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Original Research Article

Unveiling Bartter's Syndrome: A Rare Renal Puzzle in a 32 Year Old Male: A Case Report in Central India

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Abstract:

Bartter syndrome is a rare, salt-wasting tubulopathy with loss-of-function mutations in the ion channels of the thick ascending limb of the loop of Henle cause renal salt wasting, resulting in hypokalemia, hypochloremia, and hypercalciuria. It is an autosomal recessive disorder that affects one in 1,000,000 people. Clinical manifestations vary in severity and range from polyhydramnios and hypovolemia in the antenatal variant to polyuria and fatigue in the adolescent or adult-onset variant. It results from mutations in several genes, including KCNJ1, CLCNKB, CLCNKA, BSND, and ROMK, which encode ion transporters. We report a rare presentation of adult-onset Bartter syndrome. A 32-year-old man presented to the hospital with bilateral upper and lower limb weakness since 4 days. Patient also had complain of twitching and perioral numbness of face and polyuria. On presentation power in all 4 limbs were reduced, he was normotensive, His serum electrolytes revealed hypokalemia, hypocalcemia , hypomagnesemia ,urine analysis suggestive of raised urinary chloride, raised urinary potassium to creatinine ratio & raised 24 hour urinary calcium. ABG revealed metabolic alkalosis. Bartter syndrome was suspected based on serum and urinary electrolytes assessment and arterial blood gas analysis. The patient was initiated on potassium chloride (KCL) infusion and potassium chloride syrup to correct hypokalemia, calcium correction was given to correct hypocalcemia, indomethacin and spironolactone was started to prevent recurrent loss of potassium followed by which patient's symptoms resolved completely.

Keywords: Bartter's Syndrome, Hypokalemia, Renal Tubular Disorder, Metabolic Alkalosis, Hyperaldosteronism, Case Report, Central India.

Introduction

The discovery of a novel salt-wasting tubulopathy by Bartter et al. was characterized by juxtaglomerular apparatus hyperplasia resulting in hyperreninemia, adrenal cortical hyperplasia resulting in normotensive hyperaldosteronism, and hypokalemic metabolic alkalosis as a significant event in 1962 [1]. Bartter's syndrome is an uncommon genetic disorder that impairs renal tubular function, particularly in the thick ascending limb of the loop of Henle, resulting in a dysregulation of sodium, chloride, and potassium balance. Although Bartter's syndrome typically presents in childhood, late-onset forms can occur in adults and often lead to a diagnostic challenge due to the nonspecific nature of its symptoms. The disease is primarily characterized by hypokalemia, metabolic alkalosis, and elevated plasma renin and aldosterone levels, which mimic a variety of other renal and endocrine disorders. It is classified into two types based on the phenotype, neonatal (antenatal) and classical Bartter syndrome, and five based on the genotype. Except for Types 3 and 5, all other types of Bartter syndrome are usually present in the pediatric population [2]. Clinical manifestations vary in severity and range from polyhydramnios and hypovolemia in the antenatal variant to polyuria and fatigue in the adolescent or adult-onset variant.

Case Presentation:

A 32-year-old man presented to the department of general medicine with a history of bilateral upper and lower limb weakness since 4 days. Patient also had complain of twitching and perioral numbness of face and polyuria. On presentation power in all 4 limbs were reduced, he was normotensive, His serum electrolytes revealed hypokalemia, hypocalcemia , hypomagnesemia ,urine analysis suggestive of raised urinary chloride, raised urinary potassium to creatinine ratio, raised 24 hour urinary

calcium. ABG revealed metabolic alkalosis. Bartter syndrome was suspected based on serum and urinary electrolytes assessment and arterial blood gas analysis. The patient was initiated on potassium chloride (KCL) infusion and potassium chloride syrup to correct hypokalemia, calcium correction was given to correct hypocalcemia, indomethacin and spironolactone was started to prevent recurrent loss of potassium followed by which patient's symptoms resolved completely. Genetic studies were not done due to the non-availability of specialized laboratories. He had a similar episode two months ago but had no significant family history. The patient weighed 37 kg and was 165 cm tall (BMI = 13.6 kg/m^2). Systemic examination revealed hypotonia in all four limbs. Laboratory investigations are presented in Table 1. On follow-up after 2 months, the patient's condition improved and his 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 potassium supplements were prescribed.

