

Anti-Angiotensin Type 1 Receptor Antibodies Associated with Rejection in Donor HLA Antibody Negative Recipients

N. Reinsmoen, C. Lai, J. Mirocha, K. Cao, M. Naim, G. Ong, Q. Wang, H. Duong, S. Riega, M. Rafiei, J. Patel, J. Kobashigawa

Cedars-Sinai Medical Center, Los Angeles, CA

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Anti angiotensin type 1 receptor (AT1R) antibodies have been found associated with rejection in renal recipients (recips) in the absence of donor HLA specific antibodies (DSA) and with earlier onset or faster progression of microvascular remodeling in heart recipients. The aim of our study was to determine the impact of anti-AT1R on clinical outcomes including antibody mediated rejection (AMR) with or without cellular mediated rejection (CMR) in heart recipients.

Methods: Pre and posttransplant sera from 215 recipients transplanted between May 2007 and November 2011 were tested for DSA (Luminex single antigen beads) and anti-AT1R (ELISA) with high levels being defined as ≥ 17 units. Clinical parameters examined were: 5 yr AMR/CMR (\geq grade 2) and coronary artery vasculopathy (CAV).

Results: Pre and posttransplant sera from 19 recipients diagnosed with AMR and/or CMR were tested for DSA and AT1R. Ten recipients had DSA at the time of biopsy: 5 with AMR; 3 with CMR; and 2 with AMR and CMR. Of these 10 recipients, 5 had high anti-AT1R levels. Nine recipients had no DSA at the time of biopsy: 4 recipients with CMR had low levels of anti-AT1R. 5 recipients had pre and/or posttransplant high levels of anti-AT1R and no concomitant DSA: 3 with AMR, 1 with AMR+CMR, and 1 with CMR. No clear association was seen between CAV and high levels of anti-AT1R. However, marked increases (>29 unit change) in pre vs. posttransplant anti-AT1R levels were observed for 10 recipients with no AMR/CMR; 4 developed CAV.

Discussion: The presence of high levels of anti-AT1R in the absence of DSA implicates a role for non-HLA antibodies in AMR. The observation of DSA and/or high levels of anti-AT1R in 4 cases of CMR suggests antibody, perhaps non complement binding antibodies, may play a role in CMR. Thus, determining both HLA and non-HLA antibodies may be useful in determining overall immunological risk and may have long term clinical implications