Case Report

Classical Bartter's syndrome (type III) disease with normocalciuria in an Indian adult male: A case report

Sahithi Krovvidi[1], Gayatri Kammila[2], Rakesh Korrapati[3], Jaya Sai Mupparaju[3], Akhila Naraharasetty[4]

From [1]Medical Student, Department of General Medicine, [2]Assistant Professor, [3]Medical Student, NRI Medical College, Guntur, [4]Medical Student, Department of General Surgery, Dr. Pinnamaneni Siddhartha Institute of Medical Sciences, Gannavaram, Andhra Pradesh, India

ABSTRACT

Bartter's syndrome (BS), well known as salt-wasting nephropathy, is a rare genetic disorder characterized by renal defects in ion transport, leading to electrolyte imbalances such as hypokalemia, metabolic alkalosis, renal salt wasting, hypercalciuria, and increased renin-angiotensin-aldosterone system with low to normal blood pressure. This inherited disease is frequently seen in neonates and is unusual in adults. Among the five types of BS, type III, the Classic BS is normally evident in later life and is the result of mutations in the CLCNKB gene. The present case report describes a rare case of adult-onset BS type III in a 40-year-old man. Biochemical analysis revealed hypokalemia (K^+ 2.0 mmoL/L) with renal potassium wasting, metabolic alkalosis ($HCO3^-$ 28.8 mmoL/L), hypochloremia (Cl^- 86 mEq/L), normomagnesemia ($Mg\ 2^+$ 2.29 mg/dL), and normocalciuria ($Ca\ 2^+$187.2 mg/day). Our report highlights the variation in clinical characteristics and emphasizes the need for understanding genetic and biochemical analyses in suspected BS cases.

Key words: Bartter syndrome, Hypokalemia, Metabolic alkalosis, Normocalciuria

Bartter's syndrome (BS) is a salt-losing renal tubular disorder with hypokalemia, metabolic alkalosis, hyperaldosteronism, hyperreninemia, hypercalciuria, low chloride, and normal to low blood pressure [1]. It is a rare genetic disorder with an estimated occurrence of one in 10 lakh people. The majority of clinical cases occur during the prenatal or neonatal period. However, there are cases that become noticeable rarely in adults. The disease is classified clinically and genetically into five subtypes: Type 1 (SLC12A1), Type 2 (KCNJ1), Type 3 (CLCNKB), Type 4 (BSND or CLCNKA/CLCNKB), and Type 5 (CASR or MAGED2), as per the site of salt transport impairment [2]. Among these, type III occurs from polymorphisms in the chloride channel gene (CLCNKB), resulting in decreased chloride efflux and changing the transepithelial voltage gradient, which decreases sodium, potassium, and chloride resorption [3]. Type III is frequent in adults and is most difficult to differentiate clinically from Gittleman syndrome and other impaired tubulopathy.

Regardless of significant progress in knowledge since the genetic clarification of this disease, data on the prolonged impact of BS is extremely inadequate. As there is a lack of clinical studies, the need for more scientific evidence should be emphasized that could aid in diagnosis and therapy [2]. We report a case of adult-onset BS type III in a 40-year-old male due to hypokalemia, metabolic alkalosis, narmocalciurea, and normal blood pressure.

Access this article online	
Received - 11 April 2025 Initial Review - 02 May 2025 Accepted - 31 May 2025	Quick Response code
DOI: 10.32677/ijcr.v11i7.5167	

CASE REPORT

A 40-year-old male was admitted to the general medicine department, NRI General Hospital, Guntur, with complaints of headache in the bilateral frontoparietal and occipital areas, which was intermittent, lasting for 5–10 min, and mild nocturnal muscle cramps, especially in the calf region, lasting for seconds to minutes since 3 months. No history of premature (or) maternal polyhydramnios was reported. Headache was not associated with vomiting and double vision. The patient looks comparatively healthy with normal vitals. Nonetheless, he has type II diabetes mellitus with good glycemic control for the past 2 years and is an alcoholic.

