Case Report

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Hypokalemia in a young man…think Bartter syndrome type 3

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Background: Bartter syndrome is an autosomal recessive salt reabsorption disorder that results in decreased extracellular fluid volume with low/normal blood pressure.

Case presentation: A 17-year-old boy with polydipsia, polyuria, weakness in the lower limbs, and ataxic gait. His Laboratory test shows hypokalemia; hypochloremia, hypomagnesemia and metabolic alkalosis. The authors' patient was managed by fluid and electrolyte replacement, which is essential in emergency management.

Conclusion: Bartter syndrome is difficult to treat, and currently, there is no complete cure. The overall prognosis depends on the extent of receptor dysfunction, and despite these facts, most patients can live a normal life if they strictly follow their treatment plan.

Keywords: bartter syndrome type 3, BS, hypokalemic, nephrocalcinosis, young male

Introduction

Bartter syndrome is an autosomal recessive salt reabsorption disorder that results in decreased extracellular fluid volume with low/normal blood pressure[1]. It is characterized by several electrolyte imbalances, including low potassium and chloride and in some cases, hypomagnesemia. Other abnormalities include high renin, secondary hyperaldosteronism, and elevated prostaglandin E2 levels. The acid-base phenomenon is usually metabolic alkalosis. Patients often present in childhood. Different phenotypes are classified according to the location of impaired salt transport. There are five types of Bartter syndrome: Type I results from mutations in the sodium chloride/potassium chloride cotransporter gene (NKCC2), and 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 the gene encoding barttin[2,3], Type V results from mutations in extracellular calcium ion-sensing receptors and in the genes that encode the chloride channel subunits, ClC-Ka and ClC-Kb[4], We show a rare case for Bartter Syndrome Type 3.

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HIGHLIGHTS

- Bartter syndrome is an autosomal recessive salt reabsorption disorder.
- This leads to increased distal delivery of salt and excessive salt and water loss from the body.
- We must consider this syndrome when the patient complains of symptoms of hypokalemia and hypomagnesemia.

Case presentation

Case history

A 17-year-old boy with polydipsia, polyuria, weakness in the lower limbs, and ataxic gait was admitted to the Department of Nephrology. He had a history of hepatitis A (HAV) one year ago and a tonsillectomy since he was 11 years old. The past medical history was unremarkable. His vital signs were as follows: temperature 37°C, blood pressure 110/70 mmHg, heart rate 100 bpm, and O_2 saturation 99%. On physical examination, cranial nerves were normal, Chvostek was negative, the Trousseau sign was positive, the Romberg sign was negative, and there was a decrease of bowel sound with epigastric tenderness.

Investigation, treatment, and follow-up

The laboratory tests were as follows: potassium 2.3 mg/dl, chloride 96 mg/dl, magnesium 1.9 mg/dl, corrected calcium 8.1 mg/dl, albumin 5.6 mg/dl, creatinine 0.84 mg/dl, creatine phosphokinase 526 IU/l, lactate dehydrogenase 233 IU/l, and arterial blood gases (ABGs): PH = 7.46, HCO_3 = 25.7, PO_2 = 91, and PCO2 = 35.7. Twenty-four hours urine (calcium 8.15 mmol/l, sodium 107.92 mmol/l, potassium 17.8 mmol/l, magnesium 3.8 mg/l). The density of urine was 1.025, and PH = 5. An electrocardiogram (ECG) showed T wave inversion, with a prolongation of the U wave, particularly in the V3–V4 leads (Fig. 1). Echography demonstrated Nephrocalcinosis due to hypercalciuria (Fig. 2). Computed tomography scan (CT scan)

