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Case Report

Internal Medicine Section

Gitelman Syndrome in a Case of Diabetic Kidney Disease: A Diagnostic and Therapeutic Dilemma

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ABSTRACT

Gitelman syndrome is an autosomal recessive disorder that usually presents with hypokalemia, hypomagnesemia, hypocalciuria and normal blood pressure. In contrast to Bartter syndrome it presents in late adulthood. Hypokalemia in a patient of chronic kidney disease is not a usual finding. Here we present a case of intractable hypokalemia due to Gitelman syndrome with hypertension in a background of chronic kidney disease, which poses both a diagnostic as well as a therapeutic dilemma.

Keywords: Chronic kidney disease, Hypertension, Hypokalemia

CASE REPORT

A 48-year-old, male diabetic patient on irregular medications, was admitted in the hospital with complaints of fatigue, generalised weakness for the last one month. He had quadriparesis at the time of admission. The weakness started from lower limbs and then involved upper limbs, proximal weakness was more than distal and there was no diurnal variation. There was no history of vomiting, diarrhoea, fever, sensory level, bladder and bowel involvement fasciculations, muscle atrophy, bulbar symptoms, cranial nerve involvement or any drug intake.

On clinical examination, patient was alert and conscious, had pallor, blood pressure was 160/90 mmHg. Rest of the general examination showed no abnormality. On neurologic examination, he had hypotonia of all four limbs with diminished reflexes and flexor planter response. Power in both upper and lower limbs was 3/5. There was no cranial nerve, cerebellar, meningeal or sensory involvement. Examination of other systems were within normal limits.

Laboratory investigations revealed haemoglobin 10.0 gm/dL with normal blood counts. Liver function test was normal. Fasting blood sugar 221 mg/dL, post prandial blood sugar was 314 mg/dL with a glycosylated haemoglobin of 9.2%.

Electrolyte study revealed sodium 130 mg/dL, potassium 1.1 mg/dL, Calcium 8.6 mg/dL, phosphate 2.13 mg/dL, magnesium 1.0 mg/dL, Arterial blood gases revealed pH 7.55, bicarbonate 38.0 mEq/L and pCO_2 45.0 mmHg, urea was 53 mg/dL and creatinine was 2.0 mg/dL. Urine analysis revealed 3+ protein with Urine A:C ratio of 1708 mg/mg and a negative diuretic screen. Thyroid function tests were normal. Nerve conduction velocity and electromyogram studies were within normal limits.

The patient was started on intravenous potassium (10 meq/hour for first two days which was later increased to 30 meq/hour) as well as magnesium supplementation (60 meq in first 24 hours then 30 meq/day for next three days). The magnesium values normalised but potassium values remained low inspite of adequate potassium replacement. A 24 hours urine analysis was performed and hypocalciuria along with low calcium creatinine ratio was found which are summarised in the [Table/Fig-1].

Ultrasound of whole abdomen and CT scan abdomen did not reveal any adrenal space occupying lesion. A diagnosis of Gitelman syndrome was made based on above findings. Patient was started on Eplerenone (50 mg daily which was later increased to 150 mg over next seven days), oral potassium and magnesium supplementation. The patient responded and was doing well on follow up for a year but had poor compliance. He was admitted again with low potassium and succumbed to his illness due to cardiac arrest.

24 hours urinary potassium	43 mEq/day
Trans tubular potassium gradient	>38
Urinary chloride	40.8 mmol/L
24 h urinary calcium	<0.2 mg/100 mL
Urine creatinine	35.8 mg/100 mL
Urine calcium: creatinine ratio	5.6 mg/gm

[Table/Fig-1]: laboratory parameters suggesting renal loss of potassium along with hypocalciuria.

DISCUSSION

Gitelman syndrome usually presents with hypokalemia, metabolic alkalosis, hypomagnesemia, hypocalciuria, and normal blood pressure. These patients usually complain of fatigue, cramps of the arms and legs which may be severe [1]. Approximately 10 percent of affected patients have tetany at diagnosis. Polyuria and nocturia are found in approximately 50 to 80 percent of patients, respectively [2]. Surprisingly, hypertension may develop later in life. In a series of 36 patients with Gitelman syndrome from 35 unrelated families, nearly half (44%) developed hypertension later in life (median of 55 years). The reason for this observation is not known, but it may relate to prolonged exposure to elevated renin and aldosterone levels [3]. Approximately 51.7% patients of hypokalemic weakness have secondary causes, Gitelman syndrome is found in 3.4% of cases [4]. In the present case, the patient had hypertension from the beginning and with the background of diabetic nephropathy, it was a therapeutic challenge.

Bartter or Gitelman syndrome is often suspected in patients with unexplained hypokalemia, metabolic alkalosis, and a normal or low blood pressure. Gitelman syndrome is more common than Bartter syndrome [5]. In a report from the Framingham Heart Study, the prevalence of Gitelman syndrome was 1 in 40,000 compared with 1 in 1,000,000 for Bartter syndrome. These tubular defects involve sodium chloride transport and produce a clinical spectrum that mimics chronic ingestion of a loop diuretic (Bartter syndrome) or a thiazide diuretic (Gitelman syndrome).

In such patients, the presence of Bartter or Gitelman syndrome can be diagnosed after other, more common causes of unexplained hypokalemia and metabolic alkalosis have been excluded. Excluding these other causes includes a careful history, thorough physical examination, measurement of the urine chloride concentration (or fractional chloride excretion), and urine diuretic screens. Measurement of urinary calcium excretion (either a 24 hours urine collection or a spot calcium/creatinine ratio) can help differentiate between Bartter and Gitelman syndromes. Urine calcium excretion is high normal or elevated in Bartter syndrome and below normal in Gitelman syndrome [6,7]. In normal adults, the upper limit for 24 hours urinary calcium excretion is approximately 275 mg (6.9 mmol) in women and 300 mg (7.5 mmol) in men [6]. The ratio of urine calcium/creatinine in adults is considered abnormal if it is more than 200 mg/gm of creatinine (565 mmol/mol) [7].

Although data from adults are scarce, a large series of 29 adults with genetically confirmed Gitelman syndrome found that a spot urine calcium/creatinine ratio of <44 mg/gm had a sensitivity of 80% [8]. In this case 24 hour calcium was very low and urine calcium: creatinine ratio was also lower than the specified range mentioned above.

The genetic study of hypokalemic disorders is very complex and is not routinely done. The genetic testing is limited by the large size of the involved genes, the multitude of recognized mutations, the absence of "hot spots" along the gene, intrafamilial heterogeneity, and cost. The most common disorders that have a similar presentation and must be excluded are vomiting and diuretic use. Frequently, patients have both vomiting and diuretic abuse. In these cases urinary chloride is low, in contrast gitelman has very high urinary concentration in range of 40 mg/L [9].

CONCLUSION

This case is unique in its own way because of presence of hypertension which may divert the attention towards spectrum of hypokalemic disorders that present with hypertension. In this case, we conclude hypertension to be effect of diabetic nephropathy and use of eplerenone in such patients will be limited by rise in creatinine once renal insufficiency sets in.

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