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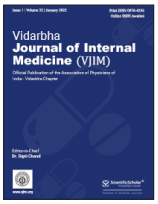

Case Report

Gitelman Syndrome – A Case Report

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ABSTRACT

Hypokalaemia is an electrolyte disorder, commonly encountered in clinical practice. Sometimes, it may present with severe life-threatening complications. We present here a case of 22-year-old female, who was admitted to intensive care unit, for severe hypokalaemia associated with cardiac and neurological complications. She had recurrence of such episodes. On detailed clinical and biochemical evaluation, she was diagnosed to have Gitelman syndrome (GS). She was treated with intravenous potassium and magnesium supplementation under cardiac monitoring and other supportive management. She was discharged in stable condition, on oral supplements, and remained stable on follow-up visits. GS is an autosomal recessive and renal tubular disorder characterised by hypokalaemic metabolic alkalosis with hypomagnesaemia, hypocalciuria, secondary hyperreninemic aldosteronism and hypotension. The disease is caused by biallelic inactivating mutations within the SLC12A3 gene encoding the thiazide-sensitive sodium chloride cotransporter expressed within the apical membrane of cells, lining the distal convoluted tubule. Since GS is an autosomal recessive trait, the recurrence risk for people with an affected child is 25%. It is very important to completely evaluate a patient with hypokalaemia to find the underlying cause. There can be various etiological factors for hypokalaemia ranging from common to rare disorders. If underlying aetiology remains undiagnosed, there may be recurrence as well as increased morbidity and mortality. GS is one such disorder, which needs prompt diagnostic evaluation and treatment.

Keywords: Gitelman syndrome, Bartter syndrome, Hypomagnesaemia, Hypokalaemia

INTRODUCTION

Gitelman syndrome (GS) is a rare disorder with prevalence of 25/1 million people. GS usually presents clinically as hypokalaemia with or without its symptoms. Hypokalaemia is an electrolyte imbalance characterised by low serum potassium levels (<3.5 mEq/L). Severe and life-threatening neurological and cardiac complications may develop when potassium levels are <2.5 mEq/L. It can be due to various causes. It is very important to find the underlying cause of hypokalaemia as just correcting potassium levels may lead to recurrence as well as severe complications.

CASE REPORT

A 22-year-old female was admitted in intensive care unit (ICU), with h/o recurrent and severe episodes of generalised weakness, cramps, muscle stiffness, tingling and headache off and on for the past 4 years. Frequency of symptoms had increased in the past 1 year and now she had symptoms daily. Patient had received anxiolytics multiple times previously due to non-specific complaints. On examination, she was anxious, pulse rate - 100/min, regular and blood pressure was 90/60 mm of Hg. She had hypotonia in all four limbs. Remainder of the clinical examination was normal. Review of old records showed serum potassium of 2.5–3 mEq/L. She was hospitalised twice and received parenteral and oral potassium. She was not on any other medications. Family history was negative for similar complaints or other medical problems. Laboratory investigations showed – Serum sodium – 136.4 meq/L, serum potassium – 2.5 meq/L, serum magnesium – 0.63 mg/dL and serum chloride – 90 meq/L. Urinary potassium – 107 meq/L (<20 meq/L), urinary chloride – 132 meq/L (110–250 meq/L) and serum cortisol was 18.5 mcg/dL. Blood gas analysis was suggestive of metabolic alkalosis. Twelve lead electrocardiogram (ECG) showed global ST segment depression. Patient was admitted in intensive care unit (ICU) in view of subtle neurological and cardiac manifestations of hypokalaemia. Mutation analysis could not be done in this patient. On the basis of clinical profile and laboratory features, patient was diagnosed to have GS She was treated with intravenous potassium and magnesium supplementation under cardiac monitoring and other supportive management. Subsequently, she was shifted to oral supplements. She was given T. Aldactone 25 mg once daily and was discharged on 3rd day. She was asymptomatic at day 10 follow-up. Follow-up laboratory tests on 10th day

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showed serum potassium – 3.6 meq/L, serum magnesium – 1.0 mg/dL and serum sodium – 138 meq/L.

DISCUSSION

GS, is an autosomal recessive renal tubular disorder characterised by hypokalaemic metabolic alkalosis with hypomagnesaemia, hypocalciuria, secondary hyperreninemic aldosteronism and hypotension.[1,2] The disease is caused by biallelic inactivating mutations within the SLC12A3 gene encoding the thiazide-sensitive sodium chloride cotransporter expressed within the apical membrane of cells lining the distal convoluted tubule.[3] Bartter syndrome is another vital hereditary condition to contemplate within the genetic abnormality of GS. Especially, Type III Bartter syndrome, which is caused by mutations in the CLCNKB gene, is clinically and biochemically overlapping with GS Bartter syndrome and usually has an earlier onset and a more severe phenotype.

