

The role of angiotensin II type 1 receptor-activating antibodies in renal allograft vascular rejection.

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Abstract

Acute rejection with vascular involvement remains a challenging problem in renal allotransplantation. Fibrinoid necrosis of the arteries with secondary thrombotic occlusions is C4d negative in 50% of cases and has the worst prognosis among all allograft vascular lesions. Nonhuman leukocyte antigen (HLA) non-complement-fixing antibodies reacting to artery-specific antigens have been speculated to be responsible for causing severe vascular injury. We recently reported the presence of agonistic antibodies against the angiotensin II type 1 receptor (AT(1)R-AA) in 16 recipients of renal allografts who had severe vascular rejection and malignant hypertension but who did not have anti-HLA antibodies. AT(1)R-AA stimulate AT(1)R and induce mediators of inflammation and thrombosis. Removal of AT(1)R-AA by plasmapheresis in combination with pharmacologic AT(1)R blockade leads to improved renal function and graft survival in AT(1)R-AA-positive patients. We have shown that the analysis of the subtle diagnostic and mechanistic differences may help to identify patients at particular risk and improve outcome of rejections with vascular pathology.