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Case Study

A Case Report On Bartter Syndrome

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ABSTRACT

Bartter syndrome is a rare inherited disorder that usually present with bunch of tubular disorders such as hypokalemia, hypochloremia and metabolic alkalosis. The primary pathogenic mechanism is defective salt reabsorption predominantly in the thick ascending limb of the loop of Henle. The kidney's reabsorption of salt is impaired by these defects, resulting in imbalances in electrolytes and fluid concentrations in the body. Potassium, calcium, magnesium, sodium, and chloride are the primary electrolytes that are affected. Treatment usually involves medications to correct the imbalance and control symptoms. This may include potassium-sparing diuretics, potassium supplements. Here we present a case of a 61-year-old female patient with Bartter syndrome.

INTRODUCTION

Bartter syndrome is a rare genetic disorder of the renal tubule and caused by impaired salt reabsorption in the ascending limb of the Henle, resulting in salt accumulation, hypokalemia, and metabolic alkalosis [1]. In 1962, Bartter et al discovered a new syndrome that was characterized by hypokalemia and metabolic alkalosis, hyperaldosteronism, and hyperplasia of the JGA [2].BS is currently recognized as a rare inherited renal tubular disorder that affects around 1 in 1,000,000 people in the world. The main cause of the disorder by the defective salt reabsorption in the thick ascending limb (TAL) of the loop of

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Henle, this can result in salt wasting, hypokalemia, and metabolic alkalosis with relatively low levels of serum chloride [3]. Damage to the sodium-potassium chloride cotransporter (NKCC2) or potassium channel (ROMK) affects sodium, potassium, and chloride transport in the thick ascending limb of the loop of Henle (TALH). Due to this, distal delivery of these ions increases, resulting in only some sodium being reabsorbed and potassium being secreted [4]. Several genes, including KCNJ1, CLCNKB, CLCNKA, BSND, and ROMK, which encode ion transporters, are the cause of mutations of Bartter Syndrome [1].

There are various types of Bartter syndrome, Type I results from mutations in the NKCC2, Type II results from mutations in the ROMK gene, Type III results from mutations in the chloride channel gene (CLC- Kb), Type IV results from the loss-of-function mutations in gene encoding barttin [5], Type V results from mutations in extracellular calcium ion-sensing receptor and in the genes that encode the chloride channel subunits, ClC-Ka and ClC-Kb [4]. Treatment strategies for Bartter syndrome can be different. Depending on the understanding of renal physiology, reported clinical observations, and individual experiences, treatment can be different. The classical pharmacological approach involves supplementing potassium chloride with indomethacin and spironolactone, which are all aldosterone antagonists. Increasing serum potassium and correcting metabolic alkalosis can be achieved by using potassium-sparing diuretics such as spironolactone, eplerenone, or amiloride in addition to potassium supplementation, which can be poorly tolerated at higher doses. Spironolactone and eplerenone act on the aldosterone receptor, but some researchers have speculated that amiloride (which directly inhibits the ENaC channel) may be more effective due to hypokalemia resulting in lower aldosterone levels.

CASE PRESENTATION

A 61 year old female patient was admitted with complaints of fever, myalgia, cough, nausea, lossed appetite, tiredness and unable to do daily routines. There was a history of OAD and Type II diabetes. The patient was on medications such as Formoterol + Fluticasone and Biphasic isophane insulin injection. Upon admission the patient was conscious and oriented. The laboratory investigations are presented in Table1. The electrolytes such as Potassium, Sodium, Calcium, and Magnesium, have declined according to laboratory investigations. The patient eGFR was reduced to 37 ml/min. The subjects electrolytes were reduced to Potassium -1.9 mmol/L, Sodium - 122 mmol/L, Magnesium - 1.3 mmol/L and Calcium - 6.8 mmol/L. Calcium-creatinine ratio of urine was 0.540, which indicated hypercalciuria. The patient had high urinary chloride excretion of 110 mmol/L, which indicate kidney dysfunction. The laboratory investigations revealed the patient had hyponatremia, hypokalaemia, hypocalcaemia, hypomagnesemia, hypochloremia and these features suggested the diagnosis of Bartter syndrome. During the hospital days the patient was treated with medications such as IV Calcium Gluconate, KCL, Magnesium sulphate, Antipyretics and other supportive measures. Patient was admitted for 7 days and the treatment included Syrup Potassium Chloride 15 ml p/o q8h, inj. Magnesium sulphate 1 ampule BD and then changed for q4h for 7 days, Inj. Calcium gluconate 1 ampule q4h for 7 days, Calcium capsule OD p/o for 7 days, Tab.spironolactone 50 mg BD for 7 days, Salt capsule p/o TDS for 7 days, Nebulization with Levosalbutamol 0.63 mg q4h for 7 days, Tab.Fludrocortisone 0.1 mg od for 7 days, Inj.Cefoperazone Sulbactam 1.5 g BD for 7 days, Inj. Pantoprazole 40 mg BD for 7 days, Capsule Oseltamivir 15 mg p/o bd for 7 days, Inj.Doxycycline 100 mg IV BD for 7 days. After 7 days of treatment, patient present complaints were