Patients of GS usually present after 6 years of age with clinical manifestations of hypokalaemia Polyuria is rare in GS patients, which is a prominent feature in Bartter syndrome. Growth parameters are normal in GS patients; however, it may be delayed in patients with severe hypokalaemia and hypomagnesaemia for prolonged duration.[4] Chronic hypomagnesaemia may cause chondrocalcinosis. The typical biochemical abnormalities in GS are hypokalaemia, metabolic alkalosis, hypomagnesaemia and hypocalciuria. Prostaglandin excretion is normal and plasma renin activity and plasma aldosterone concentration are only slightly elevated as compared to Bartter syndrome. Antenatal diagnosis for GS is routinely not advised because of the good prognosis in majority of patients in later life.

Most asymptomatic patients with GS remain untreated and undergo ambulatory monitoring with low frequency. Complaints associated with chondrocalcinosis (mainly pseudogout attacks) are caused by the deposition of calcium pyrophosphate dehydrate crystals in synovium and also the synovia and will be reduced by magnesium supplementation.[5] If symptomatic hypokalaemia persists after magnesium sulphate administration, it is treated by potassium supplements along with potassium sparing diuretics.

Detailed history should include evaluation for possible GI losses, review of medicines, assessment for underlying comorbidities, history of paralysis, hyperthyroidism or use of insulin or beta-agonists. Symptoms and signs of hypokalaemia – Leg cramps, weakness and paresis, constipation, respiratory distress, electrocardiographic (ECG) changes and cardiac arrhythmias. Laboratory tests should be done to find out the cause, severity and associated complications of hypokalaemia. These include serum glucose and magnesium levels, urine electrolyte and creatinine levels. The foremost accurate method for evaluating urinary potassium excretion is additionally a 24-h urine potassium collection; normal kidneys excrete not over 15–30 mEq/L of potassium/day in response to hypokalaemia. A more practical approach is calculation of the urine potassium-to-creatinine ratio from a spot urine specimen; a ratio >1.5 mEq/mmoL is indicative of renal potassium wasting. If no cause is identified with the initial workup, assessment of thyroid and adrenal function should be considered. Imaging of the adrenal glands (computerised tomography or magnetic resonance imaging [MRI]) if there is a suspicion of mineralocorticoid, glucocorticoid or catecholamine excess or MRI of pituitary (to exclude Cushing's disease) could even be needed. Typically, the ECG manifestation of hypokalaemia includes decreased T-wave amplitude, ST-interval depression, T-wave inversions, PR-interval prolongation and U waves. Arrhythmias related to hypokalaemia include sinus bradycardia, ventricular tachycardia or fibrillation and torsade de pointes. The treatment of hypokalaemia has four aims: (a) Reduction of potassium losses, (b) replenishment of potassium stores, (c) evaluation for potential toxicities and (d) determination of the cause, and thus prevent future episodes. Discontinuation of laxatives, use of potassium-neutral or potassium-sparing diuretics (if diuretic therapy is required), treatment of diarrhoea or vomiting, use of H2 receptor blockers in patients with nasogastric suction and effective control of hyperglycaemia, if glycosuria is present, are some common measures.

CONCLUSION

Hypokalaemia is a very common abnormality found in clinical practice. It can be caused by many factors such as excessive use of diuretics, endocrine diseases such as primary hyperaldosteronism, kidney disorders and genetic syndromes affecting the renal function, diarrhoea, vomiting, chronic laxative abuse, intestinal obstruction or infections, insulin administration, thyrotoxicosis, familial periodic paralysis and congenital adrenal hyperplasia. Hypomagnesemia may aggravate hypokalaemia and is often refractory to treatment with potassium supplements.[6,7] Hence, it is very important to completely evaluate a patient with hypokalaemia to find the underlying cause. Complete evaluation would include detailed history, complete physical examination, laboratory tests, ECG and imaging. Always look for possible neurological and cardiac complications as they are life-threatening, and treat them accordingly as per severity. Intravenous potassium correction is required if warning signs are present. Each 1 mEq/L decrease in serum potassium represents a potassium deficit of roughly 200–400 mEq. Correction typically should not exceed 20 mmoL/h, although higher rates using central venous catheters are successful in emergencies.[8] Continuous cardiac monitoring is indicated if the speed exceeds 10 mmoL/h. Potassium

should not be given in dextrose-containing solutions because dextrose-stimulated insulin secretion can exacerbate hypokalaemia.

Clinical significance

Hypokalaemia, a very common disorder, can cause severe life-threatening complications. It can be a manifestation of various commonly encountered rare diseases. Therefore, it is important to understand the underlying disorder and treat it accordingly, to prevent recurrence as well as related complications in a critically ill patient.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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