On examination, muscle spasms of bilateral lower limbs are not associated with weakness, and other systemic examinations were normal.

Laboratory tests showed polycythemia secondary to dehydration (Hb-18%, PCV-51%). The patient's thyroid levels and liver function tests were normal. Serum osmolality, electrolytes (calcium, magnesium), and creatinine were within

Correspondence to: Sahithi Krovvidi, Department of General Medicine, NRI Medical College, Chinnakakani, Guntur, Andhra Pradesh, India. E-mail: sahithikrovvidi@gmail.com

the normal range with severe hypokalemia (2.0 mmoL/L), hyponatremia (127 mmoL/L), hypophosphatemia (2.0 mmoL/L), and hypochloremia (86 mEq/L) (Table 1). High plasma renin and aldosterone levels were recorded. As the serum potassium level was low, urine was sampled to determine the renal loss. Before sending 24 h urine samples, the possible causes of pseudohypokalemia, such as leukocytosis and prolonged storage of blood samples, were ruled out. The urine potassium/gram of creatinine was 25 mEq/g, i.e., >15 mEq/g showing renal loss of potassium. Analysis of 24 h urine sample showed polyuria (3.9 L), renal hyperkalemia (135.6 mEq/day), and hyperphosphaturia (214.5 g/day), with normal urine calcium and decreased urine osmolality. Arterial blood gas indicated metabolic alkalosis (7.5 pH), 122 mmoL/L sodium, 3.2 mmoL/L lactic acid, and 28.9 mmoL/L $HCO3^-$, and he had no complaints of vomiting, profuse sweating, or any history of diuretic use.

The transtubular potassium gradient was 3, indicating distal tubule potassium secretion. On abdominal and pelvic ultrasound, hepatomegaly with altered echotexture, prostatomegaly, and bilateral nephrocalcinosis were noted. A computed tomography scan of KUB revealed bilateral medullary nephrocalcinosis and other findings in accordance with the ultrasound. In addition, urine Ca/creatinine was 1.02. An increase of 24 h urine phosphates with normal serum phosphate might be driven by tubulopathy. All these, besides hypokalemia, hypochloremic alkalosis, normocalciuria, and reduced ability to concentrate urine (due to reduced urine osmolality), led to the diagnosis as a case of BS type III. Although genetic analysis is decisive for definitive diagnosis, it was not performed owing to the cost of the test.

The patient was treated with an injection of KcL (potassium chloride) 40 meq in 500 mL normal saline and spironolactone throughout the course of the disease to maintain serum potassium levels. Owing to gastrointestinal adverse reactions and gynecomastia, spironolactone could not be continued. Serum creatine was initially elevated (1.5 mg/de) at the time of admission, and on serial monitoring, it attained normal 1 mg/dL. By the time of discharge,

Table 1: Clinical and laboratory results of the patient at the time of admission in comparison with Gitelman syndrome

Parameters	Results	Inference	Gitelman syndrome
Clinical findings			
Muscle cramps	Present		Common
Weakness	Absent		Present
Blood pressure	110/70 (120/80) mmHg	Normotensive	Hypertension
Total blood cell count			
Hemoglobin	18 (12–15) g/dL		
RBC count	6.97 (4.7–6.1) million/µL		
WBC count	13.4 (4–11) thousands/µL		
Platelet count	2.6 (1.5–4.5) lakh/µL		
PCV	51 (38.3–48.6) %		
Blood urea	47 (7–20) mg/dL		
Serum electrolytes			
Sodium	127 (135–145) mmol/L	Hyponatremia	
Chloride	86 (97–105) mmol/L	Hypochloremia	
Potassium	2.0 (3.5–5.0) mmol/L	Hypokalemia	
Calcium	8.3 (8.4–10.2) mg/dL	Normocalcemia	
Magnesium	2.29 (1.5–2.4) mg/dL	Normomagnesemia	Hypomagnesemia
Phosphorus	2.5 (2.5–4.5) mg/dL		
Serum creatinine	1.4 (0.7–1.3) mg/dL		
24 h urine analysis			
Urine volume	3.9 (0.8–2) L	Polyuria	Rare
Sodium	315.9 (40–220) mEq/day		
Potassium	135.6 (25–125) mEq/day		
Calcium	187.2 (100–300) mg/day	Normocalciuria	Hypocalciuria
Phosphates	214.5 (0.4–1.3) g/day	Hyperphosphaturia	
Urine osmolality	369.27 (500–850) mOsm/kg	Urine concentrating ability: Reduced	Intact
Arterial blood gas		Metabolic alkalosis	
pH	7.5 (7.35–7.45)		
Sodium	122 (133–146) mmoL/L		
Lactic acid	3.2 (<2) mmoL/L)		
Bicarbonate	28.9 (22–26) mEq/L		
CT KUB	Nephrocalcinosis	Present	Absent

