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Case Report

Classical Bartter syndrome in a 3 years old girl

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ABSTRACT

Bartter syndrome is rare genetic disorder of kidney characterized by hypokalemia, hypochloremia, metabolic alkalosis, hyponatremia, hypercalciuria, hyperreninemia, hyperaldosteronism with normal blood pressure. Here we report a case of 3 year old girl born of consanguious marriage, with complaints of not gaining weight with history of polyuria, polydipsia, having clinical and laboratory features of Bartter syndrome.

Keywords: Bartter syndrome, Metabolic alkalosis, Polydipsia, Polyuria

INTRODUCTION

Bartter syndrome (BS) is a rare genetic condition first described by Bartter in 1962.[1] It is a tubular disorder of kidney affecting the thick ascending limb of loop of Henle (LOH) leading to salt wasting. It is characterized by hypokalaemia, hypochloremia, hypercalciuria, metabolic alkalosis, hyperreninemic hyperaldosteronism, and a normal blood pressure.[2]

Mutations of several genes encoding the transporters and channels involved in salt reabsorption in the thick ascending limb cause different types of BS. This syndrome is associated with an increased antenatal and neonatal mortality because many patients fail to thrive. It is commonly seen in the prenatal and neonatal period. Very few cases of acquired BS are described in the literature; they are commonly associated with tuberculosis, autoimmune conditions such as Sjogren's disease, granulomatous conditions like sarcoidosis, or following administration of drugs such as aminoglycosides, loop diuretics.[3,4]

CASE REPORT

A 3 year female brought by parents complaining of not gaining weight with delay in motor milestones. There was past history of increase water intake and increased frequency of urination 15-20 times per day since one year of age. She was born of consanguineous marriage. Her antenatal, natal, postnatal period, and first year of life were uneventful with normal development. There is family history of sibling death on day one of life, whose cause is not known. Patient was having dietary deficiency of 400 kcal/day and 6 gm of protein/day.

On examination, child was wasted and stunted with weight of 5.25 kg, length of 69 cm and head circumference of 46 cm. Patient was having triangular facies, frontal bossing, large eyes, protruding ears, costochondral beading, kyphoscoliosis, widening of wrist, protruded abdomen. Blood pressure was normal, which was measured daily during hospital stay.

On laboratory investigation, serum urea-37 mg/dl, serum creatinine was 0.63 mg/dl. Serum sodium was 128 mmol/l, serum potassium was 1.8 mmol/l, serum chloride was 82 mmol/l. Arterial blood gas analysis suggestive metabolic alkalosis. Serum calcium was 1.92 mmol/l. Serum alkaline phosphatase was high. Serum osmolality was 270 mOsm/kg.

Thus patient was having hypokalemic, hypochloremic, metabolic alkalosis.

As the child was normotensive and had persistent hypokalemia in the absence of any relevant drug history like chronic loop diuretic use, we made our provisional diagnosis of Bartter and Gitelman syndrome.

Urine output of patient was 20-25 ml/kg/hr before treatment. Urine biochemical analysis showed high sodium (80 mmol/l), high potassium (36 mmol/l), and high chloride (130 mmol/l) level. Urinary calcium to creatinine ratio was 0.7 and specific gravity was 1.005. Serum magnesium was normal.

Ultrasound abdomen showed bilateral bright kidneys. Hearing assessment and audiogram were normal. The results of an x-ray of her kidney-ureter-bladder and an ultrasound scan of her kidneys were normal with no evidence of nephrocalcinosis. X-ray of spine showed kyphoscoliosis. Genetic studies, serum aldosterone level and serum renin level were not done due to non-availability of such special investigations in our institute.

On the grounds of clinical history, examination and investigations we made a diagnosis of classical Bartter syndrome.

The child was treated with oral potassium supplements, indomethacin. Appropriate dietary advice given. On follow-up, patient's urine output decreased dramatically and came to 4 ml/kg/hr. Her electrolytes became normal with a serum sodium value of 135 mmol/l potassium of 3.5 mmol/l, serum chloride 95 mmol/l. Urinary excretion of sodium, calcium decreased and calcium to creatinine ratio came to 0.4.

DISCUSSION

BS is a rare autosomal recessive renal tubular disorder that affects around 1 in 1,000,000 of the population, caused by a defective salt reabsorption in the thick ascending limb (TAL) of loop of Henle, resulting in salt wasting, hypokalemia, and metabolic alkalosis with relatively low levels of serum chloride.[1,2] In addition, patients with BS present with hyperreninemic hyperaldosteronism with normal/low blood pressure, reduced peripheral resistance, and hyporesponsiveness to antihypertensives.[5]

This syndrome is associated with an increased antenatal and neonatal mortality because many patients fail to thrive. BS has traditionally been two main clinical variants, as follows: neonatal (or antenatal) BS and classic BS.

Neonatal BS (types 1 and 2) usually presents in the newborn period. There is often preceding maternal polyhydramnios due to fetal polyuria and premature birth. Massive polyuria with life-threatening volume depletion and poor weight gain are seen. Nephrocalcinosis is universal in these types. The classic BS (type 3) phenotype is highly variable. The presentation may be like the typical 'neonatal' variant that manifests in the early neonatal period or the 'classic' variant that is characterized by childhood onset of fatigue, polyuria, polydipsia, salt craving, vomiting, dehydration, short stature, and failure to thrive; nephrocalcinosis is absent and hypercalciuria is less severe/absent. BS type 4, one distinct variant is associated with sensorineural deafness.[6]

The neonatal form differs from the classic BS by the age of onset, presence of nephrocalcinosis and very high urinary loss of sodium, calcium and chloride. Other differential diagnoses are Gitelman's syndrome (characterized by hypomagnesemia, hypocalciuria), pseudohyperaldosteronism (hypertension with no evidence of increased secretion of mineralocorticoids) and pseudo-BS due to administration of high doses of prostaglandin E1.[7]

Advances in molecular diagnostics have revealed that BS results from mutations in numerous genes that affect the function of ion channels and transporters which normally mediates salt reabsorption in the distal nephron segments.[8] Prenatal diagnosis can be made by the high chloride content of the amniotic fluid and mutational analysis of genomic deoxyribonucleic acid (DNA) extracted from cultured amniocytes obtained by amniocentesis.[9]

Therapeutic efforts should be directed to correct dehydration and electrolytic imbalance. Doses of potassium chloride supplementation should individually be titrated in accordance to the patient's needs and balanced by the renal loss.[8]

The most widely used group of medications in the treatment of classic BS is the prostaglandin synthetase inhibitors. Indomethacin, aspirin, and ibuprofen have all been tried and the best evidence comes from indomethacin.[10] Administration of indomethacin after 6-12 weeks of life is useful. Indomethacin at a dose of 1-5 mg/kg/day is most frequently used and well tolerated. Other drugs used are acetylsalicylic acid (100 mg/kg/day), ibuprofen (30 mg/kg/day) or ketoprofen (20 mg/kg/day).[11] Addition of potassium sparing diuretics may be initially effective in the control of hypokalemia but their effect is transient. Sodium chloride supplementation may be needed early in life, but high dietary salt intake is often sufficient in older children. Genetic counseling should be offered to couples whose previous siblings have suffered from the disorder.

CONCLUSION

BS is rare genetic disorder with sometimes devasting clinical manifestations such as failure to thrive. Early, appropriate diagnosis and initiation of proper therapy could avoid further progression and reduce complications of the disease.

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