Case Report: A 21-Year-Old Woman with Suspecting Gitelman Syndrome

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ABSTRACT

Introduction: Gitelman syndrome (GS) is a hereditary condition marked by a specific kidney function impairment. GS symptoms do not normally manifest until beyond the age of six years. We present a rare case of a 21-year-old woman with a background in generalized weakness, muscle cramps with tetany, fever, and dyspnea. The goal of this study is to give a case report of Gitelman syndrome suspicion.

Result: Gitelman syndrome is identified through clinical indicators and lab testing, such as low potassium and magnesium levels in the blood, metabolic alkalosis, and low calcium levels in the urine. We do a variety of physical and laboratory tests to determine the disease and rule out other possibilities. The molecular proof is difficult to get due to a lack of resources and the high expense of genetic testing, which has become one of our case report's flaws. This patient was diagnosed as suspecting Gitelman syndrome and treated for electrolyte imbalances. The patients were given replacement therapy, which comprised intravenous potassium, sodium, and chloride therapy, as well as calcium therapy. In addition, we also provided some symptomatic therapy. She was discharged five days later in fine condition. The vital signs were stable, the complaints had disappeared, the patient was well rested and eating well, and she might also move quickly.

Conclusion: This is one of the few reports of a 21-year-old lady being suspected of having Gitelman syndrome (GS). We conduct a battery of physical and laboratory tests to diagnose the disease and rule out other possibilities. We provide the appropriate therapies following the guidelines, and the outcomes are favorable.

Keywords: Gitelman syndrome; hereditary tubulopathy; hypokalemia; metabolic alkalosis; hypocalciuria.

INTRODUCTION

Gitelman syndrome is a sodium tubulopathy characterized by low potassium and magnesium levels in the blood, metabolic alkalosis, and low calcium levels in the urine. With an incidence of 1 to 10 per 40,000 people, occurs in both males and females, maybe greater in Asia, the most common hereditary tubulopathy is probably Gitelman syndrome (GS).

This is caused to a SLC12A3 genetic alteration, which produces the thiazide-sensitive sodium chloride co-transporter on chromosome 16q13 (NCC, NCCT, or TSC)³⁴. GS symptoms do not normally manifest until beyond the age of six years, and it is generally discovered in adults.³ Recently, upwards of
350 SLC12A3 mutations have already been identified in GS patients\textsuperscript{5,6}.

GS has long been considered a harmless tubulopathy, usually discovered throughout adolescence or maturity. Furthermore, the illness may be subclinical or associated with minor or vague manifestations, such as difficulty walking, fatigue, salt appetite, thirst, excessive urination, or cramps. However, accounts emphasizing the disease’s clinical heterogeneity and potential consequences have challenged this position\textsuperscript{7}.

In many situations, signs of Gitelman syndrome do not present until the age of six years. In general, symptoms include intermittent muscle weakening associated with tetany, which is occasionally associated with gastrointestinal problems, vomiting, and fever\textsuperscript{3,8}.

Gitelman syndrome is identified through clinical indicators and laboratory tests, such as low potassium and magnesium levels in the blood, metabolic alkalosis, and low calcium levels in the urine\textsuperscript{3,9}.

We describe what happened to a 21-year-old lady with a history of generalized weakness muscle cramps with tetany, fever, and dyspnea. The goal of this study is to give a case report of Gitelman syndrome suspicion.

**CASE PRESENTATION**

A 21-year-old woman was brought by her family to the Sebelas Maret University Hospital's Emergency Department with the major complaint of general weakness for 10 days. Before being taken to the hospital, the main symptom had been increasing worse for the previous four days. She was unable to carry out her everyday responsibilities as a homemaker. Her legs were too weak to stand up. Furthermore, her muscles cramped and she experienced tetany or paralysis. She also experienced paresthesias in her extremities at times.

The patient had a fever for the previous 5 days before admission. She became nauseous and vomited. Vomiting only happened once, with a volume of 50-100 cc of colored liquid, and the final part was consumed, with no blood or greenish liquid. She also reported having dizziness, heart palpitations, and dyspnea.

She admitted to urinating adequately 5-7 times per day and urinating approximately 100-200cc each time. She did not have diarrhea. She had never used laxatives or diuretics, nor had she ever abused alcohol or illegal substances. She didn't even smoke. She is a woman who has been married for two years but does not have any children. The patient was not pregnant at the time of the examination.

She had previously visited emergency departments at other hospitals numerous times and received potassium medication for hypokalemia about 5-6 months earlier.

