A CASE OF ADULT VARIANT BARTTER SYNDROME

Sami Ullah, Malik Nadeem Azam, Zubair Waheed Khan, Syed Muhammad Hassan Akhtar

Military Hospital Rawalpindi

INTRODUCTION

Bartter syndrome was first described in an article by Bartter et al in 1962 [1]. Bartter syndrome is a rare genetic disease characterized by hypokalemia, alkalosis, and normal to low blood pressure. We describe it due to the rarity of the condition and because it was described once in our country and that too in a neonate [2] whereas our patient is an adult.

CASE REPORT

A 29 years old male, with no previous medical history presented in a peripheral hospital with 20 days history of weakness, nausea, polydipsia, weight loss and irregular fever. It was followed 10 days later by weakness in proximal muscles of both lower limbs, making difficult for him to get up from sitting position. His physical examination revealed generalized wasting, a pulse of 56 beats per minute and power of +4/5 in lower limbs. However, it was normal distally and upper limbs were spared. Reflexes were intact bilaterally with a flexor plantar response. Rest of the systemic examination was unremarkable. His ECG showed prolonged QT interval of .48 sec, wide QRS complexes of .12 sec, with slightly depressed ST segments in leads II, III and aVF. Serum CK was 1198 U/L with normal LDH. Urine examination and renal profile were normal initially. CK-MB and electrolytes were not available at the location. A provisional diagnosis of Non ST Elevation Myocardial Infarction was made and he was shifted to AFIC. His ECG now showed flat T and prominent U waves in addition to previous changes. His urine examination was still normal but serum creatinine was found to be 161 umol/l, serum urea of 7.7 mmol/l, with sodium of 137 mmol/l and markedly reduced potassium of 1.1 mmol/L. ABGs were consistent with metabolic alkalosis showing a pH of 7.51, pCO2 36.3 mmHg, pO2 96 mmHg, HCO3 29.3 mmol/l. Creatinine clearance was 30.8 ml/min. Abdominal ultrasound showed medullary nephrocalcinosis. Serum Calcium was 1.41 mmol/L, phosphate 1.61 mmol/L , magnesium 0.52 mEq/L. 24 hours urinary calcium level was 6.51 mmol/l (hypercalciuria), potassium 69 mmol/l (raised), chloride 169mmol/l. Serum PTH was 10 pmol/l (increased), plasma rennin and serum aldosterone were elevated and were 15.2 ng/ml/hr (supine) and 27.9 ng/dl (supine) respectively. Pure tone audiometry was normal.

A diagnosis of Bartters syndrome (Adult Variant) was made keeping in view hypokalemic metabolic alkalosis, raised urinary chloride, calcium and a normal blood pressure along with hyperreninemic hyperaldosteronism. He was started on potassium supplements, tablet amiloride, and tablet indomethacin and ACE inhibitors. After three month he was asymptomatic, had gained 13 kgs weight with normalization of serum and urinary electrolytes.

DISCUSSION

Bartters syndrome is characterized by hypokalemia, metabolic alkalosis, hyperreninemia, hyperaldosteronism, hyperplasia of the juxtaglomerular apparatus and, in some, hypomagnesemia [3]. The renal release of vasodilator prostaglandins is increased in this condition and may explain normal blood pressure [3,4]. Bartter's syndrome differs from other causes of hyperaldosteronism in two ways: the patients are not hypertensive; and the plasma renin

activity is increased by aldosterone-induced volume expansion.

The Bartter syndrome can result from a variety of defects in renal tubular function [3, 4] in most patients: classic Bartter syndrome and Gitelman syndrome (also called tubular hypomagnesemia - hypokalemia with hypocalciuria) [5]. The primary defect is impairment in sodium reabsorption in the loop of Henle and distal tubule, respectively.

Correspondence: Brig Raja Sami Ullah, Classified Medical Specialist, Military Hospital Rawalpindi
Received: 17 Apr 2007; Accepted: 02 Aug 2007

Classic Bartter's syndrome generally presents early in life and is often, but not always, associated with growth and mental retardation [3,5]. In addition to hypokalemia and metabolic alkalosis, polyuria, polydipsia, and decreased concentrating ability are also common [3,5]. Urinary calcium excretion is increased and plasma magnesium is either normal or mildly reduced [5]. These findings are compatible with a primary defect in sodium chloride reabsorption in the medullary thick ascending limb of the loop of Henle [5].

