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PEDIATRIC BARTTER SYNDROME

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Abstract

In 1962 Bartter et al identified a new inherited renal tubular disorder characterized by hypokalemia metabolic alkalosis, normal blood pressure with hyperreninemia increased urinary loss of sodium potassium and chloride. We report a pediatric patient with Bartter Syndrome, who improved potassium and dietary supplements.

Bartter syndrome is an inherited salt-losing tubulopathy characterized by hypokalemia, hypochloremic metabolic alkalosis and normal blood pressure with hyperreninemia and increase urinary loss of sodium, potassium and chloride. Common clinical manifestations are failure to thrive, polyuria and episodes of dehydration. Bartter syndrome should be differentiated from non-renal causes of chloride loss such as vomiting, dietary deficiency and cystic fibrosis. In this condition urinary chloride concentration is invariable below 10meq/l. Urinary chloride concentration is usually >20-30meq/l in cases of Bartter syndrome. The combination of hypocalciuria with renal magnesium wasting distinguishes Gitelman syndrome from Bartter syndrome.

Case Report

A 2-year-old girl born to a non-consanguineous parent with no siblings, and was delivered pre term (6.5 months) gestation NVD at a district hospital. The baby weight was 1.020 kg and was managed in SNCU for 6 days. She remained well apparently upto 2 years of age. She developed loss of appetite along with weight loss, non-bilious vomiting , frequent loose stools and failure to thrive. For these complaints she was admitted from Pediatric OPD to ward for evaluation at the age of 2 years. Previous investigation report not available. There was no prior history of administration of any antibiotics. On examination, child weight 4.5kg (<3rd percentile), height 75 cm (<3rd percentile) Head Circumference=39cm (< 3rd percentile). She was poorly nourished and dehydrated with no facial dysmorphism. She was normotensive no localizing sign on neurological examination. Investigation showed hypokalemic hypochloremic metabolic alkalosis. (serum potassium 2.1mEq/l , chloride 91.9mEq/l ,bicarbonate 32mEq/l, pH 7.54 and pCo2 32 mm of Hg) Normal serum levels of creatinine, calcium, magnesium and increased urinary loss of chloride, potassium and calcium(chloride 29mEq/l, Ca: Creatinine 3300), urine output was 7ml/kg/hr. USG abdomen revealed features of nephrocalcinosis in both the kidneys. Taking into consideration all the above parameters a diagnosis of Bartter syndrome was made. Plasma renin of this child was unavailable. Judicious treatment was started with potassium supplements, fluid balance and dietary advice which lead to clinically improved. Blood values after 10 days from admission were sodium 134mEq/l, pottasium3.2 mEq/l, chloride 99.4mEq/l,

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bicarbonate 24mEq/l, pH 7.50 and Pco2 36mm of hg. Indomethacin was started after 20 days of admission in a dose of 2-3 mg/kg/day BD. Patient was discharged in a stable condition on 26th day after admission with advice of oral potassium supplement and oral indomethacin.

Discussion

Barter syndrome is a rare inherited salt -losing renal tubular disorder characterized by hypokalemia, metabolic alkalosis with hyperaldosteronism and hyperplasia of juxtaglomerular apparatus.[1]

Mutations of several genes encoding transpoters involved in salt reabsorption in Thick Ascending Limb cause different types of Bartter syndrome (BS)

Type I BS ->mutation in NKCC2(SLC12A1)

Type II BS->mutation in CLCKb (CLCNKB)

Type Iva-> BS mutation in bartin (BSND)

Type IVb->BS mutation in CLC-Ka and CLC-Kb(CLCNKA ,CLCNKB)

All these 4 types are recessive. Another subtype of BS considered as type IV which is a gain of function mutations of CASR and is characterized by an autosomal dominant hypocalcemic, hypercalciuria. Recently mutations in melanoma- associated antigen D2(MAGE-D2) have been implicated in a form of Antenatal BS and is characterized by very early onset of severe polyhydramnios and complete resolution of symptoms after birth.

Polyhydramnios typically develops between 20th-30th wk of gestation. In BS4 and BS-5 ->Polyhydramnios observed earlier than in BS1 and BS2.[2] BS 3 usually manifests later in life. Prenatal presentation doesn't exclude BS 3.The vast majority of patients with BS3 are diagnosed after the age of 1yr.[3]

The symptoms starts during infancy and include polyuria, polydipsia, vomiting, constipations and failure to thrive. Recurrent episodes of dehydration, muscles weakness and cramps are prominent in older children. The blood pressure is low normal. Renal biopsy shows hyperplasia of juxtaglomerular apparatus.[4]

The Pediatric form of BS differ from neonatal form by the age of onset, frequent presence of nephrocalcinosis and very high urinary loss of sodium, chloride, in neonatal form.[5] Other Differential Diagnosis are Gittleman syndrome (characterized by hypomagnesemia, hypocalciuria), Pseudo-BS (low urinary chloride) often found cystic fibrosis cases and Liddle syndrome (hypotension, low renin /low aldosterone)[6].

Prenatal diagnosis can be deduced by the high chloride content of amniotic fluid and mutational analysis of genomic DNA expected from cultured amniocytes obtained by amniocentesis [7.]

Therapeutic efforts should be directed to correct dehydration and electrolyte imbalance. Pharmacological suppression of prostaglandin formation addresses the underline pathophysiology and many clinical observational studies has shown benefits in the form of improved growth and electrolyte profile. Commonly used NSAID in BS are indomethacin (1-4mg/kg/day divided in 3-4 doses), ibuprofen (15-30mg/kg/day in 3 doses) and celecoxib (2-10mg/kg/dayin 2 doses) [8].

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Addition of potassium sparing diuretics ACE-I and angiotensin receptor blockers can help ameliorate the electrolyte abnormalities (hypokalemia in BS. A few kidney transplantation have been reported in the literature . In all cases, electrolyte abnormalities and polyuria were corrected and recurrent disease was not observed.[9]

Data on long term outcomes in BS are sparse. Lack of satisfactory control may lead to morbidity growth failure and renal insufficiency.

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