CASE REPORT

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A Rare Case of Dyselectrolytaemia – Adult Onset Bartter Syndrome

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Abstract

Bartter syndrome (BS) is a rare autosomal recessive disorder affecting salt reabsorption in the thick ascending limb of the loop of Henle. This report highlights clinicopathological findings and genetic studies of classic BS in a 43-year-old male patient who presented with persistent hypokalaemia, hypocalcaemia and hypercalciuria with low cognitive abilities and sensorineural hearing loss, diagnosed as Bartter syndrome. Genetic analysis of the patient was done which did not reveal any mutations of NKCC2 SLC12A1, KCNJ1, CLCNKA, CLCNKB and MAGE-D2. This case represents an atypical presentation of classic BS in an adult patient. Clinical and laboratory findings with persistent dyselectrolytaemia in the form of hypokalaemia, hyponatraemia, hypocalcaemia with hypercalciuria with mild sensorineural deafness and low cognitive abilities were important for diagnosis of this case.

Key words: Hypokalaemia; hypocalcaemia, hypercalciuria, sensorineural hearing loss, low cognition.

Introduction

Bartter syndrome (BS) is a rare renal tubulopathy that was first described by Bartter in 1962. The condition is characterised by polyuria, hypokalaemia, metabolic alkalosis, and hyper-reninaemic-hyperaldosteronism with normal or slightly low blood pressure due to renal loss of sodium and hyperplasia of the juxtaglomerular apparatus (JGA). The condition is also referred to as salt-wasting nephropathy[1]. The prevalence of BS is 1 in 1,000,000, compared with 1 in 40,000 for Gitelman syndrome (GS)[3]. The classification depends on the severity of the symptoms and the type of genetic mutation. Clinically, BS can be classified into two variants, antenatal/neonatal BS and classic BS, according to the onset of age. Genetically, BS can be classified into five variants according to the type of gene mutation[2]. Type V BS presents as classic BS, which is characterised by polyuria, polydipsia, and a tendency for dehydration, hypocalcaemia, hypomagnesaemia and hypercalciuria. Patients with classic BS might have symptoms in the first two years of life, but most cases are usually diagnosed at school-age or in adolescence. However, age of onset and clinical severity is highly variable[5].

Here, we present a case of late-onset BS, with typical hypokalaemia, hypomagnesaemia, hypocalcaemia, and hypercalciuria with low cognitive ability since birth and mild sensorineural hearing loss, corresponding to the features of type V BS.

Case report

A 43-year-old male patient presented to A and E with persistent vomiting, pain abdomen and altered sensorium since 3 days with no history of fever and no prior comorbidities.

He was a labourer by occupation with lower socio-economic status. His mother gave a history of mild deafness from childhood (around 10 years) and was intellectually challenged since childhood. He was a reformed alcoholic left, 2 years back and a chronic smoker with 1 pack beedis per day. There was no significant family history with and an unremarkable prenatal history. He was previously diagnosed to have suspected Wernicke's encephalopathy/Viral encephalitis but was not on follow-up. There was no use of diuretics, laxatives or nephrotoxic drugs.

On examination, the patient was moderately built and nourished with no signs of pallor, icterus, cyanosis, clubbing, lymphadenopathy or oedema and vitals were stable.

On evaluation, he had a normocytic normochromic anaemia with neutrophilic leukocytosis. Renal function tests showed hyponatraemia and hypokalaemia, for which correction was given. ABG showed hypochloraemic metabolic alkalosis with Ph 7.56, bicarbonate - 36 mmoL/lt. LFT was within normal limits. Serology for HIV, HBsAg, and Anti-HCV were non-reactive. Urine routine was normal. Amylase and lipase were within normal limits. USG abdomen and pelvis showed mild increase in renal cortical echogenicity of both kidneys with maintained corticz – medullary differentiation. 2D ECHO was normal. CT Brain was done as he had altered sensorium and showed chronic infarct in posterior limb of