She was found to be sub febrile at 37.7 degrees Celsius, with a blood pressure of 90/60 mmHg, a MAP of 70 mmHg, a heart rate of 106 bpm, and a breathing rate of 22 per minute, and pulse oximetry of 97 percent with room air.

**INVESTIGATIONS**

Physical examination demonstrated a reduction in physiological responses as well as motor strength loss in all extremities. A full blood test showed a leukocyte count of 21.19 x 10\textsuperscript{3}/L, hemoglobin of 12.4 gram/dl, hematocrit of 35%, and platelets of 430 x 10\textsuperscript{3}/L. Lymphocytes, monocytes, eosinophils, and basophils were all within acceptable limits. Neutrophils have an above-average value of 88.3 percent. SGOT was 45 U/L, SGPT was 14 U/L, creatinine and urea were 0.92 and 29 mg/dl, respectively, on blood chemistry tests. GFR was calculated to be 91 mL/min/1.73m\textsuperscript{2}.

Initial tests revealed severe
Hypokalemia (0.99 mmol/L), severe hyponatremia (124.72 mmol/L), hypochloremia (69.74 mmol/L), and hypocalcemia (0.62 mmol/L). The blood magnesium level reported normal (2.0 mg/dl).

On an ad libitum basis, the 24-hour urinary sodium excretion was 234.46 (normal range: 40-220 mmol/24 hours), potassium was 45.21 (normal range: 25-125 mmol/24 hours), chloride was 51.89 (normal range: 110-250 mmol/24 hours), and calcium was 88.1 (normal range: 100-320 mg/24 hours). During hospitalization, urine output was adequate (+ 0.9 cc/kg WB/hour).

The ABG results indicate a pH of 7.590, PCO2 of 37.0 mm Hg, and HCO3 of 35.5 mmol/L. It demonstrated uncompensated metabolic alkalosis.

She had normal plasma glucose and urinalysis results. The chest X-ray revealed that cor and pulmo were both normal (Figure 1). An ECG confirmed sinus tachycardia and anteroseptal ischemia, as well as a heart rate of 106 bpm.

We performed echocardiography, which revealed that the heart dimensions were normal. Excellent LV and RV function. Systolic and diastolic function is normal. The heart valves were in good working order (Figure 3). We discovered normal results on abdominal ultrasonography. A widal test indicated positive results for salmonella typhi O 1/320, salmonella typhi H 1/160, and salmonella paratyphi BO 1/160.

| Electrolytes          | 29Dec 2021 | 30  | 31             | 1 Jan 2022 | 3 Jan 2022 | mmol/L |
|-----------------------|-----------|-----|----------------|------------|------------|--------|
| Sodium                | 124.72    | 137.49 | 140.04        | 144.54     | 145.88     |        |
| Potassium             | 0.99      | 1.46 | 1.68          | 2.36       | 3.56       |        |
| Chloride              | 69.74     | 90.66 | 96.28         | 97.56      | 100.56     |        |
| Calcium               | 0.62      | 0.74 | 1.09          | 1.11       | 1.20       |        |
| Magnesium             | -         | 2.0  | -             | -          | -          | mg/dl  |
This patient was treated for electrolyte abnormalities as well as an illness with typhoid fever. Replacement therapy, which included intravenous potassium, sodium, and chloride therapy, as well as calcium therapy, was administered to the patients. We administered antibiotics in the form of a ceftiraxone injection of 2 grams every 24 hours, antipyretic infusion, and a proton pump inhibitor. We also gave oxygen administration therapy as needed.

The patient's symptoms, including general weakness, improved after three days of treatment. The fever, muscle cramps, episode of muscle tetany, or muscle paralysis subsided after four days of medicine. She never experienced palpitation or dyspnea again. She might be able to get enough rest and eat well. She might also move quickly. She was finally discharged five days later in good overall health.

DISCUSSION

Gitelman et al. were the first to report it in three adult patients with hypokalemia, hypomagnesemia, and hypocalciuria accompanied by periodic muscle weakness and tetany. The genetic renal tubule disease Gitelman syndrome is now well-known. Mutations in the gene coding for the thiazide-sensitive Na-Cl transporter in the distal tubule generate the major disease in this condition.6,10

GS is most common in teenagers and adults, however it can also affect children as early as the neonatal era11,12. The following are the main clinical complaints and signs that point to a diagnosis of GS table 21,13.

In this case report, we discovered that the patient experienced general weakness, muscle weakness, cramps, dizziness, paresthesias, palpitations, low blood pressure, muscle tetany, nausea, and vomiting. Consistent with signs and symptoms in most Gitelman syndrome patients (>50%)13.

