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Clinical implications of angiotensin II type 1 receptor antibodies in antibody-mediated rejection without detectable donor-specific HLA antibodies after renal transplantation.

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Abstract

BACKGROUND:

Solid-phase immunoassays have improved detection sensitivity for donor-specific HLA antibody (DSHA) and permitted the accurate diagnosis of antibody-mediated rejection (AMR). However, DSHA is not always sufficient to explain the cause of AMR. Consequently, a means of assessing non-HLA antibodies is required to determine the cause of AMR. The aim of the present study was to evaluate the clinical implications of antibodies (Abs) targeting angiotensin II type I receptor (AT1R) in recipients with AMR but without serum DSHA.

METHODS:

Non-HLA AMR cases diagnosed between January 2011 and June 2014 were included. Levels of anti-AT1R Abs (U/mL) were quantified by using AT1R assay kits (One Lambda, Calif, United States) with collected sera pretransplantation and at biopsy (cut-off value: 15 U/mL).

RESULTS:

Seventy-two patients were diagnosed with AMR during the above-mentioned period. Of them, 12 recipients (16.7%) had no DSHA. The sera of these 12 patients were tested (2 patients were only checked at time of biopsy). Nine patients (9/10) were presensitized for anti-AT1R Abs (median, 25.0 U/mL; range, 12.9 to 50.0 U/mL). Ten patients (10/12) were anti-AT1R- positive at time of biopsy (median, 23.2 U/mL; range, 11.4 to 50.0 U/mL). The mean time from transplantation to biopsy was 73 months. Eight patients experienced acute AMR, and 4 developed chronic AMR. Four patients showed negative C4d staining in peritubular capillaries (4/12). Patients were treated with plasmapheresis, low-dose intravenous immunoglobulin, and/or rituximab.

CONCLUSIONS:

AT1R Abs may play a significant role in AMR without detectable DSHA. Pretransplantation detection of AT1R Abs may be helpful for assessing the risk for non-HLA AMR.