

An unusual cause for periodic limb paralysis; Gitelman syndrome

Jayasekara JMS, Palangasinghe DR, Bodinayake CK

Professorial Medical Unit, Teaching Hospital, Karapitiya, Galle, Sri Lanka.

Correspondence: Dr. Swarnamali Jayasekara
e-mail: swarnamali2005@gmail.com
<https://orcid.org/0000-0002-6378-2463>

Introduction

Gitelman syndrome (GS) is an autosomal recessively inherited salt losing tubulopathy with a prevalence of 1-10 per 40,000 people (1, 2). The prevalence of GS is higher in Asia than other countries (2). GS is characterized by hypokalaemic metabolic alkalosis, hypomagnesaemia and hypocalciuria (3). It is typically seen in late childhood or adulthood. Symptoms are related to the degree of electrolyte disturbance. Cramps of the limbs are present among almost all and fatigability, polyuria, polydipsia, chondrocalcinosis are the other reported symptoms (1, 4). Clinical manifestations are less pronounced in heterozygotes (1).

Here we report a case of GS presented with a hypokalaemic periodic quadripareisis.

Case report

A 15 year-old previously healthy school boy noticed bilateral upper limb and lower limb weakness when he got up in the morning. Two days prior he experienced similar kind of weakness which resolved spontaneously. Weakness was not ascending and he denied dysphagia or breathing difficulty. His urinary and bowel habits were normal and there was no history of trauma.

Examination revealed flaccid quadriplegia with muscle power Grade 3/5 in upper limbs and Grade 2/5 in lower limbs. Power of neck muscles was normal and cranial nerve examination was unremarkable. All the reflexes were diminished and plantar response was normal. There was no sensory impairment. He was neither dyspnoeic nor tachypnoeic. Single breath count was more than 20. His pulse rate was 100/ minute and blood pressure was 135/65 mmHg. Respiratory system and abdominal examinations were unremarkable.

Evaluation revealed serum K^+ 2.1 mmol/L (3.5 - 5.3), serum corrected calcium 2.59 mmol/L (2.1 - 2.57), serum magnesium 0.68 mmol/L (0.66 - 1.07), pH 7.42 with HCO_3^- 28 mmol/L, 24 hour urinary calcium excretion 0.2 mmol/day (2.0 - 7.5 mmol/day) urinary excretion of sodium 126 mmol/L, urinary potassium excretion 112 mmol/L and urinary chloride excretion 140 mmol/L, supine aldosterone 343.2 pg/mL (49.3 - 175) and supine renin 36.1 pg/mL (2.7 - 32.6). Parental screening revealed asymptomatic hypokalaemia. (mother - 3.4 mmol/L, father - 3.1 mmol/L)

Intravenous potassium chloride (KCl) was commenced to correct the serum potassium deficit followed by oral KCl one tablet twice daily and he showed a remarkable response. Later he was started on spironolactone and KCl was tailed off. He was asymptomatic on subsequent clinic visits and serum potassium remained normal.

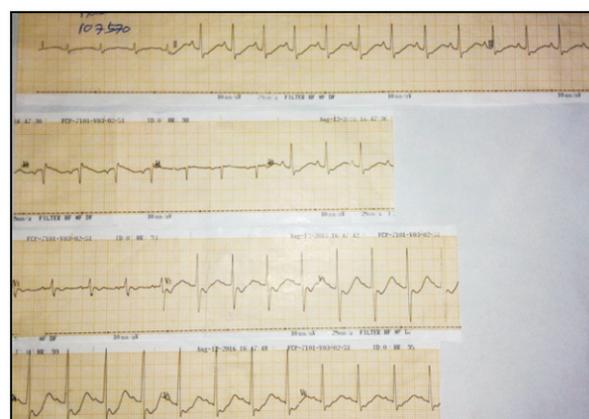


Figure 1: ECG on admission showing U waves and prolonged QT interval suggestive of hypokalaemia

Discussion

GS was first described in 1966, and its genetic basis was elucidated 30 years later. GS is unarguably the most frequent inherited tubulopathy and autosomal recessive in inheritance (5, 6). In the great majority GS is caused by mutations in the *SLC12A3* gene, which encodes the renal thiazide-sensitive sodium-chloride co-transporter (TS-NCC) that is specifically expressed in the apical membrane of cells in the distal convoluted tubule (DCT) (7).

Reduced NCC activity mimics the effects of persistent thiazide diuretic action, which include volume contraction, reduced or normal blood pressure, increased renin activity and aldosterone levels, renal potassium wasting and hypokalemia, renal magnesium wasting and hypomagnesaemia, and reduced urinary calcium excretion (1).

Impaired sodium chloride reabsorption leads to mild volume depletion and activation of the renin-angiotensin-aldosterone system (1). The combination of secondary hyperaldosteronism and increased distal flow and sodium delivery enhances potassium and hydrogen secretion at the connecting and collecting tubules leading to hypokalaemia and metabolic alkalosis (1). Hypocalciuria occurs due to loss of activity of TS-NCC which increases tubular reabsorption (3).

The diagnosis of GS is based on the clinical symptoms, biochemical abnormalities and largely one of exclusion with combination of characteristic set of metabolic abnormalities which includes hypokalaemia, hypomagnesaemia, metabolic alkalosis, secondary hyperaldosteronism, reduced urinary calcium excretion and increased urinary excretion of sodium and chloride (7,1). Other tests, such as genetic testing and measurement of the change in fractional excretion of chloride in response to loop and thiazide diuretics, are not widely performed (1).

Our patient exhibited clinical and almost all the laboratory criteria with the asymptomatic hypokalemia in both parents supporting autosomal recessive inheritance. Tubular defect of the GS cannot be corrected. Therefore treatment is life-long and is aimed at minimizing the effects of the secondary increases in renin and aldosterone production and at correcting the volume deficit and electrolyte abnormalities. Genetic counseling is utmost important as the recurrence risk for parents

with an affected child is 25% (7).

In general, the long-term prognosis is excellent and progression to renal insufficiency is extremely rare in GS (7).

Conclusions

Gitelman syndrome is one of the rare causes for hypokalaemia which is treatable and has excellent long term outcome. We achieved a good clinical and biochemical response with oral KCl followed by spironolactone.

References

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