

Results: Pre-transplant antibody studies (Labscreen PRA) had shown the presence of clearly defined antibodies to B27, DR4 and a possible weak anti-DR7. Retrospective Labscreen Single Antigen (SA) (One Lambda) testing revealed antibodies to B13 and DR7, both donor-specific antibodies. MFI values were 2000 for B13 and 5000 for DR7. The pre-transplant crossmatches (CDC and flow cytometry) were negative except for a positive B cell CDC. The patient received blood products on POD#3 and was noted to be in acute renal insufficiency. Crossmatching on POD#3 showed only a weakly positive T flow crossmatch and negative DSA. However, SA antibody studies on POD#6 showed high MFI values of 19,000 (B13) and 23,000 (DR7), and strongly positive T and B CDC and flow crossmatches. C1q studies of sera from POD#0 and #3 showed the DSA were non-complement fixing. However, by POD#6, the DS antibodies were now clearly complement-fixing. The patient expired on POD#9. Myocardium tissue from the left ventricle taken at autopsy showed positive staining for C4d.

BACKGROUND

- 66 YEAR OLD CAUCASIAN FEMALE
- INITIAL WORKUP 9/4/2009
- DIAGNOSIS: ISCHEMIC CARDIOMYOPATHY, HEPATITIS AND RENAL FAILURE
- 9/12/2009 - HEART TRANSPLANT
- 9/21/2009 - DECEASED: ACUTE HUMORAL REJECTION
- Patient HLA Type: A2,11; B37,55; Bw4,6; DR13,19; DQ6; DR51,52
- Donor HLA Type: A11,26; B7,13; Bw4,6; DR7,15; DQ12; DR51,53
- DSA Day of Transplant Anti: DR7 by LABScreen PRA; (DR7 and possible B13 by LABScreen SA, retrospective)
- * In BOLD: Mismatched Antigens

SUMMARY

- A putative “weak antibody” (as measured by MFI) at the time of transplant can be a significant risk to transplant outcome.
- A non-complement-fixing antibody can appear later as a complement fixing antibody, i.e. become C1q Positive
- Both types of antibodies can rapidly strengthen to participate in an acute rejection episode.

CONCLUSION

-DSA with relatively weak MFI values can be a significant risk to both organ and patient survival.
- Non-complement-fixing DSAs also pose a risk and can become expressed as complement-fixing antibodies in an acute immune response to mismatched donor antigens.

Antibody Testing Performed Using LABScreen PRA and LABScreen Single Antigen Beads from One Lambda, Inc. (Canoga Park, CA)