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Circulating Immune Cell Dysfunction and Apoptosis in ESRD Patients

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Background: Progressive loss of renal function is associated with a dysregulation of circulating T cells that may underlie their impaired T-cell immunity. Inflammation and apoptosis of renal cells may be central to the pathophysiology of renal disease. The Fas/Fas ligand pathway is a key initiator of both inflammation and apoptosis. However, it is not clear how dysregulation of circulating T cells contribute to the ESRD-related immune deficiency. In this study, we investigated the ESRD related changes of the T-cells and apoptosis frequency from patients.

Methods: Adult ESRD patients on HD and healthy subjects were recruited. Peripheral blood mononuclear cells were collected and staining CD4, CD8, CD45RO, CCR7 and CD95(FAS). The frequency of immune cell was measured by using flow cytometry. The frequency of apoptotic cells was calculated by scoring annexin-V binding cells after back-gating of CD4/CD8 T cells. CD95(FAS) protein levels were confirmed by Western blot analysis.

Results: A total of 25 adult ESRD patients on hemodialysis (male:female 12:13, DM 65%) and 17 healthy subjects (male:female 6:11) were enrolled in Konkuk University Medical Center. The ESRD patients revealed an increased frequency of CD4+CD25+ Treg and CD14+ cell compared with healthy subjects. However, the frequency of CD4+ and CD8+ T cells decreased in ESRD patients (Treg, HC vs. ESRD, 4.01±0.3 vs. 7.04±1.9, p=0.0001; CD4, HC vs. ESRD, 43.20±6.6 vs. 34.25±4.3, p=0.01; CD8, HC vs. ESRD, 16.54±2.9 vs. 9.43±1.9, p=0.02). The frequency of circulating central-memory(CM) subsets increased in ESRD patients, but terminal effector-memory(TEM) subsets of CD4+ and CD8+ T cells decrease in ESRD patients compared with healthy subjects. The CD4+ and CD8+ TEM cell subsets showed a statistically significant decreased in ESRD patients. In ESRD patients, the differentiation of effector memory CD8+ T cells increased, showing a significantly higher percentages of CD4+ TEM (8.7-12.3%, $P<0.05$) and CD8+ TEM cells (26.8-34.2%, $P<0.05$). The FAS and CD4+ and CD8+ TEM cell subsets apoptosis level showed a statistically significant increase in ESRD patients.

Conclusion: These results suggested that the apoptosis in TEM cell may be caused by CD95 in the progression of ESRD patients and the T cell dysregulation may play a role in ESRD-related immune deficiency.

Keywords: Apoptosis, ESRD, T cell