Bartter-Like Renal Phenotype in a Child with Donnai–Barrow Syndrome

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To the Editor: Donnai–Barrow syndrome is an autosomal recessive disorder due to mutations in *LRP2* gene that encodes megalin [1]. Low molecular weight (LMW) proteinuria is the most common renal manifestation. Here we describe a 2 y 4 mo old male child with this syndrome who presented with features of salt losing tubulopathy mimicking Bartter syndrome.

The proband was 4th born of 3rd degree consanguineous marriage. He was operated for omphalocele on day 13 of life. He had delay in growth and development and complex febrile seizures in infancy. Fundus showed chorioretinal dystrophy. Visual evoked potential (VEP) testing depicted absent waveform. Brainstem evoked response audiometry (BERA) testing indicated profound sensorineural hearing loss. One of his sibling expired in neonatal period due to diaphragmatic hernia.

He presented at 18 mo of age with fever, polyuria, vomiting, and chronic constipation. Weight was 4.6 kg (−6.7 SD), length 65 cm (−7.02 SD) and head circumference 42 cm (−4.2 SD). On examination, he had large anterior fontanelle, V-shaped hairline at center of forehead (widow's peak), wide metopic suture, hypertelorism, iris coloboma, down slanted palpebral fissures, posteriorly rotated ears, depressed nasal bridge with broad tip. Polyuria (6.6 mL/kg/h) and dehydration was present. His blood pressure was normal. Hemogram revealed microcytic hypochromic anemia (Hb 8.5 g/dL). Kidney function test suggested acute prerenal injury (AKI). He was managed symptomatically.

Following resolution of AKI (2 wk later), repeat electrolytes evaluation revealed low sodium (125 meq/L), potassium (2.6 meq/L), ionised calcium (0.9 mmol/L), phosphate (3 mg/

dL), magnesium (1.1 mg/dL) and hypochloremic (80 mmol/L) metabolic alkalosis. Spot urine electrolytes demonstrated high potassium (155 mmol/L), chloride levels (152 mmol/L) with normal spot calcium creatinine ratio (0.56 mg/mg). Ultrasound of kidneys were normal. Urinalysis showed significant proteinuria (spot protein creatinine ratio-0.6) and protein electrophoresis confirmed presence of LMW moieties (IgG > 8 mg/g, β 2 microglobulin: > 5 mg/g Cr).

Clinical exome study identified a pathogenic homozygous non sense variant c.1093C > T (p.Arg365Ter) in exon 10 coded by *LRP2* gene (based on ACMG criteria). Variants causing Bartter syndrome were not identified. The child was started on indomethacin, multivitamin and electrolyte supplements.

LMW proteinuria occurs due to disturbed resorptive function of megalin in proximal convoluted tubule [2]. In addition, there was presence of salt losing tubulopathy mimicking Bartter syndrome type 3. Hypercalciuria can be variably present in Type-3 class [3]. As whole exome sequencing or MLPA was not performed, a chance association cannot be completely ruled out.

Compliance with Ethical Standards

Conflict of Interest None.

References

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