## Case Report

# Quadriparesis in an Adult — Gitelman Syndrome

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## Abstract

A 24 years old soldier presented with sudden onset of weakness in all four limbs. There was no history of any antecedent respiratory infection, fever, diarrhoea or vomiting. Neurological examination of limbs revealed reduced tone and power in all limbs. Although the tendon reflexes were diminished they could be elicited in all limbs. Rest of the clinical examination was unremarkable. Serum potassium was 2.1 mmol/l, sodium 138 mmol/l, bicarbonate 35.3 mmol/l, urea 5.7 mmol/l, creatinine 69 umol/l and serum creatine kinase (CK) was 686 U/l. Power in the patient's limbs gradually improved to normal by following afternoon after potassium chloride infusion. Serum chloride was 93 mmol/l, bicarbonate 33.4 mmol/l, calcium 2.1 mmol/l, urine sodium 134 mmol/l, urine potassium 82 mmol/l, urine chloride 156 mmol/l and urine pH 6.0. Urinary calcium excretion was 2.2 mmol in 24 hours. Serum magnesium was 0.7 mmol/l. A diagnosis of Gitelman syndrome was made. He is doing well on spironolactone, potassium chloride supplementation and high sodium diet, maintaining serum potassium level between 3.5 and 4.5 mmol/l.

**Keywords:** Quadriparesis, hypokalaemia, Gitelman syndrome, hypomagnesaemia.

## Introduction

Gitelman syndrome (GS) is an autosomal recessive salt-losing renal tubulopathy that is characterized by hypokalaemia and metabolic alkalosis due to secondary hyperaldosteronism, hypomagnesaemia and hypocalciuria.[1] The prevalence is estimated at ~25 per million. In the great majority of cases GS is caused by mutations in the solute carrier family 12, member 3, SLC12A3 gene, which encodes the renal thiazide-sensitive sodium-chloride co-transporter in the apical membrane of cells, in the first part of the distal convoluted tubule.[2,3]

GS patients usually present above six years of age and in many cases the diagnosis is only made at adult age. Patients may present with muscle weakness, tiredness, fatigue, paraesthesias in the face and sometimes even with tetany. In general, growth is normal in GS patients, however, it can be delayed in patients with severe hypokalaemia and hypomagnesaemia.[3]

A case of severe hypokalaemia with alkalosis, hypocalciuria and low serum magnesium level presenting with severe generalized muscle paralysis is described.

## Case Report

A 24 years old soldier presented with a few hours history of sudden onset weakness in all four limbs. He had ridden a bike the previous day for 10 km and was alright till the night before. Following morning he felt weakness in the lower limbs and was unable to get up and walk. The weakness rapidly progressed in a couple of hours to involve upper limbs too, making him unable to move in the bed. He did not complain of difficulty in breathing or urinary retention. There was no history of any antecedent respiratory infection, fever, diarrhoea, vomiting or any drug intake. The patient had never experienced an episode of muscle weakness like this before. Though he gave history of tiredness, fatigue and muscle cramps off and on, he did not suffer from any other significant illness in the past. Neither his parents nor his siblings had ever experienced such symptoms.

On clinical examination, he was a young man of average built, lying supine in the bed, fully conscious and oriented, breathing normally with a respiratory rate of 16 per minute, pulse 80 beats per minute, regular in rhythm and blood pressure 110/70 mm Hg. He was well hydrated and was not even sick looking. Neurological examination revealed normal higher mental functions and normal cranial nerves. Examination of motor system in limbs revealed reduced tone and power in all limbs. Generally power was 3/5 in upper limb and 1/5 in lower limb muscles on both sides. Tendon reflexes were diminished but elicitable in all limbs. There was no sensory deficit. Rest of the systemic examination was unremarkable. The patient was regularly monitored for his respiratory status, mainly breathing rate and oxygen saturation with pulse oximeter. His respiratory rate remained within normal limits with oxygen saturation between 92 to 95 percent, without oxygen. His haemoglobin was 14.9 g/dl, Total Leukocyte Count (TLC) was $9.1x10^9$/l and platelet count $254x10^9$/l. Serum potassium was 2.1 mmol/l, sodium 138 mmol/l, bicarbonate 35.3 mmol/l, urea 5.7 mmol/l and creatinine 69 umol/l. Serum creatine kinase (CK) was 686 U/l (Reference range: upto 192 u/l). Electrocardiograph revealed decreased amplitude of T waves and prominent U waves especially in chest leads. Random plasma glucose was 109mg/dl, serum bilirubin 11 umol/l, ALT 88 U/l, alkaline phosphatase 135 U/l and albumin 50 g/dl. Power in the patient's limbs gradually improved to normal by the following afternoon after potassium chloride infusion. Subsequent electrocardiograph revealed normal amplitude of T waves and regression of U waves. Patient was kept on oral potassium supplements for the next few days, his serum potassium rose to 4.2 mmol/l and he remained completely asymptomatic. His potassium supplements were withheld to investigate the cause of hypokalaemia. Serum potassium fell to 3.2 mmol/l, sodium was 137 mmol/l, chloride 93 mmol/l, bicarbonate 33.4 mmol/l, calcium 2.1 mmol/l, spot urine sodium was 134 mmol/l, urine potassium 82 mmol/l, urine chloride 156 mmol/l and urine pH 6.0. Serum osmolality was 281 mmol/kg and urine osmolality was 762 mmol/kg. Urinary calcium excretion was 2.2 mmol in 24 hours. Serum magnesium was 0.7 mmol/l. Considering hypokalaemia and alkalosis with high urinary potassium excretion, low urinary calcium excretion and low serum magnesium level, a diagnosis of Gitelman syndrome was made and patient was put on spironolactone, 100 mg daily along with high sodium and potassium diet. He is doing well on spironolactone, potassium chloride supplementation and high sodium diet, maintaining serum potassium level between 3.5 and 4.5 mmol/l. The patient remained normotensive throughout and was not suspected to be suffering from primary aldosteronism. Magnesium replacement could not be considered due to lack of symptoms of hypomagnesaemia and absence of chondrocalcinosis.

