RETHINKING OF SIGNIFICANCE OF C4d DEPOSITION IN PTC THROUGH LONG-TERM FOLLOW-UP OF ABO-INCOMPATIBLE KIDNEY TRANSPLANTATION

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Introduction: Living donor and ABO-incompatible kidney transplantation have become global trends because of the shortage of cadaver organ donation. This is prominent in Japan. In our hospital, ABO-incompatible kidney transplantation has accounted over 30%. ABO-incompatible kidney transplantation shows a remarkable outcome with the progress in immunosuppressive treatment, however, acute humoral rejection (AHR) is the most important cause of early graft losses. The prevalence and the pathogenesis of chronic rejection after ABO-incompatible kidney transplantation remain unclear. The same criteria for acute and/or chronic antibody mediated rejection proposed for anti-HLA antibodies are available or not is an important problem, especially in terms of the significance of C4d deposition in PTC.

Methods and Materials: We examined 71 recipients after ABO-incompatible kidney transplantation, and 231 graft biopsies performed as a protocol biopsy or episode were enrolled to the study. They were analyzed with light microscopy and direct immunofluorescent method for C4d. The diagnosis of acute rejection was based on Banff scheme 1997.

Results: One hour biopsies did not show strong positive C4d deposition in PTC. Weakly diffuse deposition was noted in 16% of 55 1-hr biopsies. Approximately 60-90% of graft biopsies performed after 2-POD showed positive C4d in PTC, regardless of the time of biopsy. We have experienced pure AHR in 6 out of 55 recipients after ABO-incompatible kidney transplantation from 2-POD through 12-POD. The severity of AHR was mild to moderate, and no graft was lost due to AHR. All 8 recipients with AHR including combined type with ordinary AR showed strongly diffuse C4d deposition in PTC. Thirty-two out of 55 recipients (58%) were acute rejection free. In the biopsy specimens from AR-negative recipients, the incidence of positive C4d deposition in PTC was almost similar with AR-positive patients. Late graft biopsies after 3 months revealed 28 CAN-positive out of 51 biopsies (55%), and only 4 biopsies showed immunological chronic rejection. The incidence of C4d deposition in CAN-negative biopsies was as high as in CAN-positive ones.

Conclusion: In ABO-incompatible kidney transplantation, we have experienced only a few AHR and excellent graft survival rates were achieved. Sensitivity of C4d deposition in PTC is extremely high (100%) for AHR (including combined type). However, most of biopsy specimens after ABO-incompatible kidney transplantation show strongly positive C4d deposition as a non-specific phenomenon not related with antibody-mediated rejection (specificity is 12%). These findings may suggest that the accommodation is commonly occurred in ABO-incompatible kidney transplantation. Further studies are necessary to clarify the meaning of C4d deposition after ABO-incompatible kidney transplantation, and to elucidate the process leading to accommodation in ABO-incompatible kidney transplantation.