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스테로이드 저항성 신증후군 환자에서 WT1 유전자 분석

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Analysis of WT1 Mutations in Children with Steroid-resistant Nephrotic Syndrome

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Wilms' tumor suppressor gene (WT1) encodes a zinc finger transcription factor which plays an important role in renal and gonadal development. WT1 mutations have been found not only in patients with steroid-resistant nephrotic syndrome (SRNS) associated with Wilms' tumor and/or urogenital malformations (Denys-Drash syndrome and Frasier syndrome) but also in infants with isolated diffuse mesangial sclerosis or in children with isolated SRNS. In this study, mutational analysis for WT1 was performed in 71 children (32 boys and 39 girls) with SRNS to evaluate the incidence of WT1 mutations. Patients with congenital nephrotic syndrome were excluded. The median onset age of SRNS was 4.7 years (4 months-12.8 years). Kidney biopsy was done in 67 patients, which revealed focal segmental glomerulosclerosis (FSGS) in 53, minimal change lesion in 9, and others in 5 patients. The NPHS2 gene study revealed no mutation. PCR and direct sequencing of exon 8 and 9 of WT1 was performed using peripheral blood gDNA. Abnormal splicing mutations in intron 9, which are typical for Frasier syndrome, were detected in 3 (7.7%) girls (IVS9+4 C>T) and 1 (3.1%) boy (IVS9+5 G>A). Two girls had complete XY gonadal dysgenesis with a karyotype of 46, XY, and one girl had normal gonad morphology with a 46, XX karyotype. One boy with a 46, XY karyotype had genital abnormalities such as hypospadias. The renal pathology was FSGS in three of the patients, in whom the renal functions were maintained normally. In one girl, who presented with acute renal failure and progressed to end-stage renal disease, kidney biopsy was not performed. None of the patients developed Wilms' tumor or gonadoblastoma. WT1 mutation should be considered as one of the genetic causes of SRNS in children (5.6% of incidence in this study), especially in patients with female phenotype or male patients with genital abnormalities.