GLOMERULAR ACTIVATION OF THE LECTIN PATHWAY IN TRANSPLANT GLOMERULOPATHY

Izumi Yamamoto1, Shigeru Horita2, Takamune Takahashi3, Kazunari Tanabe4, Shohei Fuchinoue5, Satoshi Teraoka5, Motoshi Hattori6, Akimitsu Kobayashi1, Akiko Fujii7, Michio Nagata8, Yutaka Yamaguchi9

1) Division of Kidney and Hypertension, Department of Internal Medicine, The Jikei University School of Medicine, Tokyo, Japan
2) Kidney Center, Tokyo Women’s Medical University, Tokyo, Japan
3) Division of Nephrology and Hypertension, Vanderbilt University Medical Center
4), 5), 6) Departments of Urology4, Surgery5, and Pediatric Nephrology6, Tokyo Women’s Medical University, Tokyo, Japan
7) Department of Pathology, Mitsui Memorial Hospital, Tokyo, Japan
8) Molecular Pathology, Institute of Basic Medical Science, Graduate School of Comprehensive Human Science, University of Tsukuba, Tsukuba, Ibaraki, Japan
9) Department of Pathology, Kashiwa Hospital, The Jikei University School of Medicine, Chiba, Japan

Objectives: Transplant glomerulopathy (TG) is a prominent feature of chronic rejection and is characterized by double contours of the glomerular capillaries (GC). Although its morphological characteristics are clear, the pathogenesis of TG remains unclear. We demonstrated that linear and granular C4d deposits in the GC characterize TG histochemically. In general, C4d deposits arise via three complement pathways, including the lectin pathway, which is activated by the binding of mannose-binding lectin (MBL) and ficolins to carbohydrate ligands, followed by the activation of MBL-associated serine proteases (MASP) and C4.

Methods: To verify the linear and granular C4d patterns in TG, we examined glomerular activation of the lectin pathway in the glomeruli of TG patients using anti-MBL, anti-H-ficolin, anti-L-ficolin, anti-MASP-1/3 and MASP-2 antibodies, together with anti-C4d antibodies. Twenty cases of chronic allograft nephropathy (CAN) with TG were compared with ten cases of CAN without TG as a control.

Results: The glomerular activation of the lectin pathway, characterized by anti-H-ficolin antibody positivity, was observed as a granular pattern, while there was no activation in CAN without TG. Furthermore, the granular pattern of C4d deposits was co-localized with anti-H-ficolin antibody positivity.

Conclusions: These data demonstrate that the pathogenesis of GC in TG patients is activated via the lectin pathway in part.