Table 1: Laboratory investigations

Parameter	Values
CBC	Hb- 12.3 gm/dl, TLC- 7.3K, Platlet-1.47 Lakh
KFT	Urea- 18 mg/dl, Cr-0.8mg/dl
LFT	Bilirubin- 0.7mg/dl, ALT-73, AST-523
Serum Electrolyte	Na+- 133, K+-1.7, Mg-1.5, Cl-86, Ca-6.5 mmol/L
ABG	PH-7.48, PCO2-43.4, HCO3- 32.3, Ca-0.76
24 Hr Urinary Calcium	270 mg/day (100-250)
UKCr	62 mmol/gm
Ur Ca/Cr	0.97(<0.12)
Urinary Chloride	423 meq/day (110-250)

Discussion

Bartter's syndrome is a group of rare inherited renal disorders that affect the renal tubules, particularly in the loop of Henle. The condition is caused by mutations in the genes encoding for specific ion channels involved in sodium, potassium, and chloride reabsorption. The classic features of Bartter's syndrome include:

- **Hypokalemia**: Due to excessive potassium excretion in the urine.
- **Metabolic alkalosis**: Secondary to loss of hydrogen ions in urine.
- **Hyperaldosteronism**: Compensatory increase in aldosterone to preserve sodium.
- **Normal or low blood pressure**: In contrast to other causes of secondary hyperaldosteronism (such as primary hyperaldosteronism or renovascular disease).

Although Bartter's syndrome often presents in childhood, adult-onset forms can present with subtle symptoms, making diagnosis more challenging. Bartter syndrome most typically affects children as well as adolescents. Fever, polyuria, polydipsia, vomiting, cramps, dehydration, constipation, growth delays, and failure to thrive are common clinical presentations seen in neonates.

In addition to the above-mentioned symptoms, neonates also exhibit signs like sensorineural deafness, big eyes, protruding ears, strabismus, and a drooping mouth [2]. On the other hand, adults frequently present with weakness, fatigue, polyuria, polydipsia, and a salt craving [3]. This case is notable for its presentation in a 32-year-old male, with symptoms including generalized weakness, polyuria, and cramps, which led to a delayed diagnosis. The differential diagnosis for this patient included other causes of hypokalemia and metabolic alkalosis, such as hyperaldosteronism, diuretic abuse, and other renal tubular disorders. The characteristic finding of elevated renin and aldosterone levels, coupled with a negative history for diuretic use and normal renal function, helped steer the diagnosis towards Bartter's syndrome.

In Bartter syndrome, serum/blood levels of renin and aldosterone are also elevated. An arterial blood gas in Bartter syndrome will show metabolic alkalosis. Confirmation of the diagnosis of Bartter syndrome can be made by genetic testing, such as next-generation sequencing, which includes testing for the following genes: SLC12A1, KCNJ1, CLCNKB, CLCNKA, BSND, and MAGED2 [4]. However, the genetic studies were not done in this case due to non-availability of specialised labs in resource limited setting.

Other disorders like Gitelman syndrome, cystic fibrosis manifesting as a pseudo-Bartter syndrome, and Bartter-like syndrome have features overlapping with Bartter syndrome. Gitelman syndrome is also a rare, recessive, salt-wasting tubulopathy but with impaired salt reabsorption in the DCT (distal convoluted tubule). Previously, Bartter syndrome was distinguished from Gitelman syndrome by some clinical features, such as early onset, severity, presence of hypercalciuria, polyhydramnios, or growth retardation. Recent research has revealed that Bartter syndrome

patients might experience delayed presentation, and some characteristics, including hypercalciuria, are not always present [5]. Cystic fibrosis and Bartter syndrome are rare hereditary diseases with overlapping clinical manifestations such as dehydration, failure to thrive, and similar electrolyte abnormalities [6]. Nephrotoxic agents (such as aminoglycosides, amphotericin B, and heavy metals) and anorexia nervosa have also been reported to be associated with Bartter-like syndrome [7].

Management

The management of Bartter's syndrome primarily focuses on correcting electrolyte imbalances and providing supportive care. The patient was started on potassium supplementation, oral chloride, and nonsteroidal anti-inflammatory drugs (NSAIDs), which inhibit prostaglandin synthesis and reduce the renal potassium wasting.

NSAIDs are considered the first-line treatment for most forms of Bartter's syndrome, as they inhibit the renal prostaglandin production, which is involved in the pathology of the disease. In this case, the patient responded well to treatment, with resolution of his symptoms and normalization of serum potassium levels.

Some patients with Bartter syndrome will develop chronic kidney disease due to chronic hypokalemia, multiple episodes of dehydration, and nephrocalcinosis. However, the prognosis is usually good with strict adherence to the treatment and regular follow-up [8].

Conclusion

This case report highlights the importance of considering Bartter's syndrome in the differential diagnosis of unexplained hypokalemia and metabolic alkalosis, especially in adults who present with nonspecific symptoms. Early diagnosis and appropriate treatment, including potassium supplementation, chloride replacement, and NSAIDs, can significantly improve the patient's quality of life. Bartter's syndrome remains a rare but important consideration in patients with persistent electrolyte imbalances, and clinicians must maintain a high index of suspicion for timely diagnosis and intervention.

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