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심한 저마그네슘 혈증 및 저칼슘혈증으로 발현한 CLCNKB 유전자 이상 1례

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A Novel CLCNKB Gene Mutation: Severe Hypomagnesemia and Hypocalcemia

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Bartter syndrome (BS) is an autosomal recessive inherited renal tubular disorder characterized with low or normal blood pressure, hypokalemic metabolic alkalosis and hyperreninemic hyperaldosteronism and classified into 5 genotypes according to underlying mutant genes. Type III BS is caused by loss-of-function mutations in the CLCNKB gene encoding for basolateral ClC-Kb and the most common genotype in Korean patients with BS. Type III BS manifests with hypokalemia, hypercalciuria, or nephrocalcinosis. CLCNKB gene mutation also cause Gitelman syndrome (GS) which is distinguished from other hypokalemic tubulopathies by the presence of both hypomagnesemia and hypocalciuria. We describe the pediatric patient with severe hypomagnesemia, hypocalcemia with hypercalciuria and hypokalemic periodic paralysis caused by CLCNKB gene mutation difficult to categorise as type III BS or GS. A 10-year-old boy was referred to our consultation due to persistent hypokalemia and hypomagnesemia. He had the birth history of maternal polyhydramnios and normal full term spontaneous delivery. He had the past medical history of muscle cramps and rigidity six years ago. At that time, the laboratory findings in other hospital showed hypokalemia, hypocalcemia with mild hypercalciuria, severe hypomagnesemia, and nephrocalcinosis. At that time, the levels of renin and aldosterone were elevated. He had been treated with potassium and magnesium oral supplements, amiloride, and spironolactone for 6 years. He showed persistent hypomagnesemia in spite of magnesium oral supplement and was given intermittent magnesium intravenous supplement. His height and body weight were all more than the 50th percentile and physical examination was normal. After referral, the investigations showed normal renal function, low serum potassium and magnesium, elevated urinary potassium and hypercalciuria. Kidney ultrasonography showed bilateral medullary nephrocalcinosis or renal stone. These findings were not fully compatible with any kind of tubulopathy, however, the presumed diagnosis includes type III BS, type V BS, GS, or familial hypomagnesemia with hypercalciuria and nephrocalcinosis. The genetic study revealed no mutation in CLDN16 gene. Genetic tests for SLC12A3 gene mutation present in GS came negative. Genetic test for CASR gene present in type V BS was negative. CLCNKB gene mutation analysis revealed a heterozygous c.139G>A in exon 13 [p.Gly(GGG)465Glu(GAG)]. The patient is now being treated with potassium and magnesium oral supplements, and indomethacin without muscle weakness or muscle cramps. Even though this change in CLCNKB gene is not known mutation, the clinical findings and in silico prediction are suggestive of causative mutation.

Key Words: 바터 증후군, CNLCNKB 유전자, 저마그네슘 혈증
Bartter syndrome, CLCNKB gene, Hypomagnesemia