

Case Report

Gitelman's syndrome - incidentally detected in an elderly female

Rahul R.*, Raghava Sharma

Department of General medicine, K.S Hegde Medical Academy, Mangalore, Karnataka, India

Received: 27 January 2016

Accepted: 27 February 2016

***Correspondence:**

Dr. Rahul. R.,

E-mail: jvk1433@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Potassium is critical for many important cell functions. Hereditary tubulopathies can also present in adults with symptoms of recurrent hypokalemia. A 60 year female who was worked up for persistent hypokalemia during repeated admission with different etiology and presenting complaints. Bartter's syndrome and Gitelman's syndrome represent distinct variants of primary renal tubular hypokalemic metabolic alkalosis and are easily distinguished on the basis of urinary calcium levels. Therapeutic options in gitelmans syndrome include supplementation of potassium and magnesium along with avoiding sodium depletion.

Keywords: Gitelman's syndrome, Elderly, Recurrent hypokalemia, Metabolic alkalosis

INTRODUCTION

Potassium is critical for many important cell functions. 98% of total body potassium is intracellular and kidney plays a dominant role in potassium homeostasis. GI loss, diuretics use, chronic kidney disease and starvation are the major causes for hypokalemia in adults. Hereditary tubulopathies can also present in adults with symptoms of recurrent hypokalemia. They can present later in life due to a missed diagnosis at a younger age or patient being asymptomatic.¹ This report reviews Gitelman's syndrome, in a 60 year old female and emphasizes clinical and laboratory characteristics of the disease.

CASE REPORT

A 60 years old female came to us with history of vomiting, diarrhea, loss of appetite and generalized edema of 2 months duration and generalized weakness. She was a known case of diabetes, hypertension, bronchial asthma, mood disorder and was on metformin, deriphylline, sodium valproate for the above. There was no history of diuretic therapy, laxative abuse, excess alcohol intake, liquorice ingestion or any β agonist use. There was no history of fever or worsening of weakness

following exertion or after heavy carbohydrate meal. None of the other family members had any similar complaints or any history of parental consanguinity.

On examination revealed a thin female with height of 148 cms and weight of 37 kg who was conscious but dull. She was icteric, and had pedal edema. Her blood pressure was 130/80 mm of Hg and was afebrile. Systemic examination revealed soft, non-tender abdomen with hepatomegaly. There were no focal neurological deficits or any muscle weakness. Other systems were within normal limits. Blood investigations showed normal hemoglobin, total leukocyte count, ESR and platelet counts. Her urea and creatinine were 13 mg/dl and 0.68mg/dl respectively. Serum sodium 137 mEq (136-145 mEq), serum potassium 2.8 mEq/L (normal range 3.5-5 mEq/L), and serum chloride 96 mEq/L (96-106 mEq). Liver function test showed total bilirubin 5.3 (normal range 0-1 mg/dl), direct bilirubin 3.8 (normal range 0-0.25 mg/dl), indirect bilirubin 1.5 (normal range 0-0.75 mg/dl), total protein 5.0 (normal range 6.6-8.3 mg/dl), albumin 3.0 (normal range 3.5-5 mg/dl), globulin 2.0 (normal range 2.3-3.5 mg/dl), SGOT 279 (normal range 0-40U/L), SGPT 71 (normal range 0-40U/L), alkaline phosphatase 197 (normal range 60-170 U/L),

prothrombin time was also increased with an INR of 1.41. All her symptoms were attributed to acute hepatitis-secondary to valproic acid and malnutrition. Abdominal ultrasound showed mild hepatomegaly with fatty liver. Hypokalemia was thought to be due to gastrointestinal loss. CT abdomen done on a later date showed features highly suggestive of IBD with intussusceptions but colonoscopy was not done as patient was not willing for that. She was treated conservatively with intravenous potassium correction, vitamin k and other supportive measures. Hepatotoxic drugs were stopped. She was symptomatically better and was discharged.

