A rare case of Gitelman syndrome in a 37-year-old male

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ABSTRACT

Hypokalemia refers to a deficiency of potassium in the bloodstream with or without clinical signs and symptoms. It is a common electrolyte disbalance found in all age groups. There are many causes of hypokalemia and though rare but certain renal tubular channelopathies as Gitelman syndrome (GS), Bartter syndrome, and Liddle syndrome can also be manifest with altered arterial blood gas, blood pressure, and hypokalemia. In the presented case, a 37-year-old man with generalized weakness, muscle cramps, and hypotension was found to have hypokalemia. Ruling out the possible common causes of hypokalemia with hypotension and alkalotic pH and his resistance to potassium replacement was investigated for renal tubular channelopathies. He was found to have blood and urinary parameters favoring GS. He showed marked improvement in his symptoms on Aldactone. This has opened our minds to try to see for these channelopathies as potential causes of hypokalemia and improvement of the same on addressing the defect.

Key words: *Channelopathies, Gitelman syndrome, Hypokalemia*

Hypokalemia is a common electrolyte problem, particularly in pediatric and geriatric patients. In most cases of hypokalemia, unreplenished gastrointestinal or urinary losses are a major cause. Thinking about tubulopathies such as Gitelman syndrome (GS), Bartter syndrome, or Liddle syndrome is a different insight into approach and better outcomes. GS is an autosomal recessive salt-losing renal tubular defect that causes hypokalemia and metabolic alkalosis [1].

CASE REPORT

A 37-year-old male came with complaints of pain in the calf, thighs, back, and generalized weakness with easy fatigability and malaise for 1–2 years. He was having bilateral lower limb weakness for 2 days and finding difficult to walk. On further asking, he also admitted that he is often thirsty and diaphoretic. There was no history of any chronic or acute illness, symptoms suggesting of urinary tract infection, gastroenteritis, inflammatory bowel disease (IBD/IBS), any drug usage, or addiction.

On examination, his vitals were stable with SpO_2 96% (@ room air), pulse rate 100 bpm (regular), and blood pressure 90/56 mmHg. Random blood sugar was 134 mg/dl. His deep tendon reflexes were absent in bilateral lower and upper limbs and planters were mute.

The electrocardiogram showed the presence of U wave and an initial electrolytes workup showed hypokalemia (1.4 mmol/l) and hypomagnesemia (0.35 mmol/l) with normal sodium (4.1 mmol/l). The arterial blood gas (ABG) analysis showed pH – 7.56, primary metabolic alkalosis with bicarbonate – 17 mmol/l, and pCO_2 – 43 mmHg. Even a detailed history could not suggest any reason to explain the cause of hypotension with hypokalemia and alkalosis. A magnetic resonance imaging brain with a screening of the spine showed normal study as well the cerebrospinal fluid analysis failed to show any abnormality. The renal function tests, liver function tests, complete blood count, and routine and microscopic examinations of urine were within the normal limits. The ultrasound abdomen was normal. Intravenous potassium supplementation in correct replacement dose could not check the potassium and his symptoms. Further biochemical study revealed raised active renin level-110IU (N-4.4-46IU) and 24 h urinary calcium excretion was markedly reduced – 0.79 mmol/l (N-2.5-7.9). Further investigation revealed elevated plasma – active renin (281.7 μU/ml; NR 4.4–46.1), normal aldosteronemia (15.2 ng/ml), increased urinary excretion of sodium (145.8 mmol/l; NR 20–110), and chloride (190 mmol/l; NR 55–125). The estimated glomerular filtrate rate (modification of diet in renal disease) was 90 ml/min/1.73 m^2. Urinary prostaglandin E2 was normal. Based on the above findings, a provisional diagnosis of renal tubular channel defect was made with investigations favoring GS.

The patient was given intravenous potassium for 6 days at the hospital with correction of potassium to 2.8 mmol/l and regaining or neurological reflexes. He was started on potassium-sparing diuretics Aldactone – 50 mg twice a day and was discharged. After 15 days, he came with potassium to be 3.56 without any oral or IV supplements with an improvement of all the symptoms and

general well-being. The patient is maintained on it and is doing well.

DISCUSSION

Electrolyte imbalance is a common but life-threatening problem seen with various vague clinical pictures. Hypokalemia is a common clinical problem which if not addressed may be life threatening.

A common approach to hypokalemia is its relation with the blood pressure and pH in ABG [1]. In the presented case, the patient had vague symptomatic hypotension and persistent hypokalemia which he 1st time got diagnosed at our center. The ABG revealed metabolic alkalosis and biochemistry further had hypomagnesemia. Vomiting and diuretics are common causes. They were excluded by high urinary chloride excretion and no history of drug abuse. The rare but possible differential diagnoses were the tubulopathy of Gitelman and Bartter syndromes. Bartter syndrome was less likely because it usually presents early and a more severe, urinary calcium excretion is often high and normal or mildly reduced serum magnesium. Thus, our final diagnosis was GS, an autosomal recessive salt-losing renal tubulopathy.

In the majority of the cases, the disease is due to silencing mutations in the gene coding renal thiazide-sensitive sodium-chloride cotransporter (NCC) at the epithelial cells of the distal convoluted tubule [2]. It is characterized by hypomagnesemia, hypocalciuria, and secondary hyperaldosteronism that induce hypokalemia and metabolic alkalosis. Clinical manifestations mimic long administration of thiazide diuretics [3].

GS is often not diagnosed until late childhood or even adulthood. Cramps, paresthesia, and easy fatigue are common complaints. Most patients complain of recurrent carpopedal spasms with vomiting, diarrhea, or fever. Chondrocalcinosis may occur in later life and may be due to hypomagnesemia [4]. Blood pressure is lower in the general population.

The diagnosis of GS is done on clinical symptoms and biochemical abnormalities, which include hypomagnesemia, hypokalemia, metabolic alkalosis, and hypocalciuria. These patients have a poor natriuretic response to a thiazide, but good natriuresis with furosemide, indicating defect located to be at the distal tubule. DNA mutation analysis is the gold standard for diagnosis [1,4].

Most asymptomatic patients remain untreated and go unnoticed. The hypokalemia will be corrected and symptoms may subside. A combination of amiloride, spironolactone, or eplerenone with potassium chloride is often used [5].

CONCLUSION

Hypokalemia is a common electrolyte abnormality that we encounter in our daily practice. If not addressed properly, it can manifest with a life-threatening cardiac insult (arrhythmia) and death. Renal tubular channelopathies such as Liddle syndrome, Bartter syndrome, and GS are rare causes of hypokalemia but should be kept in differential if the patient has altered blood pressure (hypotension/hypertension), alkalotic pH, and non-response to the conventional replacement that we give for hypokalemia. As in our case, no one has thought of the same, despite adequate correction of potassium, he did not improve at all, and as was started on Aldactone, his potassium got corrected and symptoms improved.

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