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Clinical significance of late onset antibody-mediated rejection without donor-specific anti-HLA antibodies in kidney transplantation

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Introduction: Late onset antibody-mediated rejection (AMR) is a leading cause of allograft failure after kidney transplantation. Although the presence of donor-specific antibodies (DSA) is no longer required for AMR diagnosis according to Banff 2017 classification, the clinical significance of late onset AMR without DSA remains unclear.

Methods: We analyzed 137 cases of late onset AMR (> 6 months after transplant) that meet the Banff 2017 histologic criteria for AMR. All cases were diagnosed by for cause biopsy and grouped into DSA-positive (n=116) and DSA-negative (n=31) AMR groups.

Results: The diagnosis of AMR was made on median 87 months after transplantation. Two groups had similar histological pictures and graft renal function at the time of biopsy. Of the DSA-negative AMR group, 19 patients were tested for antibodies against angiotensin II type 1 receptor and 6 of them had antibodies (31.6%). In total, 85.7% of patients received AMR-specific treatment, including rituximab, plasmapheresis, and/or intravenous immunoglobulin. During a median follow-up of 41 months after AMR diagnosis, 48 patients lost their grafts. The 5-year death censored graft survival rates were 61.6% for DSA-positive AMR and 70.6% for DSA-negative AMR ($P = 0.752$). Multivariable analysis revealed that young age, interstitial fibrosis/tubular atrophy (ci+ct score), transplant glomerulopathy (cg score), and impaired renal function at the time of biopsy were independent risk factors for death-censored graft loss. During the follow-up, graft renal function after AMR diagnosis was comparable between DSA-positive and DSA-negative AMR.

Conclusion: DSA-negative late onset AMR have similar clinical outcomes compared to DSA-positive AMR.