She was readmitted three weeks later with two episodes of generalized tonic clonic seizures, altered sensorium, generalized weakness, decreased appetite and decreased movement on left side of the body. There was no history of any vomiting or diarrhea during present admission. On examination she was conscious and disoriented with blood pressure of 140/90 mm of Hg. She was pale, icteric and had pedal edema. Patient was febrile and Central nervous system examination revealed left sided gaze preference, weakness and babinski sign on left. CT brain was normal except age related atrophic changes and small vessel ischemic changes, probably lacunar infarct. Her liver function was better than last admission with total bilirubin of 3.7 mg/dl, SGOT 124, SGPT 32. She had leukocytosis and her urine routine was suggestive of urinary tract infection and urine culture grew *E.coli*, which explains the cause of fever at the time of admission.

Her blood investigation during the second admission showed hypokalemia, which made us check for its cause. Her urea and creatinine were normal, 20 mg/dl and 0.53 mg/dl respectively. The blood and urine investigations are given in Table 1 and Table 2. ECG was normal during both the admissions.

Table 1: Laboratory data-serum (second admission).

Serum	Value	Normal range
Serum potassium	2.4 mEq/L	3.5-5 mEq/L
Serum chloride	92mEq/L	96-106mEq/l
Serum bicarbonate	30.1 mEq/L	24-28 mEq/L
Blood pH	7.52	7.35-7.45
Serum magnesium	1.6 mg/dl	1.8-2.4 mg/dl

Urine specific gravity was normal. Her thyroid function test, serum rennin, serum aldosterone and serum cortisol levels were normal. All her three children's were worked up with serum electrolytes and urinary sodium and potassium which were all within normal limits.

Patient was treated with oral magnesium, spironolactone and potassium supplementation. Her symptoms improved and was discharged with advise to continue same medications. On initial follow up her serum electrolytes were normal and were lost to follow up latter. No genetic

studies were carried out as patient was not willing, which was one of the drawback in this case.

Table 2: Laboratory data-urine (second admission).

Urine	Value	Normal range
Urinary calcium	1.0 mmols/24 hour	2.5-7.5 mmols
Urinary sodium	74.75 mmol/24 hour	40-220 mmols
Urinary potassium	28.12 mmols/24 hour	25-150 mmols
Urinary chloride	122.95 mmols/24 hour	110-250 mmols
Urinary magnesium	34 mg/24 hour	1.2-29.2 mg
Urine osmolality	301 mOsm/kg	50-1400 mOsm/kg

DISCUSSION

Gitelman's syndrome, also referred as familial hypokalemia- hypomagnesemia, is an autosomal recessive salt-losing renal tubulopathy. In majority cases, it's the result of mutation in the SLC12A3, which encodes the thiazide sensitive Nacl transporter that is specifically expressed in the first part of the distal convoluted tubule. In our patient, diagnosis of Gitelman syndrome was based on hypokalemic hypochloremic, metabolic alkalosis with hypomagnesaemia and hypocalciuria.

The reduced sodium reabsorption in the distal convoluted tubule leads to volume depletion, resulting in hyperreninaemic hyperaldosteronism and hypokalemia, though not as severe as would result from a lesion in the loop of Henle. Loss of activity of the thiazide sensitive transport increases tubular calcium reabsorption, leading to the classic finding of hypocalciuria in Gitelman's syndrome.² Bartter's syndrome and Gitelman's syndrome represent distinct variants of primary renal tubular hypokalemic metabolic alkalosis and are easily distinguished on the basis of urinary calcium levels.³ Rodriguez-Soriano et al were the first to suggest that hypocalciuria may be useful in distinguishing the Gitelman's syndrome from classic Bartter's syndrome.⁴ It is less certain whether changes in calcium excretion provide insight in to the renal tubular pathophysiology of these syndromes. The greater urinary calcium excretion in patients with classic Bartter's syndrome is consistent with impaired reabsorption in the ascending limb of loop of Henle. Alternatively the hypocalciuria of Gitelman's syndrome suggests the involvement of the distal convoluted tubule, where reduced chloride absorption is associated with augmented calcium absorption.³

Usual mode of presentation of Gitelman syndrome is with weakness, fatigue, muscle cramps and nocturia in adolescents and young adults. In some cases Gitelman's

syndrome (GS) is found by chance because of measurement of serum electrolytes for other reason.⁵ Female patients with the same mutations are relatively asymptomatic compared with their male counterparts. The nature and position of the SLC12A3 mutation combined with male gender, seems to be a determinant factor in the severity of GS.⁶ In our patient also it was found by chance because of her persistent hypokalemia. She was also asymptomatic except the generalised weakness and persistence of hypokalemia during her second admission which made us look for the cause. Chronic vomiting may be a differential diagnosis for Gitelman's syndrome, which can be easily diagnosed by low urine chloride concentration.² But it was not done in our patient during her first admission.