We discovered persistent hypokalemia, metabolic alkalosis, and hypocalciuria in our patient using diagnostic criteria for suspected Gitelman syndrome. The magnesium level in the blood was normal (2.0 mg/dl). However, Gitelman syndrome, or GS, can manifest with mean serum magnesium levels, which has been described in roughly 20–40% of GS cases in one study14.

In this patient, the 24-hour urinary potassium excretion was 45.21, if urine potassium is greater than 30 mEq/24 hours, or 15 mEq/L or TTKG is greater than 7, potassium is lost through the kidneys15. This patient also had hypocalsiuria, with calcium urine levels of 88.1 mg/24 hours (normal range: 100-320 mg/24 hours).

| Table 2. Clinical Signs and Symptoms Seen in Gitelman Syndrome Patients1,13 |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| Most common (> 50% of patients) | Prominent (20%-50% of patients) | Occasional (<20%) | Rare (case report) |
| Salt craving | Joint pain | Early manifestation (before age 6) | Convulsion |
| Dizziness | Polyuria | Inability to thrive | Ventricular tachycardia (VT) |
| Muscle weakness | Lightheadedness | Growth retardation | Rhabdomyolysis |
| Tiredness | Chondrocalcinosis | Pubertal delay | A lack of sharpness of vision |
| Cramps | Prolonged QT interval | Loss of balance | Pseudotumor cerebri |
| Nocturia | Febrile Episodes | Ataxia | Sclerochoroidal calcifications |
Table 3. Gitelman Syndrome Diagnostic Criteria

| Feature                                      | Criteria                                                                 |
|----------------------------------------------|--------------------------------------------------------------------------|
| Chronic hypokalemia (3.5 mmol/l)             | in the presence of renal potassium squandering (potassium-creatinine ratio >2.0 mmol/mmol) |
| Alkalosis metabolic                          |                                                                          |
| Hypomagnesemia (0.7 mmol/l [1.70 mg/dl])     | combined with improper renal magnesium wasting (fractional magnesium excretion >4%) |
| Adults with hypocalciuria                    | (spot calcium-creatinine ratio less than 0.2 mmol/mmol [0.07 mg/mg])       |
| Renin activity or levels in the blood        |                                                                          |
| Chloride excretion fraction > 0.5 percent    |                                                                          |
| Blood pressure is low or normal-low.         |                                                                          |
| Renal ultrasonography is normal.             |                                                                          |

Characteristics that rule out a GS diagnosis

- Use of laxatives or thiazide diuretics
- Kidney disease runs in the family and is passed down in an autosomal dominant form.
- Hypokalemia is not present (unless renal insufficiency is present); hypokalemia is inconsistent in the absence of substitutive medication.
- There is no metabolic alkalosis.
- Renin concentrations are weak.
- Hypercalciuria; decreased urinary potassium production (potassium-creatinine ratio of 2.0 mmol/mmol).
- Increased extracellular fluid volume manifests as hypertension.
- Unilateral kidneys, nephrolithiasis, nephrocalcinosis, and cystic kidneys are revealed by ultrasound of the kidneys.
- Polyhydramniosis and hyperechogenic kidneys in the womb.
- Before the age of three years.

Criteria for determining a GS diagnosis

- Biallelic inactivating mutations in SLC12A3 have been discovered.

Table 4. Characteristics that distinguish the Bartter and Gitelman syndromes

| Feature                        | Classic Bartter syndrome | Gitelman syndrome |
|--------------------------------|--------------------------|-------------------|
| Onset age                      | childhood                | childhood or later|
| Hidramniosis materna           | rare                     | absent            |
| Symptoms of polyuria and polydipsia | present               | rare              |
| Dehydration                    | frequently occurs        | absent            |
| Tetany                         | rare                     | present           |
| Retard growth                  | present                  | absent            |
| Calcium in urine               | normal or excessive      | weak              |
| Serum magnesium                | weak on occasion         | weak              |
| Urine prostaglandins (PGE2)    | Excessive or normal      | normal            |
Clinical signs and biochemical abnormalities are used to make the diagnosis. The first and most important aberration to seek in the differential diagnosis of Gitelman syndrome is Bartter syndrome (BS), especially type III.

Table 4 provides detailed manifestations of Bartter syndrome (BS) and Gitelman syndrome (GS). Patients with BS type III (classical BS) can appear with excessive urination and excessive thirst at any age until adulthood, followed by developmental delays if diagnosis and therapy are postponed. Hypercalciuria and excessive urine prostaglandin E2 (PGE2) synthesis are frequent in patients18,19. Due to phenotypic differences, determining between BS and GS is not always easy. Although genetic diagnosis is possible, its application is limited by expensive cost and limited access18.