Figures in parenthesis indicate reference values

the serum potassium level had improved from 2.0 to 3.6 meq/L. Consequently, the patient recovered from headache and limb pain.

DISCUSSION

The present study reports a case of BS in a 40-year-old patient who presented with headache and bilateral lower limb pain incidentally, with hypokalemia, hypochloremia, metabolic alkalosis, reduced ability to concentrate urine, and normocalciuria corresponding to the typical characteristics of type III BS. Subsequently, it was supported by nephrocalcinosis. Although hypercalciuria may occur in BS, patients with BS3 commonly have normocalciuria [4]. In addition, the patient had no family and personal history of nephrocalcinosis, nephrolithiasis, hypocalcemia, and hypomagnesemia, supporting the diagnosis as a case of type III BS and excluding other types of BS. The pathogenesis of BS includes hyperplasia of the juxtaglomerular complex, elevated levels of renin and aldosterone following increased potassium loss, and metabolic alkalosis, which is regarded as a principal cause of prostaglandins, kallikrein, and bradykinin abnormalities [5].

Among five types (BS1-5) of BS, BS1, BS2, BS4, and BS5 present antenatally. BS3 is called classic BS and normally manifests later in life, mainly in adulthood [3]. Recently, adult-onset BS2, BS4, and BS5 have been reported [6-8]. Nevertheless, the clinical symptoms and age susceptibility are quite variable in BS3: polyuria and tendency of dehydration, hypokalemia, normocalciuria or hypercalciuria, proteinuria, and the lack of urolithiosis, including rare signs of hypokalemic paralysis [2]. Abdominal sonography in a 45-year-old female with classic BS revealed a lack of renal stones and nephrocalcinosis, but biochemical studies revealed hypercalciuria [9]. Whereas, in the present case, nephrocalcinosis with normocalciuria was noticed. Although nephrocalcinosis and hypercalciuria are present in most BS patients (other than BS3), the occurrence of symptomatic urolithiasis in BS seems to be comparatively low [10]. Renal impairment was not noticed in the present case in accordance with the earlier reports.

Many patients with classic BS have clinical features that are more or less identical to Gitelman syndrome (GS). Normomagnesemia, normocalciurea/hypercalciurea, and nephrocalcinosis are regular features in BS, whereas GS is a main consideration in patients with hypomagnesemia, hypocalciuria [11], and hypertension [12]. Urinary concentrating ability appears intact in GS [13].

Hypokalemia patients are known to be more prone to arrhythmias and sudden cardiac death, making it crucial for health-care professionals to better understand the condition for an accurate diagnosis and treatment of BS. In view of the deferred consent of the patient to undergo genetic testing due to cost and also technically challenging analysis of the CLCNKB gene in detecting mutation [4], the genetic predisposition in the present case could not be established. However, CLCNKB mutations can also underlie the antenatal BS, neonatal BS, and Gitelman-like phenotypes [14,15]. Depending on clinical and laboratory findings, the patient was treated with parenteral administration of potassium chloride. Treatment resulted in significant improvement in serum potassium, and the patient was advised for routine check-ups once or twice a year to analyze the continuing result of the treatment.