improved. Hence the patient discharged with the advice of Syrup. Levodropropizine 5 ml TDS for 7 days, Tab. Calcium 500 mg BD for 7 days, Tab. Spironolactone 50 mg for 7 days, Biphasic isophane insulin injection 40-40-30 u s/c to continue, Tab. Ferric pyrophosphate OD for 7 days, Salt capsule BD for 7 days and Formoterol + fluticasone 6/250 mcg 1-0-1 with Inhaler.

Table 1

BLOOD TEST RESULTS	NORMAL VALUE
Potassium -1.9 mEq/L	3.5-5.2 mEq/L
Sodium – 122 mEq/L	135-145 mEq/L
Magnesium - 1.3 mg/dL	1.7-2.2 mg/dL
Calcium - 6.1 mg/dL	8.5-10.5 mg/dL
eGFR - 37 ml/min	≥ 90 ml/min
Phosphorus – 2.8 mg/dL	2.5-4.5 mg/dL
Urine chloride – 110 mEq/L	110-250 mEq/L
Calcium creatinine ratio – 0.540 mg/dL	< 0.14 mg/dL

DISCUSSION

Bartter syndrome is a disorder that causes salt loss that is inherited and is triggered by a mutation in either potassium-sodium chloride cotransporter (NKCC2) or the potassium channel (ROMK) found in the TAL of the loop of Henle. The sodium absorption capability of TAL's was reduced, hence an increase in sodium delivery to the distal and increased sodium absorption from the distal tubular segments, in exchange for potassium and hydrogen ions. As a result of hydrogen loss, absorption of bicarbonate ions also increases, leading to metabolic alkalosis. Defective absorption of chloride leads to elimination of positive luminal load, resulting in hypercalciuria and hypermagnesuria [4]. In Bartter's syndrome, serum/blood renin and aldosterone levels are also elevated. Arterial blood gas in Bartter's syndrome suggests metabolic alkalosis. The diagnosis of Bartter syndrome can be confirmed by genetic testing, such as next-generation sequencing, which includes testing for the following genes: SLC12A1, KCNJ1, CLCNKB, CLCNKA, BSND, and MAGED2 [6,7]. Hypokalemia, often in the range of 2-3 mmol/L, is due to increased urinary potassium loss due to activation of the renin-angiotensin-aldosterone system and hyperaldosteronism due to salt and water depletion due to failure to reabsorb sodium from the TAL. From the loop of Henle or DCT. The main focus of treatment is its correction [8]. Hypokalemia and hypochloremia occur in almost all cases of Bartter's syndrome. Assessment of urinary electrolytes is also key in the evaluation of these patients [6,7]. Deekshitha Alla et.al [10], through their case report revealed that a 27-year-old man presented with a history of weakness in his upper and lower limbs. Hypokalemia, metabolic alkalosis, and hypochloremia were the features that led to the diagnosis of Bartter's syndrome. Due to the non-availability of specialized laboratories, genetic studies were not conducted. He was started on potassium chloride infusion and potassium chloride syrup. The patient's limb weakness were greatly improved after volume and potassium repletion, and they were discharged. They were advised to drink a lot of coconut water and eat a diet that was high in potassium. On follow-up after 2 months, the patient's electrolytes normalized with a serum sodium value of 137 mEq/L and potassium of 3.5 mEq/L. The patient was advised to eat potassium-rich foods and prescribed potassium supplements. Another case report by Yayik Supriyani et.al [11] depict a case report of a 52-year-old male with patient with complaints of weakness in both legs increasing since 1 day ago.

