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생체 신이식 후 이식 초기에 관찰되는 Th17 증가의 임상적 의의

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Clinical Significance of the Increase of Th17 During the Early Post-transplant Period after Living Donor Kidney Transplantation

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Accumulating evidence suggests that Th17 cells play a role in the development of chronic allograft injury in transplantation of various organs. However, the influence of current immunosuppressants on Th17-associated immune responses has not been fully investigated. We performed two separate studies. First, we prospectively investigated the changes in Th17 cells in peripheral blood mononuclear cells (PBMCs) collected before and 1 month and 3 months after kidney transplantation in 26 patients taking tacrolimus. Second, we measured the proportion of Th17 in the PBMCs of 20 kidney transplant recipients with long-term follow-up. The association between the proportion of Th17 and graft function was evaluated in early and long-term recipients. We further investigated whether tacrolimus has a direct suppressive effect on Th17 in vitro. In the early posttransplant period, the percentage of Th17 cells and the proportion of IL-17-producing cells in the CD4+ effector memory T cells (TEM) subset were significantly increased at 3 months after transplantation compared with before transplantation ($p<0.05$), whereas Th1/Th2 cells and TEM cells were significantly decreased. The degree of increase in Th17 during the early posttransplant period was significantly associated with allograft function at 1 year after transplantation ($r=0.4$, $p<0.05$). In patients with long-term follow-up, Th17 levels were also affected by graft function. The patients with chronic allograft dysfunction (CAD) showed higher Th17 levels than patients without CAD. In vitro, tacrolimus suppressed Th1 and Th2 cells in a concentration-dependent manner, but did not suppress Th17 cells even at high concentration. This suggests that current immunosuppression based on tacrolimus is inadequate to suppress Th17 cells in kidney transplant recipients, and upregulation of Th17 may be associated with the progression of CAD.

Key Words: 신장이식, 만성 이식신기능 저하, Th17
Kidney transplantation, Chronic allograft dysfunction, Th17