

Clinical Relevance of Non-HLA-Antibodies after Intestinal and Multivisceral Transplantation



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Non-HLA-allo- and autoantibodies are involved in allograft rejection in kidney and heart transplantation. Their role in intestinal transplantation (ITX) has not yet been described. We examined the development of anti-Angiotensin II-Type I receptor antibodies (anti-AT1R) and anti-Endothelin-Type A receptor antibodies (anti-ETAR) in association with the clinical course and histopathological findings of 20 ITX-recipients.

Between 06/2000 and 08/2011, 30 patients with a median age of 37.6±9.8 years received an isolated intestinal graft (n=18) or a multivisceral transplantation (MVTX, n=12). Since 2005 anti-AT1R and anti-ETAR were screened regularly. Levels of >12 U/l were considered as highly-positive. All non-HLA antibody levels were evaluated retrospectively in regards of simultaneous rejection episodes or other clinical events.

Anti-AT1R and anti-ETAR levels were determined in 20 out of 30 ITX- and MVTX-recipients. Fifteen of the 20 patients (75%) developed high levels of either anti-AT1R, or anti-ETAR, or both. Twelve of the 15 patients (80%) had rejection episodes around the time of positive non-HLA antibody sampling. Rejection episodes were either exclusively cellular rejections (n=4) or mixed cellular and antibody-mediated rejections (AMR) with positive detection of donorspecific anti-HLA antibodies (DSA, n=8). The other 3 patients showed non-donorspecific anti-HLA antibodies and viral infections (n=2) during the time of anti-AT1R- or anti-ETAR antibody detection, but did not have any signs of rejection.

Our data suggest that antibody-mediated mechanisms targeting antigens beyond HLA- may additionally trigger and accelerate immune responses. Given the possibility of pharmacologic targeting of both receptors, future studies will focus on the explanation of mechanisms how non-HLA antibodies may enhance allograft rejection and deteriorate long-term allograft survival after ITX and MVTX.

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