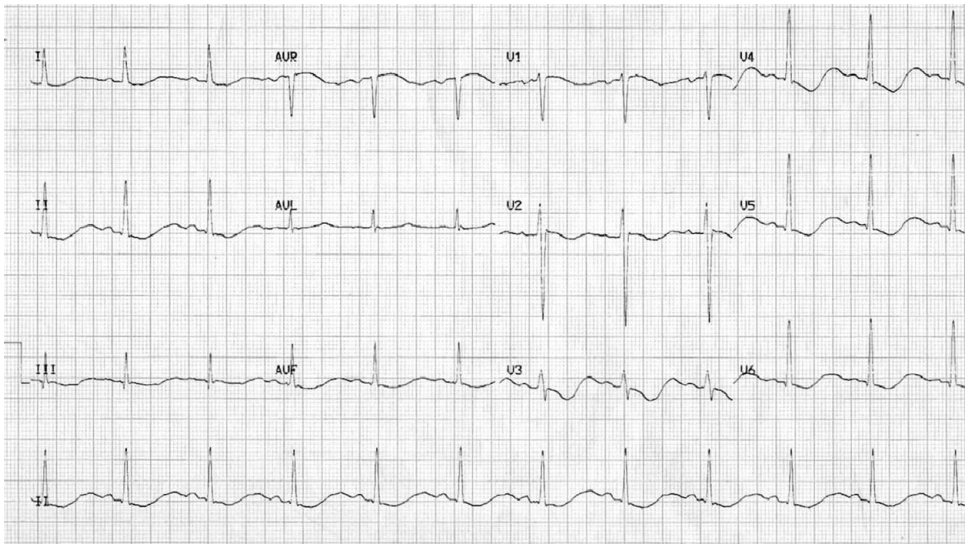

Figure 1. An electrocardiogram showed T wave inversion with a prolongation of the U wave.

showed pulpal calcifications (Fig. 3). Throughout the illness, the child has been taking potassium chloride and spironolactone as supplements to keep their serum potassium levels stable. However, the child's tubular function was still damaged. His duration of hospital stay was about 2 weeks. At discharge, his serum potassium was 2.89 mmol/l, serum creatinine was 0.4 mg/dl, hypochloremia and hypomagnesemia were still present. Follow-up: the return of laboratory values to natural.

Discussion

Bartter syndrome is a rare genetic syndrome characterized by tubular damage at the level of the thick ascending limb of the loop of Henle. The genetic mutations responsible for the development of this disease are diverse, leading to the classification of this syndrome into five types (Table 1)[5]; all these types are autosomal recessive except for type 5, which is X-linked recessive. Type 4 is further divided into subtypes a and b.

The onset of the disease varies depending on the type, with types 1, 2, and 4 manifesting prenatally or in the neonatal period. However, type 3, also known as classic Bartter syndrome, may have a delayed onset but can also manifest prenatally or in the neonatal period[6]. In our case, a 17-year-old has been diagnosed

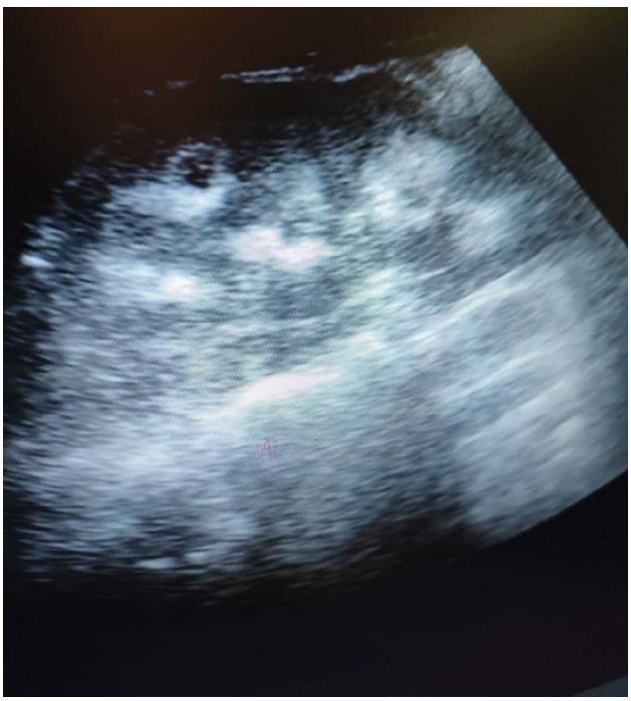

Figure 2. An echography showed nephrocalcinosis due to hypercalciuria.

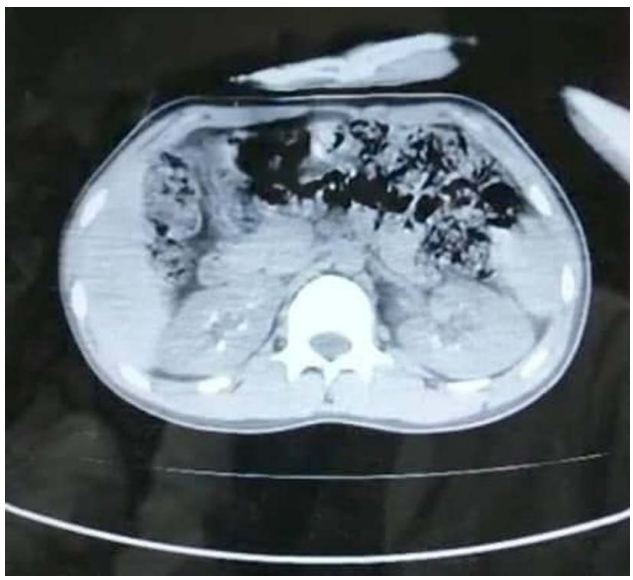

Figure 3. A computed tomography scan showed pulpal calcifications.