Our patient had hypomagnesaemia. The mechanism of hypomagnesaemia in Gitelman's syndrome and its relationship with normocalcaemic hypocalciuria are complex and still not well understood. Several mechanisms have been described, one of which postulates that genetic mutations that result in the reduced expression of TRP6 Mg channels in the duodenum and DCT results in intestinal and urinary magnesium loss and hypomagnesaemia.⁷

Reduced expression of the NCCT was described by Loffing et al in their experimental study on mice.⁷ They concluded that acute intratubular hydrochlorothiazide (HCTZ) infusion decreases the expression of the apical NCCTs with a consequent abrupt intracellular Ca⁺ passive diffusion that could induce distal convoluted cell (DCC) apoptosis. As a result, there is a reduction in the absorptive surface area in these tubular segments of the DCT, where the expression of TRPM channels regulates Mg²⁺ absorption.

In addition, inactivation of the NCCT might be responsible for reduced distal magnesium transport as well as up-regulation of calcium absorption in the DCT resulting in hypocalciuria.⁸

Therapeutic options in Gitelman's syndrome include supplementation of potassium and magnesium along with avoiding sodium depletion. Increased sodium delivery to distal nephron increases potassium excretion. In sodium wasting or in patients supplemented with sodium in the diet, the increased potassium excretion will require potassium supplementation in large quantities and potassium sparing diuretics to maintain normal range of plasma potassium levels. Modest amount of potassium

supplementation with or without potassium sparing diuretics may be required in the absence of salt wasting.⁹

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

REFERENCES

1. Tabasum A, Shute C, Datta D, George L. A man with a worrying potassium deficiency. *Endocrinology, Diabetes & Metabolism Case Reports.* 2014;2014:130067. doi:10.1530/EDM-13-0067.
2. Brenner RM, Brenner BM. Disorders of the kidney and urinary tract. In : Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL Editors. *Harrison's Principles of Medicine*, 15th ed. McGraw-Hill: NewYork; 2001. p. 1601-2.
3. Gitelman HJ. Hypokalemia, hypomagnesemia and alkalosis: A rose is a rose- or is it? *J Pediatr.* 1992;120:79-80.
4. Rodriguez-Soriano J, Vallo A, Garcia-Fuentis M. Hypomagnesemia of hereditary renal origin. *Pediatr Nephrol.* 1987;1:465-72.
5. Bettinelli A, Bianchetti MG, Girardin E, Caringella A, Cecconi M, Appiani AC, et al . Use of calcium excretion values to distinguish two forms of primary renal tubular hypokalemic alkalosis: Bartter's and Gitelman's syndrome. *J Pediatr.* 1992;120:38-43.
6. Riveira-Munoz E, Chang Q, Godefroid N, Hoenderop JG, Bindels RJ, Dahan K, Devuyst O. Transcriptional and functional analyses of SLC 12 A3 mutations: new clues for the pathogenesis of Gitelman syndrome. *J Am Soc Nephrol.* 2007;18:1271-83.
7. Loffing J, Loffing-Cueni D, Hegyi I, Kaplan MR, Hebert SC, Le Hir M, et al. Thiazide treatment of rats provokes apoptosis in distal tubule cells. *Kidney International.* 1996;50:1180-90.
8. Kamel KS, Oh MS, Halperin ML. Bartter's, Gitelman's, and Gordon's syndromes. From physiology to molecular biology and back, yet still some unanswered questions. *Nephron.* 2002;92(Suppl 1):18-27.
9. Robson WL, Arbus GS, Balfe JW. Bartter's syndrome. *Am J Dis Child.* 1979;133:636-8.

Cite this article as: Rahul R, Sharma R. Gitelman's syndrome - incidentally detected in an elderly female. *Int J Res Med Sci* 2016;4:1257-9.