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선천성 신증후군의 유전자 검사

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Genetic Study of Congenital Nephrotic Syndrome

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Objectives : Congenital nephrotic syndrome (CNS) is defined as nephrotic syndrome which manifests in utero or during the first 3 months of life. Recent genetic studies disclosed that mutations in each of the NPHS1 (encoding nephrin), NPHS2 (encoding podocin), WT1 (encoding a nuclear transcriptional factor, WT1), and LAMB2 (encoding laminin β 2 chain) genes have been implicated in CNS. In this study, genetic study was done in children with CNS to know the relative frequency of causative mutations in these four genes as well as genotype- phenotype correlations.

Patients and Methods : Twelve unrelated Korean patients with CNS were recruited. Direct exon sequencing of NPHS1, NPHS2 and LAMB2 gene and the relevant exons 8 and 9 of WT1 gene were performed.

Results : Disease- causing mutations were detected in ten (83%) patients (NPHS1, NPHS2, WT1, and LAMB2: 33%, 8%, 33%, and 8%, respectively). Family history was positive in two patients (one with NPHS1 mutations, and the other with no mutation). Three patients with WT1 mutations had ambiguous genitalia and/or diaphragmatic hernia, and one patient with LAMB2 mutations developed retinal detachment. The renal biopsy of one of the patient with NPHS1 mutations revealed membranous nephropathy, however, his younger brother, who has the same mutations, had renal lesion compatible with CNS of Finnish type. Among nine patients who were followed-up more than 1 year, seven developed end- stage renal disease. Renal transplantation was performed in three patients, and none of them had recurrent disease in their graft kidneys.

Conclusion : The overall incidence (83%) of causative mutations in these four genes in this study was similar to that from a recent European study (85%). However, the incidence of NPHS2 mutation was lower and that of WT1 mutation was higher in this study. Accompanying other organ involvement may give a useful clue for clinical diagnosis in patients with CNS

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