A CASE OF ADULT ONSET BARTTER’S SYNDROME

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ABSTRACT
Bartter’s syndrome consists of genetically heterogeneous group of disorders presenting with features of salt losing tubulopathy of frusemide type which is characterised by polyuria, hypokalaemia, hypochloraemia, metabolic alkalosis, normal blood pressure with hyerreninemic hyperaldosteoneism. We report a case of 25 year old male presenting with paraparesis and Bartter like phenotypic presentation. We report this case because of its presentation in adults which is rare.

Keywords: Bartter’s Syndrome, Diuretic Abuse, Hypokalaemia, Metabolic Alkalosis

INTRODUCTION
Bartter’s syndrome, a hereditary disorder linked to mutation in five genes (Lee et al., 2012) with autosomal recessive (type1-4) or autosomal dominant pattern (type 5) mode of inheritance. These genetic defect affect ion transport channels in thick ascending loop of Henle and distal convoluted tubule. 30% of the filtered Na and Cl is reabsorbed in thick ascending limb, which when affected lead to defective reabsorption is the main pathology. The antenal variants are type 1, 2 and 4 with defect in NKCC2, ROMK and BARTTIN, a β subunit for CLCKa and CLCKb transport channels respectively. Type 3 (classical variant) present with early childhood or continue into adulthood, defect in CLCNKb channel and nephrocalcinosis is not a constant feature. Type 5 (hypocalcaemia with bartter) due to gain of function mutation in CaR channel, so it is associated with hypoparathyroidism (Yamamoto et al., 2000) and hypomagnesimia (Waldegger, 2008). The main differentials to be excluded are Gitelman syndrome and pseudo Bartter (diuretic abuse and surreptitious vomiting, cystic fibrosis). The prevalence of Gitelman syndrome was 1 in 40,000 compared with 1 in 1,000,000 for Bartter syndrome (Ji et al., 2008). The lower prevalence of Bartter syndrome in the population may be due at least in part to prenatal or neonatal death resulting from the disorder before it could be diagnosed. So, its presentation in adults is rare (Xiumin et al., 2013; García Castaño et al., 2013; Simon et al., 1997).

CASES
A 25 year old male who is an alcoholic, smoker, presented with sudden onset weakness of both legs for 1 day. History of difficulty in using both upper and lower limbs. He has a history of strenuous exercise following which he developed this deficit.

Patient had a previous history of similar episode in past for which he took treatment and was not on regular follow up. Patient had no history of gastro intestinal loss. No history of drug intake like insulin, diuretic, antibiotics.

Patient was born to non-consangunieous parents. No history of similar episode among family members. On examination- BP-110/70 mmHg, PR-98/min, SPO2-90%, single breath count was 10. Neurological examination- power of both upper and lower limb were 1/5. Hand grip was 80%. Deep tendon reflexes were absent. Sensory, autonomic and cranial nerve examination were normal. No deafness or growth retardation.

Investigation revealed Serum potassium-1.7meq/L, serum sodium-146meq/L, random blood sugar-100mg/dl, arterial blood gas analysis showed pH-7.46, HCO3-25.4 mmol/L, pCO2- 37.3 mmHg, Na+-146 mmol/L, K+-2.84 mmol/L. Urine potassium was 24 mmol/day and Trans tubular gradient was 5.63 indicated increased distal potassium secretion. Urine chloride level was 111mmol/day, urine calcium/creatinine ratio was 0.311. Serum magnesium was 2.00mg/dl. Thyroid function test was normal. Hypokalemia, normal blood pressure, metabolic alkalosis, hypercalciuria, normal magnesium level lead to diagnosis of Bartter’s syndrome.
DISCUSSION
In Bartter’s syndrome, most common mutated gene is KCNJ1. Deafness points to BSND defect, neonatal history of hyperkalaemia later followed by hypokalaemia points to KCNJ1 defect, CLCNKB defect has severe metabolic alkalosis. The genetic defects affect the ion transport channels in thick ascending loop of Henle and distal convoluted tubule. Gitelman syndrome is differentiated from Bartter's by its late presentation and it is thiazide like salt losing tubulopathy. Features like hypo magnesia, hypocalciuria and chronic hypercalciuria (Waldegger, 2008) occur only in Gitelman not in Bartter’s syndrome.

The features of Bartter’s include polyuria, polydipsia, and decreased concentrating ability (Kurtz, 1998; Stein, 1985). Chronic fatigue, muscle weakness, cramps, constipation and recurrent vomiting, paralysis. Growth retardation, hypokalaemic nephropathy and nephrocalcinosis are some long term effects.

Our patient presented with sudden onset weakness of lower limbs with preserved sensory and autonomic functions. He had no feature of polyuria or polydipsia.

Dysfunction of the channels described previously lead to hypokalemia, hypochloremia, hypercalciuria. Hypokalemia is due to compensatory mechanism that is activated to absorb more NaCl downstream. This also leads to metabolic alkalosis.

Hypomagnesemia occurs in 20% of cases (Walsh et al., 2011). hypercalciuria and nephrocalcinosis occur in type 1,2 not in type 4, rare in type 3. Stimulation of renin-angiotensin axis and activation of TGF-β is responsible for renal changes (Yamamoto et al., 1996). Even with high angiotensin II they have low/normal blood pressure due to renal release of prostaglandin E2. Prostaglandin E2 production due to increased cyclooxygenase 2 (COX2) expression (Kömhoff et al., 2004). So, these patients do not develop hypertension or its complications (Pagnin et al., 2006).

Our patient presented with hypokalaemia, hypochloremia, metabolic alkalosis, with hypercalciuria. Serum magnesium levels were normal. Nephrocalcinosis was absent. Patients’ blood pressure was normal. Urine potassium was elevated. Transtubular potassium gradient (TTKG) was >4. Urine chloride and urine calcium creatinine ratio was elevated. USG and CT abdomen was normal.

Treatment includes oral potassium supplementation (1 to 3mmol/kg/day) mainly potassium chloride is preferred. NSAID (indomethacin 2 to 4 mg/kg/day) and high dose spironolactone (2 to 5 mg/kg) or amiloride (10 to 15 mg/kg) can be given. Increasing oral salt intake is not acceptable as it leads to more potassium loss.

Our patient was treated with oral potassium chloride supplementation and patient recovered from weakness.

The prognosis of Bartter’s syndrome depends on the type, among which type 3 and 5 appear to be less severe than type 1 and 2. In long term 25% develop mild impairment of kidney (Jeck et al., 2001). Only few data’s about long term follow up of adult patients with Bartter’s syndrome is available. End stage renal disease is uncommon in Bartter’s syndrome (Puricelli et al., 2010).

REFERENCES


