사이클로스포린 장기투여가 신장 내 보체계 및 조절인자의 활성화에 미치는 영향

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Purpose : Complement activation has been associated with the onset of acute inflammatory reactions leading to complications such as acute graft rejection and ischemia-reperfusion injury in renal transplantation, and deposition of C4d is an important marker of antibody-mediated rejection in chronic allograft nephropathy. This study was performed to investigate complement in cyclosporine (CsA)-induced renal injury.

Methods : We first evaluated whether or not complement is activated in CsA-induced renal injury. Second, we investigated regulatory proteins which controls complement activation. Mice on a low salt (0.01%) diet were given vehicle (VH, olive oil, 1 mL/kg/day), or CsA (30 mg/kg/day), and sacrificed at 1 and 4 weeks. Activation of complement system was evaluated with expression of C4d, C3 and membrane attack complex (MAC). Regulatory protein (CD46, CD55 and CD59) were also evaluated.

Results : Compared to the VH group, the CsA group showed increased immunoreactivity of C4d, C3 and MAC expression at 1 week, and further increase of was observed at 4 weeks. Localization of C4d and C3 with double labeling with α-smooth muscle cell revealed that these were predominantly expressed on renal tubular cells in injured area. MAC was also localized at luminal side of renal tubular cells. Regulatory proteins (CD46, CD55 and CD59) were also increased in CsA-treated mice kidneys compared with VH-treated mice kidneys.

Conclusion : CsA-induced renal injury activates components of complement system and its regulatory proteins. Main site of complement activation is renal tubular cell. This finding provides a useful parameter for differential diagnosis between antibody-mediated rejection and chronic CsA nephropathy in chronic allograft nephropathy.