Gitelman syndrome patients who are asymptomatic frequently do not require therapy, although they do require inpatient monitoring once or twice annually. A diet heavy in salt and potassium is advised.

Electrolyte correction, analgesics, and potassium-sparing diuretics, either alone or in combination with ACE In/ARB except for a few cases, the results and prognosis were excellent, and patients recovered entirely from their first clinical manifestations. Hypokalemia may also need high potassium chloride dosages, 500 mmol/day in adult, yet low stomach tolerance is frequent. If symptoms are present, hypokalemia is applied in the treatment of amiloride (5–10 mg /1.73 m2 per day) and spironolactone (200-300 mg/d) as well as KCl administration (13 mmol/kg per day divided into 3–4 doses). To avoid developing hypotension, amiloride medication should be begun at a lower dose at first18,20.

When a patient appears unwilling to consider taking medicines or when a substantial potassium shortage is producing cardiac arrhythmias, quadriplegia, breathing difficulties, or rhabdomyolysis, intravenous potassium chloride (KCl) may be required.

Dilute KCl in saline to 40 mmol/L. Because greater potassium concentrations are exceedingly irritating, resulting in discomfort and vein sclerosis, a maximum of 50 mmol/L should be delivered into a peripheral vein at a rate of 10 mmol/hour. Central venous lines typically have a peak of 80 mmol/L and a pace of 20 mmol/hour (depending on hypokalemia, ECG monitoring). If the patient's blood sugar level climbs beyond 10 mmol/hour, he or she should be monitored in a greater environment or location21.

Replacement therapy for electrolyte imbalances was delivered to our patient, which comprised intravenous potassium, sodium, and chloride therapy, as well as calcium therapy. In our case report, spironolactone and KCL are also given as oral supplements.

This case report has several flaws. The molecular proof is impossible to get due to a lack of resources and the high expense of genetic testing. The suspicion of Gitelman syndrome pathology in this patient provides a strong clinical diagnosis based on a history of recurrent electrolyte disorders, clinical symptoms, laboratory evidence, and drug response.

Genetic counseling is required since Gitelman syndrome is autosomal recessive. Gitelman syndrome adults have a minimal chance of having Gitelman syndrome children (1 in 400). Because most patients have a fair prognosis, antenatal diagnosis for Gitelman syndrome is not suggested22.

The prognosis for the long term is typically good. Problems such as nocturia and polydipsia, as well as musculoskeletal and constitutional symptoms, can make everyday tasks difficult and have a detrimental impact on patient's quality of life. There is indeed a chance of developing abrupt cardiac arrhythmias in the context of serious hypokalemia, hypomagnesemia, and alkalosis, which can be deadly. Noncompliance with
medication, the occurrence of simultaneous diarrhea or vomiting, or competitive activities that cause potassium and magnesium loss through perspiration are all factors that might trigger these episodes.

CONCLUSION

Gitelman syndrome (GS), is a hereditary condition marked by a specific kidney function impairment. Gitelman syndrome is diagnosed using clinical signs and lab results. Asymptomatic Gitelman syndrome patients often do not require treatment. Analgesics, potassium-sparing diuretics, and electrolyte replenishment with and without ACE In/ARB in nearly every case were the standard therapy.

This case report describes a rare case of suspected Gitelman syndrome. This patient was diagnosed with suspected Gitelman syndrome from the signs and symptoms felt by the patient history of generalized weakness, muscle cramps with tetany, fever, and dyspnea. We do various physical and laboratory tests to determine the disease and eliminate other possibilities. The patient was treated for electrolyte imbalance. The patients were given replacement therapy, which consisted of intravenous potassium, sodium, and chloride therapy and calcium therapy.

In addition, we also provide some symptomatic treatment. Finally, she was discharged five days later in good condition. The vital signs were stable, the complaints had disappeared, the patient was well rested and eating well, and she might also move quickly.

In the long term, the prognosis of Gitelman syndrome is usually favorable. We must be aware of the problems that might develop in a state of hypokalemia, hypomagnesemia, and substantial alkalosis as doctors, particularly abrupt cardiac arrhythmias, which can be fatal. Recognizing the signs and symptoms of Gitelman syndrome, doing a thorough physical examination, conducting targeted investigations to establish a diagnosis, and prescribing appropriate therapy are all critical for positive patient outcomes.

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