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Case Report

Bartter Phenotype Unmasked by Use of Loop Diuretics -

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ABSTRACT

Bartter's syndrome is a rare genetic disorder manifesting predominantly in the antenatal or early neonatal period. Bartter like syndrome, sometimes referred to as Acquired Bartter syndrome can manifest at any age depending on the precipitating event. We report a case of Bartter phenotype in a patient of diabetes mellites unmasked by the use of loop diuretics.

Keywords: Bartter's syndrome; Metabolic alkalosis; Hypokalemia

Key Message: Severe hypokalemia precipitated by diuretic use requires evaluation for underlying tubular disorder and /or hyper aldosterone state.

INTRODUCTION

Bartter's Syndrome (BS) is a rare genetic condition described by Bartter and coworkers in 1962 [1]. The prevalence of BS is 1 in 1,000,000 [2]. It usually occurs due to genetic defects in one of the genes involved in NKCC2 (NA^+-K^+-$2Cl^-$) transport across luminal membrane of the thick ascending limb of the loop of Henle (TAL). Bartter like syndrome occurs due to conditions and/or drugs which interfere with NKCC2 transport across the thick ascending limb of the loop of Henle. This case is unique in the sense that the Bartter phenotype was precipitated by loop diuretics which unmasked the underlying tubular defect.

CASE HISTORY

A 40-year-old gentleman, presented with two weeks history of bilateral ankle edema and a one-week history of severe weakness. He had type 2 diabetes and had been on metformin for one month. The weakness was generalized but was more so in his bilateral lower limbs. He was unable to get up from sitting posture. There was no history of loose stools or recurrent vomiting. He denied any lower limb paresthesia, bowel or bladder disturbance. The patient had been on torsemide 20mg daily for the last two weeks.

On examination, the patient was conscious and well oriented to time, place, and person. His BP was 100/70 mmHg and his pulse was 86/min. His cardiovascular, respiratory and abdominal examination was normal. Neurological examination revealed normal higher mental functions and cranial nerves. Examination of the motor system revealed hypotonia in all 4 limbs. He had grade 3/5 and grade 4/5 power in bilateral lower and upper limbs respectively. Bilateral knee jerks were sluggish. His sensory exam was normal. Plantar reflex was bilateral flexor. There was no sensory or autonomic involvement.

Laboratory evaluation showed blood urea 31 mg/dl, serum creatinine 0.8mg/dl, sodium ion (Na^+) 134 meq/L, potassium ion (K^+) 1.3 meq/L, serum albumin 3.4 g/dl, random blood glucose 126 mg/dl, and HbA1c of 6.6. Arterial blood gas revealed a pH of 7.69, partial pressure of carbon dioxide of 55mmHg, serum bicarbonate of 60.2 meq/L. Further evaluation revealed urinary potassium of 40 meq/l with Transtubular Potassium Gradient (TTKG) of 12.73. This was suggestive of renal potassium loss. Urinary Calcium to Urinary Creatinine (UCa/UCr) ratio was 0.4. His thyroid function tests were normal and his 24 hour urinary protein was 760 mg per day. Hypokalemic metabolic alkalosis with renal potassium loss was thought to be due to loop diuretic use. The patient was given potassium supplementation 200 meq per day (iv plus oral). Potassium level reached to 4.0 meq/L and weakness improved. The patient was discharged home on day 4 on spironolactone 50 mg daily and telmisartan 20 mg daily. On follow up in 2 weeks serum potassium was 3.0 meq/l. The dose of spironolactone was increased to 100 mg daily and the dose of telmisartan was increased to 40 mg daily. On subsequent follow up in another 2 weeks patient had a recurrence of symptoms. Serum potassium was 2.1 meq/L. The patient had been off loop diuretics for more than a month. The patient was again hospitalized for life-threatening hypokalemia. Investigations revealed urinary potassium of 20 meq/L, and Transtubular Potassium Gradient (TTKG) of 10.77 despite being on spironolactone 100 mg daily and telmisartan 40 mg daily. Urinary Calcium to Creatinine (Uca/UCr) ratio continued to be high at 10.46. Arterial blood gas analysis revealed pH 7.60, bicarbonate of 41 meq/L and partial pressure of carbon dioxide of 42 mmHg. The serum magnesium level was 1.8 mg/dl. The diagnosis of Bartter phenotype was made. Bartter phenotype was unmasked by use of torsemide. We couldn't find any obvious cause for his Bartter phenotype and was likely idiopathic. His received potassium chloride 200 meq/day (iv plus oral) and the dose of spironolactone increased to 200 mg daily. The patient was discharged home on potassium chloride 100 meq per day maintenance, spironolactone 200 mg daily and telmisartan 40 mg daily. His potassium on follow-up 1 week later was 4.1 meq/l.

His serum aldosterone levels and plasma renin activity couldn't be done as the patient had been on diuretics.

DISCUSSION

Bartter's syndrome is a rare genetic disorder described by Bartter and coworkers in 1962 [1]. BS can occur due to various genetic defects leading to reduced activity of one of the several electron transporters in the thick ascending limb of the loop of Henle. Five main genetic defects are described. Defective function of the NKCC2 (Na^+-K^+-$2Cl^-$) cotransporter in the luminal membrane [3], the luminal potassium channel [4], and the basolateral chloride channel [5] are the causes of BS types I, II, and III, respectively. Type IV BS is associated with sensorineural deafness due to reduced activity of kidney-specific chloride channels (ClC-Ka and ClC-Kb) [6]. Defects in the Calcium-Sensing Receptor (CaSR) in the basolateral membrane of the thick ascending limb can impair sodium chloride transport and generate a mild Bartter phenotype called type V [7]. Bartter like syndrome is known to be associated with infections like tuberculosis, granulomatous disorders like sarcoidosis, autoimmune disorders like Sjogren's. Several drugs like Aminoglycosides, colistin, Amphotericin B, antitubercular drugs like capreomycin and loop diuretics have been reported to give Bartter like phenotype. Loop diuretics block NKCC2 (Na-K-2Cl) cotransporter in the luminal membrane and give rise to Bartter like syndrome. Our patient didn't have any family history suggestive of Bartter's syndrome and since he presented for the first-time following loop diuretic use, it was thought to be the likely reason for hypokalemic metabolic alkalosis in the first instance. However, since the patient continued to be severely hypokalemic despite being on spironolactone and telmisartan, an underlying tubular disorder

unmasked by use of loop diuretic appears to be the most likely etiology. Less than 7% of patients taking thiazides and less than 1% of patients taking furosemide exhibit a decrease in serum potassium below 3.0 meq/L [8,9]. For this reason, it is appropriate to consider the possibility of other causes for hypokalemia in patients whose serum potassium falls to less than 3.0 meq/L during diuretic therapy. The patient is presently on oral potassium chloride replacement 100 meq daily along with spironolactone 200 mg daily and telmisartan 40 mg daily. He is currently asymptomatic with normal serum potassium.

Whether there is any association between Diabetes mellites and BS is not clear. However, hypokalemia is known to worsen diabetes control and diabetic control is improved following Potassium replacement [10,11].

CONCLUSION

Bartter like syndrome should always be kept as a differential for a normotensive patient with hypokalemic metabolic alkalosis. Development of severe hypokalemia precipitated by diuretic use warrants search for underlying tubular disorder or hyper aldosterone state.

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