

Case report**A successful pregnancy for a young hypothyroid woman with Gitelman Syndrome: A rare case study report****Zahra Kashi¹, Adele Bahar², Marjan Mouodi³, Ozra Akha^{3*}**¹Sexual And Reproductive Health Research Center, Mazandaran University Of Medical Sciences, Sari, Iran And Diabetes Research Center, Mazandaran University Of Medical Sciences, Sari, Iran²Diabetes Research Center, Mazandaran University of Medical Sciences, Sari, Iran ^{3,*}Tehran University of Medical Sciences, Tehran, Iran

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Abstract

It is widely assumed that Gitelman syndrome is a rare genetic disorder with such electrolyte imbalance as hypokalemia and hypomagnesaemia. The impact of hypothyroidism on Gitelman syndrome and its management is not clear. In this case study, a hypothyroid young woman referred to our endocrine clinic for muscle cramp after the hypothyroidism management. Based on Laboratory and clinical findings, the woman was diagnosed to have been suffering from Gitelman syndrome and the treatment with magnesium, potassium and oral Spironolactone began immediately. After two years of treatment, the woman experienced a successful planned pregnancy.

Keywords: Gitelman syndrome, Hypothyroidism, Pregnancy**Introduction**

It is generally assumed that Gitelman syndrome is a rare genetic disorder with autosomal-recessive manner, characterized by low blood pressure, metabolic alkalosis and hypokalemia, which could supposedly be due to the impairment of an important sodium chloride transporter in distal tubule (1, 2). It is also claimed that hypomagnesaemia and hypocalciuria are other manifestations of this disorder (3). It is estimated that the prevalence of Gitelman syndrome is 25 per million. The prevalence of heterozygotes type is approximately 1% in Caucasian (1, 4). It is believed that due to the severe electrolyte disturbance, especially hypokalemia, the tubular defects in sodium-chloride transport are similar to those of the long-term use of chronic thiazide intake (5). It is highly recommended that Gitelman syndrome be taken into account in differential diagnosis of persistent hypokalemia (6). It is also estimated that the salt excretion that occurs in this inherited tubulopathy can lead to clinical symptoms observed in this syndrome. The disruption of sodium absorption can also lead to

decreased volume and the activation of the renin-angiotensin system.

It is speculated that the secondary hyperaldosteronism and increased sodium delivery can increase potassium and hydrogen secretion in tubules (7). The pregnancy in these patients is, as a result, disquieting for both physicians and patients. The Gitelman syndrome was reported to be associated with thyrotoxicosis and thyroiditis, but not with hypothyroidism (8-10). In this report, we will introduce a young hypothyroid woman with Gitelman syndrome, who experienced a successful maternal and fetal outcome after the diagnosis and treatment.

Case report

A 25-year-old woman was referred to our endocrine clinic for the follow-up and control of hypothyroidism. She reported she had been suffering from the limbs cramp for three months, which was more severe at the night. She was receiving 900 mcg levothyroxine per week and was euthyroid. The basal (before receiving levothyroxine) Thyroid Stimulating Hormone (TSH) and thyroxine (T4) were 19 IU/L and

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83 mic/dl, respectively. Anti-thyroid peroxidase antibody was positive. On physical examination, the blood pressure was 90/60 mm/Hg, the weight was 60 kg, the heart rate was 82 per minute, and the respiratory rate was 18 per minute. Laboratory examinations showed the serum calcium of 9.0mg/dl , the phosphate of 3.3 mg/dl, the creatine phosphokinase (CPK) of 106 , the Lactate dehydrogenase (LDH) of 416, the potassium of 2.8meq/l (low), the magnesium of 1.50 mg/dl(low), the renin of 135mic/ml (high), and the aldosterone of 54ng/dl (high).

The woman was not taking diuretics. Urine electrolytes 24h calcium and potassium were low and high, respectively. The arterial blood gas showed the metabolic alkalosis (Table 1). It should be noted that the electrocardiogram and renal sonography were normal.

It is worth mentioning that the Gitelman syndrome diagnosis was established based on renal wasting hypokalemia, which is associated with hypomagnesemia, hypocalciuria, hyperreninemic hyperaldosteronism, and metabolic alkalosis. Oral potassium, magnesium supplement and spironolactone 100 mg per day were subsequently prescribed and began to be used on daily basis. It should be mentioned that the use of levothyroxine tablet was also continued. After one week, the plasma potassium was 4meq/l, and the patient reported less limb cramps. After two years of treatment, while the patient was euthyroid (TSH=2 mic/dl), the spironolactone tablet was discontinued due to a pregnancy plan. One month prior to the conception and in the first month of pregnancy, the patient received oral levothyroxine 1400 mic/week and a high dose of potassium and magnesium. The serum potassium range was 2.6 to 3 meq /l.