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left internal capsule with age disproportionate cerebral atrophy. MRI Brain showed mild diffuse cerebral atrophy – disproportionate to age. RFT was monitored regularly. Patient had persistent hypokalaemia and correction was given for the same. On the 4th day of hospitalisation he developed tetany (Trousseau's sign and Chvostek's sign were positive). Serum calcium and magnesium were low and correction was given for the same. Upon re-evaluating the history and examination, the patient gave a history of polyuria and polydipsia since 1 year. Release reflexes were present (glabellar tap and palmomental reflexes). His serum calcium, magnesium, electrolytes were monitored regularly and correction was given for the same. Spot urine calcium, magnesium, sodium and potassium were within normal limits. 24-hour urinary calcium, sodium, and magnesium were high. 24-hour urinary potassium was within normal limits. Input and output monitoring was done daily. Upper gastrointestinal endoscopy was done which showed gastric erosions and treatment was given for the same. On suspicion of adult onset Bartter syndrome, Tab Indomethacin 75 mg once daily was introduced following which the patient improved significantly, both clinically and biochemically. Genetic analysis was done which did not reveal any mutations of NKCC2 *SLC12A1, KCNJ1, CLCNKA, CLCNKB* and *MAGE-D2*. After 1 month, his reports were serum pH: 7.326, serum bicarbonate: 21.7 mmoL/L, serum potassium: 4.3 mEq/L. Subsequently, repeat calcium, magnesium, electrolytes are within normal limits and polydipsia and polyuria had recovered.

Discussion

Bartter syndrome was first described by Bartter *et al* in 1962[1]. Bartter syndrome can be inherited or acquired. Inherited Bartter syndrome is divided into five subtypes: types I-IV are due to a loss of function mutations and type V due to gain of function mutation. Types I, II, and IV are usually called antenatal Bartter syndrome while type III is called adult-onset/classical Bartter syndrome. Type V Bartter syndrome can be distinguished from all other types by the presence of hypocalcaemia and hypomagnesaemia. In addition to this, there are several acquired causes of Bartter syndrome, including autoimmune disorders like Sjogren syndrome, Hashimoto thyroiditis, scleroderma, and several drugs like aminoglycosides, loop diuretics, amphotericin, etc[4].

Bartter syndrome is classified into different subtypes according to the gene mutations involved: type I BS is caused by mutations in NKCC2 (*SLC12A1*); type II BS is caused by mutations in ROMK (*KCNJ1*)18; type III BS is caused by mutations in CLC-Kb (*CLCNKB*)19; type IVa BS is caused by mutations in barttin (*BSND*) 20 and type IVb BS is caused by mutations in CLC-Ka and CLC-Kb (*CLCNKA* and *CLCNKB)*. All these four types are recessive disorders. An additional distinct subtype of BS, considered as type V BS by many investigators, is ascribed to gain-of-function mutations of *CASR* and is characterised by an autosomal dominant hypocalcaemic hypercalciuria. More recently, mutations in melanoma-associated antigen-D2 (*MAGE-D2*) have been implicated in a transient form of antenatal BS, also referred to as type V BS according to some reports. This newly recognised form of BS is characterised in most cases by a very early onset of severe polyhydramnios and complete resolution of symptoms after birth[6].

Types I, II, and IV have a neonatal presentation, while in type III, the symptoms begin in the first 2 years of life, but diagnosis is made later, at school age or adolescence.

The pathophysiology of Bartter syndrome is related to defect in the sodium/potassium/chloride co-transporter, or potassium channel in thick ascending limb of the loop of Henle. This leads to reduced reabsorption of sodium, potassium and chloride in the thick ascending limb of the loop of Henle. This in turn results in the delivery of these ions to the distal segments where only some sodium is reabsorbed and potassium is secreted[7].

Patients with Bartter syndrome exhibit a blunted pressor response to exogenous administration of angiotensin II. Recent reports suggest that overproduction of prostaglandins by the kidney plays a major role in the pathogenesis of this syndrome. Thus, administration of indomethacin, an inhibitor of prostaglandin synthesis, was followed by clinical and chemical improvement in the patients and recovery of their vascular sensitivity to angiotensin II as seen in our patient[8].

The classical pharmacological therapy includes potassium chloride supplementation, prostaglandin inhibitor (indomethacin), and aldosterone antagonist (spironolactone)[6]. Our patient improved with indomethacin. Indomethacin inhibits PGE2 which is overexpressed in Bartter syndrome. There are a few reports of Bartter syndrome in adults[7].

Conclusion

Though Bartter syndrome is diagnosed at a young age, an adulthood presentation is possible due to phenotypic variation as in our case.

References

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