A Case of Bartter's Syndrome Presenting in Adulthood

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Keywords. bartter syndrome, hypokalemia, metabolic alkalosis

Bartter's syndrome is a rare disorder usually presenting antenatal or in childhood and is characterized by hypokalemia, metabolic alkalosis, hyperaldosteronism and normal blood pressure. We report a case of adult-onset Bartter's syndrome in a 38 year old male who presented with lower limb weakness.

IJKD 2020;14:65-7
www.ijkd.org

INTRODUCTION

Bartter's syndrome is an autosomal recessive disorder that often presents in childhood and is characterized by hypokalemia, metabolic alkalosis, with normal blood pressure. It was first described by Bartter and colleagues in 1962.[1] Clinical features include failure to thrive, growth and mental retardation and polyuria and polydipsia. This condition is diagnosed on antenatal examination or in early childhood, and presentation in adults is very rare.

CASE PRESENTATION

A 38 years old man, farmer by profession, presented to us with fatigue, lethargy and lower limb weakness for a few months. He complained of bilateral flank pain and polyuria along with the above symptoms. For these symptoms he reported using analgesics off and on. However, he denied history of use of laxatives, diuretics, and herbal medicines. He did not report any exacerbation of symptoms with exercise or excessive carbohydrate intake. There was a history of nephrolithiasis two years ago which was managed medically. Family history was positive for nephrolithiasis as well. On examination, he appeared to be volume depleted, and his pulse was 90/min and blood pressure was 90/60 mmHg. There was decreased power in all four limbs, more so in the lower limbs. His blood urea nitrogen was 41 mg/dL, creatinine = 2.3 mg/dL, sodium = 132 mEq/L, potassium = 1.5 mEq/L, chloride = 94 mEq/L, bicarbonate = 29.5 mEq/L, calcium = 8.1 mg/dL, magnesium = 2.0 mg/dL, phosphorus = 2.3 mg/dL, and uric acid was 5.6 mg/dL. Arterial blood gas showed pH of 7.48, $pCO_2$32 mmHg, pO_2 113 mmHg, and HCO_3 25 mEq/L. Urinalysis revealed a pH of 7. There was proteinuria +2 but no hematuria, or active urinary sediment.

Twenty-four-hour urinary excretion of sodium was 294 mEq (40–220 mEq), potassium 152 mEq (25–125 mEq), chloride 283 mEq (110–250 mEq), oxalate 53.1 mEq (7-44 mEq), protein 1108 mg, and calcium 472mg (100–300 mg), with urine osmolality of 464 mOsm/kg. His transtubular potassium gradient (TTKG) was 9 indicating renal potassium wasting. Further investigations showed that serum renin was 275.7 mIU/mL (range: 4.40–46 mIU/mL), and serum aldosterone of 22.6 ng/dL (range: 1.5-13.3 ng/dL). Ultrasound showed normal-sized kidneys with bilateral medullary nephrocalcinosis. In view of normal BP, polyuria, metabolic alkalosis, hypokalemia, increased renin and aldosterone, increased urinary sodium, potassium, chloride and calcium excretion and medullary nephrocalcinosis, diagnosis of Bartter syndrome was made. The patient was started on a potassium rich diet, potassium replacement, and spironolactone 50 mg twice a day. Five days later his labs showed serum creatinine = 1.5 mg/dL, sodium = 138 mEq/L, potassium = 3.5 mEq/L, chloride = 92 mEq/L, bicarbonate = 26.5 mEq/L. His symptoms improved and he was discharged home. One month later, on a follow-up visit, his labs were serum creatinine = 1.4 mg/dL, sodium = 138 mEq/L, potassium = 4.2 mEq/L, bicarbonate = 26.5 mEq/L.

Case Report

DISCUSSION

The primary defect in Bartter's syndrome is in sodium chloride reabsorption in the medullary thick ascending limb (TAL) of the loop of Henle resulting in increased delivery of sodium to the distal tubule, results in increased urinary potassium losses and hydrogen ion secretion eventually leading to hypokalemia, metabolic alkalosis and secondary hyperaldosteronism due to volume contraction. The reduced chloride absorption in TAL inhibits voltage driven absorption of calcium leading to increased renal calcium excretion causing nephrocalcinosis.

Bartter syndrome is classified into five types on the basis of the affected transport proteins in loop of Henle as a result of gene mutations. Types I, II, and IV are classified as antenatal Bartter syndrome and are usually present in the neonatal period. Type III or the classical Bartter syndrome presents in the first two to five years of life. Late manifestations in type III Bartter syndrome include proteinuria and impaired kidney function as a result of nephrocalcinosis. Type V Bartter syndrome (usually called autosomal dominant hypocalcaemia or autosomal dominant hypoparathyroidism) is due to a gain-of-function mutation in the calcium-sensing receptor and is distinguished from the other types by the presence of hypocalcaemia and hypomagnesaemia. Treatment of Bartter's syndrome is aimed at correcting electrolyte abnormalities with potassium supplementation and the main stay of therapy is use of aldosterone antagonists i.e. spironolactone. In patients with Bartter syndrome, there is overproduction of prostaglandin E2, as a consequence of salt wasting which further reduces sodium chloride absorption at the TAL. Therefore indomethacin and Ibuprofen (prostaglandin inhibitors) have long been used in the treatment of severe cases.

Our patient was a middle aged gentleman who had had hypokalemia, metabolic alkalosis, high urine potassium and chloride excretion, high serum renin and aldosterone levels, normal serum magnesium, hypercalciuria and nephrocalcinosis. Other conditions with similar metabolic abnormalities are sometimes called Pseudo-Bartter syndromes and include laxative abuse, furosemide abuse, bulimia, Sjogren's syndrome, sarcoidosis and cystic fibrosis.[2,3] A Bartter syndrome like phenotype has been described in the literature associated with long-term use of certain drugs, such as Aminoglycosides, Colistin and Amphotericin B.[4-7] All of these were ruled out in our patient because lack of relevant history and a high urinary chloride excretion and hence a diagnosis of idiopathic Bartter syndrome like phenotype was made.

Though Bartter's syndrome is usually diagnosed in pediatric age groups, an adulthood presentation is possible due to phenotypic variation. So far only a few reports of Bartter's syndrome presenting in adulthood have been described in the literature.[8-13] To the best of our knowledge this is the first case report of adulthood presentation of Bartter syndrome from Pakistan. Our patient responded well to oral potassium supplementation and spironolactone and the metabolic abnormalities were reversed. We avoided using indomethacin/ibuprofen in our case in view of the reduced estimated glomerular filtration rate and mild non-nephrotic range proteinuria. These findings are in contrast to those reported in literature. Almost all adult patients described so far have had well-preserved renal function. We attribute proteinuria and renal impairment to prolonged intake of analgesics and nephrocalcinosis. We intend to closely follow his renal function and proteinuria and will add Renin-angiotensin-Aldosterone system (RAAS) inhibitors to the treatment protocol.

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Received July 2019
Revised September 2019
Accepted November 2019