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Induction of Accommodation by Anti-Complement Component 5 Antibody-Based Immunosuppression in ABO-Incompatible Heart Transplantation

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Objectives: Plasmapheresis in combination with immunoglobulin and rituximab is often used to induce accommodation in ABO-incompatible (ABOi) living-donor transplantation; however, this regimen cannot be applied to cases of ABOi deceased-donor transplantation. Here, we investigated whether an anti-complement component 5 (C5) antibody-based regimen can induce accommodation in ABOi heart transplantation.

Methods: Both IgM and IgG anti-blood type A antibodies were induced in wild-type mice by sensitization using human blood type A antigen. Heterotrophic ABOi heart transplantation was performed from human blood type A-transgenic C57BL/6J mice to sensitized wild-type DBA/2 mice.

Results: Either anti-C5 antibody or conventional triple immunosuppressants (corticosteroid, tacrolimus, mycophenolate mofetil) alone did not induce accommodation in majority of ABOi heart allografts, whereas their combination induced accommodation in more than 70% of cases despite the presence of anti-A antibodies. The combination therapy markedly suppressed the infiltration of T cells and macrophages into ABOi allografts, despite mild deposition of IgG and C4d. T cell activation and differentiation into Th1, Th2, and Th17 cells were suppressed along with CD49d^{high}CD4⁺ T and follicular helper T cells in the combination treatment group. CD24⁺ B cells including both CD24⁺CD23⁺ marginal zone B cells and CD24⁺CD23⁻ T2-marginal zone B cells, were increased in the accommodation group.

Conclusions:

C5 inhibitor-based immunosuppression induced accommodation in murine ABOi heart transplantation, presenting a promising strategy for ABOi deceased-donor transplantation.