Table 1

Batter's syndrome classification according to gene defect and clinical manifestation.

Disorder	OMIM	Inheritance	Gene	Protein	First presentation	Specific clinical findings
BS Type 1	601678	AR	*SLC12A1*	NKCC2	Antenatal	Nephrocalcinosis
BS Type 2	241200	AR	*KNCJ1*	KNCJ1	Antenatal	Postnatal transient hyperkalemia, Nephrocalcinosis
BS Type 3	607364	AR	*CLCNKB*	ClC-Kb	Variable	Variable
BS Type 4a	602522	AR	*BSNC*	Barttin	Antenatal	Sensorineural deafness, sever polyhydramnios
BS Type 4b	613090	AR	*CLCNKA and CLCNKB*	ClC-Ka and ClC-Kb	Antenatal	Sensorineural deafness, sever polyhydramnios
BS Type 5	300971	XLR	*MAGED2*	MAGE-D2	Antenatal	Transient Bartter syndrome, nephrocalcinosis

BS, Bartter syndrome.

with Bartter syndrome type 3 or classic type. This type is caused by a mutation in the CLCNKB gene, which encodes for channels that allow chloride to pass into the renal tubule, represented by the CIC-Kb channel. This gene is located on chromosome 1p36.13[7]. Despite the presence of aldosteronism, blood pressure values are typically normal in patients, which is characteristic of Bartter syndrome. The reason for this is due to a renal loss of sodium[8]. Additionally, hyperaldosteronism enhances potassium secretion, completing the pathogenic cycle[9].

The characteristic presentation of this syndrome is the presence of hypokalemia with metabolic alkalosis, which results from the excretion of hydrogen ions in the urine, along with an increased production of bicarbonate. This leads to elevated levels of bicarbonate. However, our patient had bicarbonate levels within the normal range despite having metabolic alkalosis.

Most cases of concurrent metabolic alkalosis and hypokalemia are associated with chronic conditions. The most common causes of metabolic alkalosis with hypokalemia are related to volume and chloride depletion, such as vomiting (or nasogastric suction) or diuretic use. In these situations, there is an initial loss of both potassium and acid equivalents through the gastrointestinal or urinary tracts, with additional urinary losses often occurring due to increased aldosterone (resulting from volume depletion) and other intrarenal mechanisms. In the absence of volume depletion or diuretic use, the presence of both metabolic alkalosis and hypokalemia should raise suspicion of primary or secondary

