미세변화신증후군의 병인

연세대학교 의과대학 소아과학교실, 세브란스 어린이병원 소아청소년과

신 재 일

Pathogenesis of Minimal Change Nephrotic Syndrome

Jae Il Shin, M.D., PhD.

The Institute of Kidney disease, Department of Pediatrics,
Yonsei University College of Medicine, Severance Children's Hospital, Seoul, Korea

Idiopathic nephrotic syndrome (INS) is the most common glomerular disease in children. Minimal change nephrotic syndrome (MCNS) accounts for about 70% of INS in children, and 25% in adults. The characteristic finding of MCNS is the absence of inflammation or deposition of immune complex in the renal glomeruli. Since the 1970s, INS has been considered to be a disorder of T cell function. Recently, however, the pathophysiologic mechanisms of MCNS have been investigated by genetic, cellular and molecular studies and various hypotheses have been suggested.

MCNS was suggested to be a systemic disorder of T cell function and cell-mediated immunity due to several clinical observations such as the rapid occurrence of relapse after infections or immunization, hyporesponsiveness of lymphocytes to mitogens and decreased delayed hypersensitivity. The underlying mechanism, although not fully demonstrated, is that the immune system, perhaps through T cell dysfunction, releases a factor that induces the pathological changes in podocytes.

Some authors also reported that various alterations in cytokine production during MCNS and especially, tumor necrosis factor-α and interleukin (IL)-13 levels often increase during relapse.

Another evidence was on the a permeability factor and it was demonstrated that systemic infusion of supernatants of cultured peripheral blood mononuclear cells or T cells of patients with the relapse of MCNS induced proteinuria in rats.

Also, many genes involving the innate immune response are upregulated in MCNS. In some children with MCNS, the relapses occur after various viral or bacterial infections, suggesting that activation of the innate immune system might be related to podocyte dysfunction causing proteinuria.

Immuno-ultrastructural studies in patients with MCNS have shown that the expression of nephrin was diminished in the active phase of MCNS. The failure to restore normal nephrin signaling might be due to an antagonistic pathway abnormally upregulated in podocytes in the active phase of MCNS.

Recently, one study demonstrated that IL-13 overexpression in the rat could also lead to podocyte injury with downregulation of nephrin, podocin, and dystroglycan and a concurrent upregulation of B7-1 (CD 80) in the glomeruli, inducing a minimal change-like nephropathy. Also, another study showed that urinary CD80 was increased in minimal change disease patients while it was not commonly present in the urine of patients with other glomerular diseases.

In summary, recent clinical and experimental data show that the pathogenesis of MCNS is complex, but

among various mechanisms, insights from murine models suggest that persistent CD80 expression in podocytes, possibly initiated by antigens or cytokines may contribute to the development of proteinuria in MCNS. However, further studies are required to understand the interplay of immune system dysfunction and proteinuria in the pathogenesis of MCNS.