Having identified the gender of the fetus and been confirmed that the fetus was a female, spironolactone tablet was prescribed and started to be used at a dose of 12.5 mg daily and increased to 50 mg/d with the serum potassium range of 3.1 to 3.4. The other serum electrolytes were acceptable during the pregnancy. The patient experienced an uncomplicated pregnancy and delivered a healthy baby weighing 3700 grams. After birth, the spironolactone dosage increased to 100 mg/d. After four years, the patient's baby is fully healthy, but the patient need more spironolactone dosage (> 200mg/day) to maintain the serum potassium level above 3 meq /l .

Table 1. Lab test results for a young hypothyroid woman with Gitelman Syndrome

Parameter	Patient lab	Normal range
Thyroid stimulating hormone (TSH) (IU/l)	3.9	0.5-5
Serum potassium (meq/l)	2.5	3.5-5
Serum magnesium (mg/dl)	1.50	1.7-2.3
Serum calcium (mg/dl)	9.1	8.5-10.2
Serum phosphorus(mg/dl)	3.7	2.5-5
Serum sodium (NA) (meq/l)	142	135-150
Serum chlorine (CL) (meq/l)	92	98-106
Serum albumin (mg/dl)	4.5	4-5
Serum 25 OH vitamin D ₃ (ng/ml)	53	30-70
Renin(upright) (mic/ml)	135	4.4-46.1
Aldosterone(upright)(ng/dl)	54	4-31
PH (acidity)	7.50	7.35-7.45
Bicarbonate (hco ₃ ⁻)(meq)	29.1	22-26
Partial pressure of carbon dioxide (Pco ₂) (mmHg)	37.2	35-45
Creatinine (mg/dl)	0.9	0.5-1.2
Urine specific gravity	1020	1003-30
24-hour urine potassium (meq/d)	65	25-100
24-hour urine chlorine (mmol/l)	133	140-250
24-hour urine calcium (mg/d)	28	100-300

Discussion

The Gitelman syndrome was named after Hillel J. Gitelman who discovered it in 1966 (11). Unlike many patients with Barter syndrome who are symptomatic at birth, the patients with Gitelman syndrome are not usually recognizable until the end of childhood or adulthood(12). Most adult patients with Gitelman syndrome are symptomatic and experience severe clinical manifestations (13). It is estimated that clinical symptoms are less severe in the heterozygote type. It is also believed that muscle cramp is reported by almost all patients and could be severe. This can be attributed to a decrease in plasma potassium and magnesium levels. It is further speculated that the cause of magnesium reduction could be due to the increase in

renal excretion as well as decreases in digestive absorption. About 10% of patients were diagnosed with tetanus at first. It is claimed that severe renal salt loss could lead to hypotension and fatigue. It is worth noting that polyuria and nocturia were reported in 50 to 80 percent of cases, respectively, which could be due to salt and water excretion (14). In addition, chronic hypokalemia is supposed to be one of the causes of diabetes insipidus. It is also conjectured that severe and chronic hypomagnesemia could be associated with chondrocalcinosis. In the same vein, the Gitelman syndrome was reported to be associated with thyrotoxicosis and hypokalemic periodic paralysis (8-10). It is vividly unclear whether or not the hypothyroidism could mask the symptoms of the Gitelman syndrome.

The patient in our report reported limbs camp when the thyroid function test was normal. Panhypopituitarism, according to the result of a research study, was reported to be associated with Gitelman syndrome in a 57-year-old case (15). This case was known as primary hypothyroidism (low T4, and TSH 9.06 μ U/l) at first and received the levothyroxine tablet. It should be noted that after the confirmation of panhypopituitarism, the diagnosis of secondary hypothyroidism was also made. It is worth noting that at the time of Gitelman diagnosis, the patient was euthyroid.

Most patients with Gitelman syndrome require oral potassium and magnesium in addition to the angiotensin-converting enzyme inhibitor treatment they receive, which is true about our patient, as well. It is estimated that the Gitelman syndrome has been known for over fifty years. There have been many improvements in treatment and follow up, leading to the improved quality of life in patients and increasing the chance of pregnancy. Therefore, the proper management of these patients is very important during pregnancy. It is commonly believed that the Gitelman syndrome management during pregnancy is difficult and the fetal demise may occur (16). In addition, the hypothyroid women are at the risk of some complications during pregnancy. It is worth noting that our patient experienced an uneventful pregnancy without reviving parenteral potassium.

One of the limitations of this study was that we did not do molecular genetic testing for the diagnostic confirmation of Gitelman syndrome. It is presumed

that genetic testing is a helpful method, which can detect the mutations of the genes causing this syndrome; nevertheless, it is not generally used for the confirmation of a diagnosis.

In conclusion, Gitelman syndrome can be managed during pregnancy with oral potassium and magnesium. Spironolactone can also be managed without any maternal-fetal complications, especially in female fetus. Overall, the hypothyroidism effect on Gitelman syndrome manifestation is not clear, and whether hypothyroidism can ameliorate the clinical symptoms of the Gitelman syndrome needs future investigations.

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Conflicts of Interest

None declared.

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