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Bartter 증후군 한국인 소아환자에서의 유전학적 배경

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Genetic basis of Bartter syndrome in Korean Children

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Bartter syndrome (BS) is characterized by renal salt wasting, hypokalemic metabolic alkalosis and normotensive hyperreninemic hyperaldosteronism. BS is clinically classified into antenatal (aBS) and classic BS (cBS), and also into 5 subgroups according to underlying mutant genes; *SLC12A1* (BS I), *KCNJ1* (BS II), *CLCNKB* (BS III), *BSND* (BS IV), and *CASR* (BS V). We analyzed clinico-genetic features of Korean children with BS. Total 20 unrelated children with BS (7 males and 13 females) were recruited. The clinical findings were retrospectively studied. Mutational analysis of the 5 genes was done using PCR amplification and direct sequencing. In addition, semiquantitative PCR amplification to detect large deletions of *CLCNKB* was done in some cases with BS III. All patients presented with typical clinical features of BS. Clinical diagnosis was aBS in 5 cases and cBS in 15. Three patients had one or more affected sibling. All 5 cases with aBS had history of polyhydramnios as well as prematurity and/or fetal growth retardation. Hypercalciuria was noted in 3 (60%) cases with aBS and 10 (67%) with cBS, while nephrocalcinosis was detected in 3 (60%) with aBS and 3 (20%) with cBS. Hypomagnesemia was noted in 1 (20%) case with aBS and 4 (27%) with cBS. Among 5 cases with aBS, three were BS III, one BS II, and one BS IV with nerve deafness. All 15 cases with cBS were BS III. Among total 18 patients (36 alleles) with BS III, p.W610X was detected in 19 alleles (53%), total deletion in 6 (17%), partial deletion in 2 (6 %), small insertion or deletion in 3 (8%), and missense mutation in 6 (17%). All patients have been treated with oral potassium with/without prostaglandin inhibitors, potassium sparing diuretics or oral magnesium. During follow-up, one case with aBS/BS III developed chronic renal insufficiency due to recurrent episodes of dehydration, and two cases with cBS developed chronic renal failure due to chronic drug-induced interstitial nephritis and accompanying focal segmental glomerulosclerosis, respectively. In conclusion, BS III is the most common subtype (90%) in Korean BS. Among *CLCNKB* mutations, p.W610X was the most common (53% of the alleles), which suggests a founder effect. Screening for large deletions in CLCNKB, which is the second most common mutation, should be included in the genetic study for patients with BS. Renal function should be followed up carefully in patients with BS.

Key Words : Bartter 증후군, 유전형, 돌연변이
Bartter syndrome, Genotype, Mutation