## Discussion

The diagnosis of Gitelman syndrome is based on clinical symptoms and biochemical abnormalities. The most typical biochemical abnormalities in GS are hypokalaemia, metabolic alkalosis, hypomagnesaemia and hypocalciuria. Serum potassium concentration is comparably low ($2.7 \pm 0.4$ mmol/L) to Bartter syndrome. Serum magnesium concentration is low (less than 0.65 mmol/l). The patient had a serum magnesium level of 7 mmol/l, and never showed features of tetany. In a few GS patients magnesium

concentration is easily maintained in the normal range early on, which may lead to a false diagnosis of Bartter syndrome, and drops below normal only with time.[4] Urinary calcium concentration is usually less than 0.2 mmol/mmol creatinine and rarely exceeds 0.5 mg/kg/day. Hypomagnesaemia and hypocalciuria have always been considered obligate features for GS. This assumption has recently been disputed by Lin et al.[5] They reported two families with molecularly proven GS, in which male patients had severe hypokalaemia, and were symptomatic with episodes of paralysis, impaired urinary concentration ability, but with normal serum magnesium and urinary calcium excretion. Remarkably, female GS patients within these families, carrying the same causative mutations as the male patients, were asymptomatic, had less severe hypokalaemia, intact urine concentration ability, but did have hypomagnesaemia and hypocalciuria.[5] Although this was a small study, the authors concluded that gender may affect phenotypic expression in GS and that hypomagnesaemia and hypocalciuria may not be invariant features of the disorder.

Prostaglandin excretion is normal and plasma renin activity and plasma aldosterone concentration are only slightly elevated compared to Bartter syndrome. The patient remained normotensive throughout and was not suspected to be suffering from primary aldosteronism so serum aldosterone levels and plasma renin activity were not measured.

Most asymptomatic patients with GS remain untreated and undergo ambulatory monitoring (generally by nephrologists) with low frequency (1-2 times per year). At each visit complaints related to hypokalaemia (fatigue, muscle weakness, constipation, cardiac arrhythmias) and hypomagnesaemia (tetany, cramps, paraesthesias, joint and muscle pain) as well as serum levels of K+, bicarbonate and Mg2+ should be evaluated.[4]

Symptomatic hypokalaemia should be treated with potassium sparing diuretics like amiloride and aldactone, starting with a low dose to avoid hypotension. All patients should be encouraged to maintain a high sodium and high potassium diet. Patients showing symptoms of hypomagnesaemia or chondrocalcinosis should receive lifelong supplementation with magnesium preparations.[6] The patient has been doing well on spironolactone and high sodium and potassium diet. Magnesium replacement has not been considered due to lack of symptoms of hypomagnesaemia and absence of chondrocalcinosis.

Growth and puberty delay in some patients with severe GS can be corrected by adequate Mg2+ and K+ supplementation and a growth-promoting effect of indomethacin was also reported in GS patients.[7] Cardiac work-up is recommended to screen for risk factors of cardiac arrhythmias.[8,9]

In general, the long-term prognosis of Gitelman syndrome is excellent. However, the severity of fatigue may seriously hamper some patients in their daily activities. Progression to renal insufficiency is extremely rare in GS.[4]

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