Transplantation. 2014 Jun 9. [Epub ahead of print]

Association of Anti-Human Leukocyte Antigen and Anti-Angiotensin II Type 1 Receptor Antibodies With Liver Allograft Fibrosis After Immunosuppression Withdrawal.

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Abstract

BACKGROUND: Many pediatric patients who receive a living-donor **liver** transplant undergo **withdrawal** of **immunosuppression** (IS). For them, the high incidence of long-term progressive graft fibrosis is of particular concern.

METHODS: We conducted a cross-sectional study including 81 pediatric patients who underwent IS **withdrawal** after living-donor **liver** transplant at Kyoto University Hospital and whose serum samples and pathological data could be obtained during the analysis period. We examined the association of donor-specific anti-human leukocyte antigen (HLA) antibody (DSA) and angiotensin II type 1 receptor antibody (anti-AT1R Ab) with posttransplant graft fibrosis. Normalized mean fluorescence intensity (MFI) 5,000 or higher and anti-AT1R Ab concentrations 17 U/mL or higher were both considered high level. The patients were classified into an advanced fibrosis group (AFG) (Ishak score≥3) and a control group (CG) (Ishak score≤2).

RESULTS: Only one patient demonstrated DSA class I. Among those who demonstrated DSA class II, more AFG patients than CG patients demonstrated high-level mean fluorescence intensity, although the difference was not significant (64% vs. 39%; P=0.053). The incidence of high-level DSA-DRB1, however, was significantly higher in the AFG than that in the CG (40% vs. 4%; P<0.001), but there was no significant difference in DSA-DQB1 or DSA-DRB345. High-level anti-AT1R Ab was significantly more frequent in the AFG than in the CG (65% vs. 36%; P=0.02). All patients with both high-level DSA-DRB1 and high-level anti-AT1R Ab were found to have advanced fibrosis (P<0.001).

CONCLUSION: Anti-AT1R Ab and DSA-DRB1 may be candidates as biomarkers of graft fibrosis; both HLA and non-HLA immunity may be involved in graft fibrosis after IS **withdrawal**.

PMID: 24914568 [PubMed - as supplied by publisher]

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