Prostaglandins, which directly stimulate renin release, contribute to the electrolyte abnormalities in Bartter syndrome as evidenced by the increase in urinary prostaglandin excretion and the ability of prostaglandin synthesis inhibitors to reverse most of the biochemical and hormonal changes, except sodium reabsorption [6]. Prostaglandin excretion appears to be normal and prostaglandin synthesis inhibitors are of little benefit in Gitelman syndrome [5]. This difference parallels the differences in response to diuretic administration. Loop diuretics (similar to Bartter syndrome) increase urinary prostaglandin excretion, at least in part via increased prostaglandin synthesis in the thick ascending limb. Thiazide diuretics (similar to Gitelman syndrome) produce little or no increase in prostaglandin excretion.

The diagnosis of these somewhat similar disorders is one of exclusion. Surreptitious vomiting and diuretic use are the two other major causes of unexplained hypokalemia and metabolic alkalosis in a normotensive patient. Measurement of renin and aldosterone levels is not helpful, since there is hypersecretion of renin in all of these conditions. However, vomiting is associated with a low urine chloride concentration (<18 meq/L, due both to hypovolemia and hypochloremia) and, in some patients, with characteristic physical findings, such as scarring on the dorsum of the hand and dental erosions from exposure to acid in the gastric secretions. Diagnosis of diuretic abuse can be confirmed (in the absence of a positive history) only by a urine assay for diuretics. The urine chloride concentration is variable, being high if the diuretic is still acting but low (due to volume depletion) if the diuretic effect has worn off. Patients with Bartter or Gitelman syndrome tend to be clinically euvolemic, with chloride excretion being equal to intake. The net effect is a urine chloride concentration that is usually above 16 mmol/l.

Treatment (life-long) is aimed at minimizing the effects of the secondary increases in prostaglandin and aldosterone production. The combination of a NSAID and a potassium-sparing diuretic, in higher than usual doses to more completely block distal potassium secretion can raise the plasma potassium concentration toward normal, largely reverse the metabolic alkalosis, and partially correct the hypomagnesemia [6 - 8]. A similar improvement in the plasma electrolyte picture can be achieved by the use of an angiotensin converting enzyme (ACE) inhibitor which diminishes the production of angiotensin II and aldosterone [8].

Most patients require oral potassium and magnesium supplementation, since drug therapy is usually incompletely effective. Diarrhea frequently limits the dose of magnesium given and the magnesium that is absorbed tends to be excreted in the urine. In addition, patients with impaired transport in the loop of Henle have diminished potassium as well as sodium and chloride reabsorption at that site. In this setting, blocking distal potassium secretion with amiloride and/or an ACE inhibitor will not reverse the reabsorptive problem in the loop, resulting in persistent potassium wasting. Hypomagnesemia can also contribute to urinary potassium loss via an uncertain mechanism.

REFERENCE

1. Bartter FC, Pronove P, Gill JR Jr, MacCardle RC. Hyperplasia of the juxtaglomerular complex with hyperaldosteronism and hypokalemic alkalosis. A new syndrome. Am J Med. 1962; 33: 811-28.
2. Parkash J, Salat MS, Khan IA. Neonatal Bartter Syndrome. J Coll Phy Surg Pak. 2006; 14: 8: 548-50.
3. Stein JH. The pathogenetic spectrum of Bartter's syndrome. Kidney Int. 1985; 28:85.
4. Fujita T, Ando K, Sato Y. Independent roles of prostaglandins and Renin - angiotensin system in abnormal vascular reactivity in Bartter's syndrome. Am J Med. 1982; 73:71.
5. Bettinelli A, Bianchetti MG, Girardin E. Use of calcium excretion values to distinguish two forms of primary renal tubular hypokalemic alkalosis: Bartter and Gitelman syndrome. J Pediatr. 1992; 100:38.
6. Vinci JM, Gill JR Jr, Bowden RE. The kallikrein-kinin system in Bartter's syndrome and its response to prostaglandin synthetase inhibition. J Clin Invest. 1978; 61: 1471.
7. Griffing GT, Komanicky P, Aurecchia SA. Amiloride in Bartter's syndrome. Clin Pharmacol Ther. 1982; 31:711
8. Hene RJ, Koomans HA, Dorhout Mees EJ. Correction of hypokalemia in Bartter's syndrome by enalapril. Am J Kidney Dis. 1387; 9:180.