

# Severe Hyponatremia and Hypocalcemia in Gitelman Syndrome: A Case Report

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## Abstract

Gitelman syndrome (GS) is a recessive salt-losing tubulopathy due to a mutation of genes encoding the sodium chloride cotransporters and magnesium channels in the thiazide-sensitive segments of the distal convoluted tubule. In this paper we describe a 69-year-old lady with GS who presented with severe hyponatremia and hypocalcemia which are very rare complications associated with this syndrome. We are discussing the mechanisms involved in the development of these rare manifestations in this case report.

**Keywords:** Gitelman syndrome; Hyponatremia; Hypocalcemia

## Introduction

Gitelman syndrome (GS) is caused by inactivating mutations in the gene for the sodium chloride channel (thiazide-sensitive NCC) of the distal convoluted tubule, called SLC12A3 [1]. Usual age of presentation is late childhood or early adolescence. GS is characterized by hypokalemia, hypomagnesemia, metabolic alkalosis and low urinary calcium excretion [2]. They also have normal serum sodium and calcium, hyperuricemia and inappropriately high urinary potassium, magnesium and chloride usually [3]. In this paper we present a case of GS with severe hyponatremia and hypocalcemia which was hardly described in the literature.

## Case Report

A 69-year-old lady was presented with fatigue for 1 week.

She did not give any history of diabetes mellitus or hypertension and was not on any drugs. On examination she was pale and the blood pressure was 130/80 mm Hg. She appeared adequately hydrated on clinical examination and examination of respiratory, cardiovascular, neurological systems and abdomen were unremarkable. Investigations showed hemoglobin 10.9 g/dL (microcytic hypochromic), total WBC count 9,600/ $\mu$ L, platelet count  $2.4 \times 10^9$ /L, ESR 65 mm in 1 h. Urinalysis showed 2 - 4 leucocytes/high power field. There was no albuminuria or visible RBC in the urine. Chest X-ray was normal and electrocardiogram showed U waves and flattened T waves. Her biochemical parameters revealed RBS 127 mg%, urea 27 mg/dL, creatinine 1.1 mg/dL and uric acid 2.0 mg%. Tests on liver function, thyroid function and serum cortisol showed normal results. The serum and urinary electrolytes, arterial blood gas analyses are shown in Table 1. Urine culture was sterile and ultrasonography of abdomen was normal. The trans-tubular potassium gradient was seven. Since the patient had hypokalemia with high trans-tubular potassium gradient, metabolic alkalosis, normal blood pressure, hypomagnesemia, high urinary chloride and hypocalciuria, a diagnosis of GS was made. In addition to the usual electrolyte abnormalities she also had severe hyponatremia, hypocalcemia and hypouricemia.

She was treated with parenteral potassium, calcium and magnesium initially along with spironolactone. The sodium level improved with fluid restriction and hypertonic saline, and electrolytes showed improvement after 7 days. She was discharged with advice to continue oral potassium, calcium and magnesium supplements.

## Discussion

Evaluating a patient with dyselectrolytemia is an interesting academic exercise for the physician especially if some unusual complications are encountered. The combination of hypokalemic metabolic alkalosis with hypomagnesemia and hypocalcemia are the characteristic electrolyte abnormalities described with GS. Serum sodium and calcium are usually normal in patients with GS. In this paper we describe a patient who had the classical features of GS with severe hypo-

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**Table 1.** Serum and Urinary Electrolytes, Arterial Blood Gas Analysis

	Patient value	Normal range
Serum (mmol/L)		
Sodium	110	135 - 145
Potassium	1.8	3.5 - 5.0
Bicarbonate	32	22 - 26
Calcium	1.475	2.2 - 2.67
Phosphorus	1.35	0.8 - 1.5
Magnesium	0.29	0.7 - 1.1
Measured serum osmolality (mOsm/kg)	235	285 - 295
Urine osmolality (mOsm/kg)	234	80 - 1,350
24 h urine analysis		
Sodium (mmol/24 h)	210	Variable
Potassium (mmol/24 h)	36	Variable
Urinary chloride (mmol/L)	87	Variable
Urinary calcium creatinine ratio	0.079	Variable
Arterial blood gas analysis		
pH	7.59	7.35 - 7.45
PCO <sub>2</sub> (mm Hg)	31	35 - 45
PO <sub>2</sub> (mm Hg)	64	80 - 105
HCO <sub>3</sub> (mEq/L)	30	22 - 26

natremia and hypocalcemia.

Hyponatremia was described with GS for the first time by Schepkens et al in 2001 in two patients [3]. The phenotype of GS is identical to that with the chronic use of thiazide diuretics [1]. Thiazide induced hyponatremia has features similar to that of SIADH [4]. Thiazides are “Saluretic”, whereas frusemide causes water diuresis, “aquaretics”. Various mechanisms have been attributed to thiazide induced hyponatremia. Thiazide induced hyponatremia occurs when the intake of free water is greater than the amount the kidneys can excrete. In subjects with a moderate impairment of free-water excretion, a thiazide will cause hyponatremia if fluid intake is excessive. Hyponatremia can even appear in those with more serious impairment of free-water excretion with ordinary fluid intake [5]. In patients with GS a similar mechanism may result in hyponatremia which resembles SIADH. Thus GS patients are prone to developing hyponatremia in a manner similar to that seen with thiazide diuretics. But hyponatremia is unusual in GS patients since they achieve a balance between water intake and free-water excretion under

normal circumstances. Our patient under study had a normal volume status clinically, hypoosmolar hyponatremia, hypouricemia with an inappropriately high urinary osmolality and sodium, all consistent with SIADH. So the probable cause for hyponatremia in our patient is likely to be as discussed above.

Patients with GS have significant hypomagnesemia. Chronic hypomagnesemia is closely associated with hypocalcemia, which is caused by impaired parathyroid hormone (PTH) secretion or the refractoriness of bone and renal tubules to PTH [6]. In general, PTH-induced release of calcium from bone is substantially impaired when the plasma magnesium concentration falls below 0.8 mEq/L (1 mg/dL or 0.4 mmol/L). In comparison, it appears that more severe hypomagnesemia [7] occurs only when there is diminished PTH secretion.

Pantanetti et al [8] and Nakamura et al [9] describe two patients with GS in whom hypocalcemia developed due to hypomagnesemia. The combination of two rare complications, namely hyponatremia and hypocalcemia, in our case

makes this a unique case of GS and throws open scope for more study and research.

### Sources of Support

None.

### Conflicts of Interest

None.

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