CONCLUSION

BS, though a rare genetic disorder, should be considered in the medical diagnosis of adults with hypokalemia and metabolic alkalosis. Knowledge of clinical diversity in BS is significant for initiating diagnosis and effective management. Early and accurate molecular diagnosis is vital for distinct therapy. Education of the patient is also equally important. Hence, the limited research and paucity of knowledge require filling with more scientific studies, which would aid health-care professionals in a better understanding of the prognosis of disease.

REFERENCES

1. Park JW, Chung YJ, Yeum CH, Lee JJ, Yoo KS, Kim SW, *et al*. A case of adult-onset Bartter's syndrome. Korean J Intern Med 1995;10:60-3.
2. Konrad M, Nijenhuis T, Ariceta G, Bertholet-Thomas A, Calo LA, Capasso G, *et al*. Diagnosis and management of Bartter syndrome: Executive summary of the consensus and recommendations from the European rare kidney disease reference network working group for tubular disorders. Kidney Int 2021;99:324-35.
3. Naesens M, Steels P, Verberckmoes R, Vanrenterghem Y, Kuypers D. Bartter's and Gitelman's syndromes: From gene to clinic. Nephron Physiol 2004;96:65-78.
4. Cha EJ, Hwang WM, Yun SR, Park MH. An adult case of Bartter syndrome type III presenting with proteinuria. J Pathol Transl Med 2016;50:160-4.
5. Baehler RW, Work J, Kotchen TA, McMorrow G, Guthrie G. Studies on the pathogenesis of Bartter's syndrome. Am J Med 1980;69:933-8.
6. Hussain A, Atlani M, Goyal A, Khurana AK. Type-5 Bartter syndrome presenting with metabolic seizure in adulthood. BMJ Case Rep 2021;14:e235349.
7. Elfert KA, Geller DS, Nelson-Williams C, Lifton RP, Al-Malki H, Nauman A. Late-onset Bartter syndrome type II due to a homozygous mutation in KCNJ1 gene: A case report and literature review. Am J Case Rep 2020;21:e924527-1-7.
8. Heilberg IP, Tótoli C, Calado JT. Adult presentation of Bartter syndrome type IV with erythrocytosis. Einstein (Sao Paulo) 2015;13:604-6.
9. Chiang WF, Lin SH, Chan JS, Lin SH. Hypokalemic paralysis in a middle-aged female with classic Bartter syndrome. Clin Nephrol 2014;81:146-50.
10. Seys E, Andrini O, Keck M, Mansour-Hendili L, Courand PY, Simian C, *et al*. Clinical and genetic spectrum of Bartter syndrome type 3. J Am Soc Nephrol 2017;28:2540-52.
11. Al Shibli A, Narchi H. Bartter and gitelman syndromes: Spectrum of clinical manifestations caused by different mutations. World J Methodol 2015;5:55-61.
12. Berry MR, Robinson C, Karet Frankl FE. Unexpected clinical sequelae of gitelman syndrome: Hypertension in adulthood is common and females have higher potassium requirements. Nephrol Dial Transplant 2013;28:1533-42.
13. Walsh PR, Tse Y, Ashton E, Iancu D, Jenkins L, Bienias M, *et al*. Clinical and diagnostic features of Bartter and gitelman syndromes. Clin Kidney J 2018;11:302-9.
14. Jeck N, Konrad M, Peters M, Weber S, Bonzel KE, Seyberth HW. Mutations in the chloride channel gene, CLCNKB, leading to a mixed Bartter-gitelman phenotype. Pediatr Res 2000;48:754-8.
15. Zelikovic I, Szargel R, Hawash A, Labay V, Hatib I, Cohen N, *et al*. A novel mutation in the chloride channel gene, CLCNKB, as a cause of gitelman and Bartter syndromes. Kidney Int 2003;63:24-32.

Funding: Nil; Conflicts of interest: Nil.

How to cite this article: Krovvidi S, Kammila G, Korrapati R, Mupparaju JS, Naraharasetty A. Classical Bartter's syndrome (type III) disease with normocalciuria in an Indian adult male: A case report. Indian J Case Reports. 2025; 11(7):301-303.