Infantile Bartter Syndrome with Sensorineural Deafness

Alternative Names
BSND
Bartter Syndrome, Type 4
Bartter Syndrome, Type 4, Digenic

WHO International Classification of Diseases
Endocrine, nutritional and metabolic diseases

OMIM Number
602522

Mode of Inheritance
Autosomal recessive

Gene Map Locus
1p31, 1p36, 1p36

Description
Variants of inherited hypokalemic tubulopathies follow autosomal recessive inheritance and share characteristic clinical features: renal salt-wasting, hypokalemic metabolic alkalosis, and normotensive hyperreninemic hyperaldosteronism.

The neonatal variant of Bartter syndrome can be now classified genetically into four subtypes. In type I Bartter syndrome, the sodium potassium-2 chloride (NKCC2) luminal channel is mutated. In type II Bartter syndrome, the luminal ROMK potassium channel is affected. Type III Bartter syndrome is related to mutations in the basolateral ClC-Kb chloride channel. The recently identified form of Bartter syndrome includes infants with uniformly concomitant sensorineural deafness (BSND), a condition originally described in an Arab Bedouin kindred.

Molecular Genetics
Infantile Bartter syndrome with sensorineural deafness is caused by mutations in the Barttin gene. The gene encodes a beta-subunit for basolateral chloride channels in the distal tubule, including ClCKb.

Epidemiology in the Arab World

Lebanon
Jeck et al. (2001) conducted a study on the clinical data of members of a consanguineous family from Lebanon with hypokalemic salt-losing tubulopathy with chronic renal failure. In the index female case of the family, prenatal course and postnatal renal salt and water wasting suggested the diagnosis of hyperprostaglandin E syndrome/antenatal Bartter syndrome. Beginning at three months of age, renal ultrasound showed hyperechoic kidneys. At 1 year of age, complete sensorineural hearing loss was diagnosed. At 2 years of age, renal biopsy showed marked tubulointerstitial fibrosis and global glomerular sclerosis. During the second pregnancy in the family, polyhydramnios and fetal hydrops with ascites and pleural effusions were diagnosed at 17 weeks of gestation. At 30 weeks of gestation, a male infant was born by cesarean section because of fetal distress. Vomiting that was resistant to indomethacin treatment was a major problem in the medical care of the preterm infant and led to introduction of continuous partial parenteral nutrition. The elder patient received a cochlear implant at the age of three years with positive effect on speech development.

Palestine
Landau et al. (1995) described five children with infantile Bartter syndrome and sensorineural deafness, two sisters and their three male cousins, born to an extended Bedouin family with multiple consanguineous marriages. The age of affected children ranged between 1 month and 16 years. They presented some clinical variability with regard to the course of the renal disease and especially its early manifestations and severity. However, sensorineural deafness was uniform, severe, and of very early onset in all patients (1 month). In three of the cases, the typical electrolyte...
imbalance and facial appearance were detected neonatally.

In year 2003, Shalev et al. conducted a retrospective analysis in 13 infants with Bartter syndrome with sensorineural deafness. All pregnancies were complicated by polyhydramnion and premature birth. All patients have sensorineural deafness, as well as hypokalemic metabolic alkalosis. Persistent hypercalciuria or nephrocalcinosis were absent in most children. All children have been treated with indomethacin (2 mg/kg/d) and potassium supplementation. Kidney biopsies from two 7-year-old patients revealed mild focal tubulointerstitial fibrosis and minimal mesangial proliferation but no glomerulosclerosis. Shalev et al. (2003) concluded that early renal function deterioration is not a uniform finding among children with Bartter syndrome with sensorineural deafness mutations.

References

Contributors
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