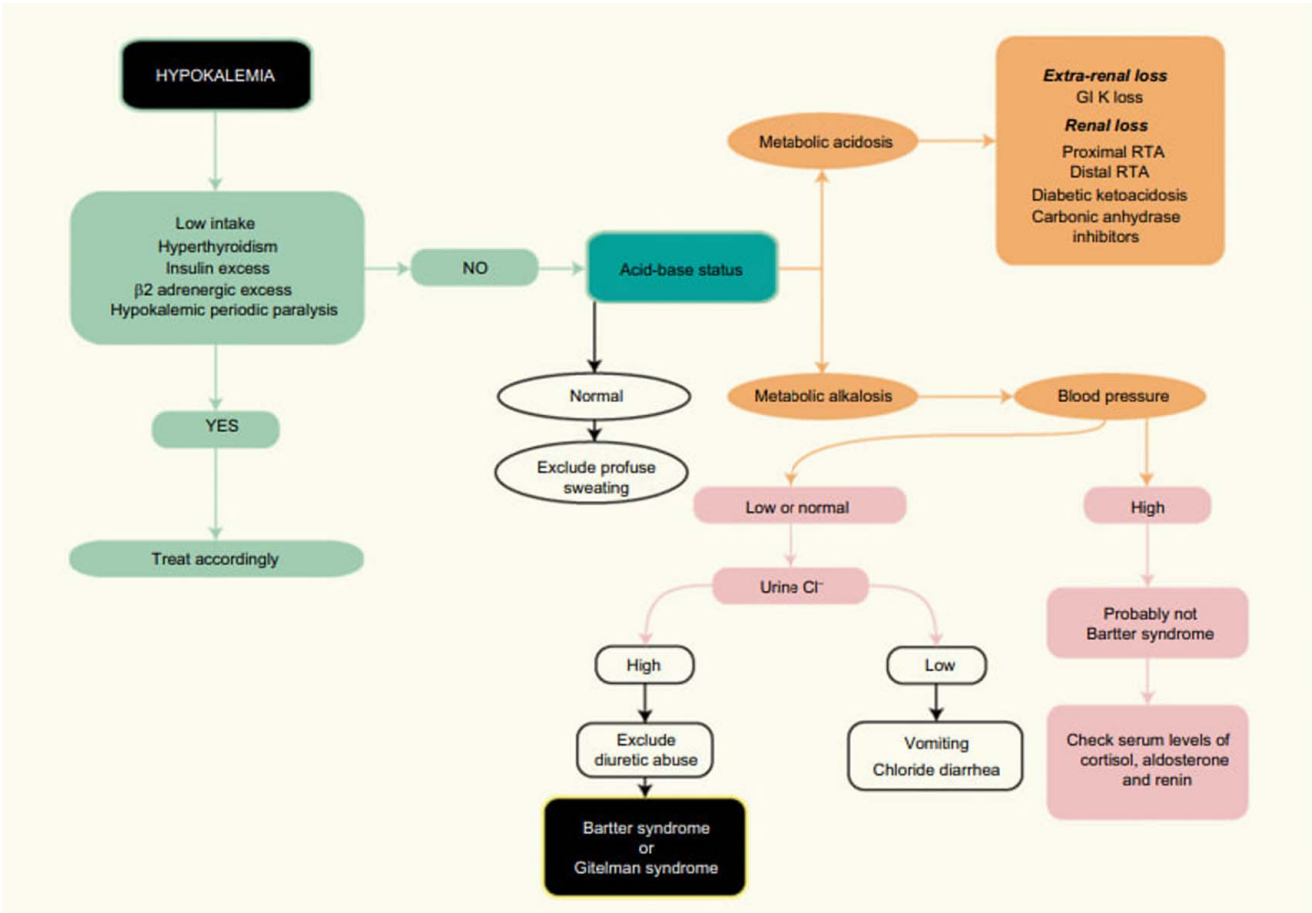

Figure 4. Flowchart for the differential diagnosis of metabolic alkalosis with hypokalemia in adult patients.

hyperaldosteronism[10]. In our case, It was a genetic cause that resulted in metabolic alkalosis and hypokalemia. So, hypokalemia with metabolic alkalosis and normal blood pressure leads to thinking about either renal causes or extra-renal causes, such as diuretic abuse. However, after denying the use of diuretics, the options remain either Bartter syndrome or Gitelman syndrome, and further investigations have proven Bartter syndrome (Fig. 4).

Most medical literature reports a sodium deficiency in patients; on the contrary, this is not inevitable, as in our patients whose sodium levels were normal. In addition to sodium deficiency, Bartter syndrome is characterized by hypochloremia, hypocalcemia, and hypomagnesemia.

Renal biopsy is generally not an indication for the diagnosis of Bartter syndrome. Hyperplasia of the juxtaglomerular apparatus has been observed but can be mild or even absent. Signs of chronic tubulointerstitial nephropathy can occur during evolution[11]. Therefore, due to economic constraints, genetic study was not available and clinical diagnosis was relied upon. The most prominent of these manifestations is a lack of muscle tone, which is a typical manifestation in classic Bartter syndrome[6].

The first change in the ECG associated with hypokalemia is a decrease in the amplitude of the T wave. As the potassium deficiency continues, the T wave inverts and the U wave appears prolongated, especially in the V3–V4 directions[12], which is consistent with our case.

Regarding the treatment of our patient, taking into account the pathophysiology of Bartter syndrome, fluid and electrolyte replacement is essential in emergency management, and several studies in the medical literature consider prostaglandin inhibitors as an important treatment in this condition, as is the use of non-steroidal drugs. Anti-inflammatory medications, especially indomethacin.

Conclusion

Bartter syndrome is a renal tubular salt-wasting disorder in which the kidneys cannot reabsorb sodium and chloride in the thick ascending limb of the loop of Henle. This leads to increased distal delivery of salt and excessive salt and water loss from the body. This syndrome must be considered when a patient complains of symptoms of Hypokalemia and hypomagnesemia.

Methods section: the work has been reported in line with the SCARE 2023 criteria[13].

Ethics approval

Not applicable because all date belong to the authors of this article.

Patient consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

S.H. and A.H.D.A. and H.A. and B.S. and N.K. and Q.H. are co-first authors. All contributed equally in this paper and all authors attest that they meet the current ICMJE criteria for Authorship. S.H. is the supervisor and contributed to editing and reviewing the final version. A.H.D.A. contributed to drafting, editing, reviewing, and bibliography. H.A. is the corresponding author, also, contributed to drafting, editing, reviewing, and bibliography. B.S. contributed to drafting, editing, reviewing, and bibliography. N.K. contributed to drafting, editing, reviewing, and bibliography. Q.H. is the supervisor who diagnosed the patient and reported the data of the case, contributed to editing and reviewing the final version. All authors reviewed and accepted the paper.

Conflicts of interest disclosure

There are no conflicts of interest.

Research registration unique identifying number (UIN)

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Data availability statement

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