Weakness in both legs has increased since 1 day ago. The patient experienced sudden weakness after working, but it wasn't accompanied by weakness in their arms. Their complaints are becoming more severe, making walking difficult. The patient's laboratory examination showed that they had 1.7 mmol/L of potassium, which was a sign of hypokalemia. Examination of kidney function found levels of urea 9 mg/dl and creatinine 0.4 mg/dl, indicating normal kidney function. Examination of blood gas analysis showed results of metabolic alkalosis with a Ph value of 7.5, a pCO2 value of 34, a pO2 value of 119, and an HCO3- value = 46 mmol/L. The urine potassium analysis resulted in potassium levels of 22 mmol/day, urine osmolarity of 140 mOsm/kg H2O at serum osmolarity of 274 mOsm/kgH2O, and TTKG of 28, which shows that hypokalemia is caused by potassium leakage from the kidneys. In this patient, the molar ratio of urine calcium and creatinine was 0.22, which indicated hypercalciuria. In this patient, there was high urinary chloride excretion of 74.7 mmol/L. The patient was diagnosed with Bartter syndrome. Treatment is carried out by administering Potassium chloride tablets 3 x 600 mg orally while monitoring electrolytes regularly. In our case, the findings that favoured the diagnosis of Bartter syndrome was the electrolytes examination. The lab reports shows electrolytes such as Potassium, Sodium, Calcium, Magnesium and Chloride have declined according to laboratory investigations. The subjects electrolytes are showed in Table 1. Calcium-creatinine ratio of urine was 0.540, which indicated hypercalciuria. The patient had high urinary chloride excretion of 110 mmol/L, which indicate kidney dysfunction. Due to the patient refusal, the genetic studies were not conducted. The laboratory investigations revealed the patient had hyponatremia, hypokalaemia, hypocalcaemia, hypomagnesemia, hypochloremia and these features suggested the diagnosis of Bartter syndrome. Additionally, our case demonstrated a combination of hypomagnesemia and hypocalciuria, further supporting this diagnosis. Comparing to the case report of Yayik Supriyani et. al [11], we observed a decrease in the molar ratio of urine calcium to creatinine in our case, which signals hypercalciuria, along with increased urinary chloride excretion. Through comparison, we discovered that patients with Bartter syndrome exhibit abnormalities in electrolytes such as sodium, potassium, chloride, and magnesium. Upon analysing our case alongside two previously mentioned case reports, we concluded that hypokalemia and hypochloremia are consistent features of Bartter syndrome. The patient was treated according to the standard treatment guidelines during the hospitalization. During the hospitalization, the patient was treated with medications such as IV Calcium Gluconate, KCL, Magnesium Sulfate, and other supportive measures. Patient was admitted for 7 days and the treatment included Syrup Potassium Chloride 15 ml p/o q8h, Inj. Magnesium sulfate 1 ampule BD and then changed for Q4H for 7 days, Inj. Calcium gluconate 1 ampule q4h for 7 days, Calcium Capsule OD p/o for 7 days, Tab.Spironolactone 50 mg BD for 7 days, Salt Capsule . Since Bartter syndrome is a rare condition, it is important to take special attention and care by the health care providers for treating the patients and also to take an appropriate critical approach in evaluating risks and harms.

CONCLUSION

This case report underscores the diagnosing and managing of Bartter syndrome, a inherited autosomal recessive condition resulting in defects of renal tubular excretion and reabsorption of electrolytes. Through our patient's case, we have elucidated the typical clinical presentation of Bartter syndrome, including hypokalemia, hypochloremia, and, in some instances, hypomagnesemia and hypocalciuria.

Collaboration between clinicians, nephrologists, and geneticists is essential for accurate diagnosis, genetic counselling, and comprehensive care.

The treatment focuses on Potassium chloride supplements are preferred because of the coexisting chloride deficiencies in these patients. Spironolactone, a specific aldosterone antagonist it binds competitively to the receptors present at the aldosterone-dependent sodium-potassium exchange site in the DCT, it increases water excretion while retaining potassium [9].

Moving forward, continued research efforts are needed to deepen our understanding of Bartter syndrome pathophysiology and to explore novel therapeutic approaches aimed at improving patient outcomes. By sharing our experiences and insights, we hope to contribute to the collective knowledge base and enhance the care provided to individuals affected by Bartter syndrome.

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