Gitelman Syndrome in a Pregnant Woman

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Case Report

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Abstract

Background: Gitelman syndrome (GS) is an autosomal recessive inherited salt-losing tubulopathy resulted from a loss-of-function mutation in the gene SLC12A3 encoding the thiazide-sensitive sodium-chloride cotransporter (NCCT) protein located in the distal renal tubules. Investigations revealed hypokalemia, metabolic alkalosis, hypomagnesemia, hypocalciuria and increased activity of renin-angiotensin-aldosterone system. There have been very few case reports on Gitelman syndrome in pregnancy, and some cases showed adverse consequences of the fetus.

Case presentation: We presented a case report of a pregnant female with hypokalemia, a large amount of intravenous potassium was required to maintain a relatively normal level of serum potassium.Therefore, further laboratory examinations and whole blood DNA sequencing were carried out. The patient was eventually diagnosed with Gitelman syndrome. In terms of treatment, the amount of potassium supplementation was gradually reduced, and magnesium supplementation was intermittently provided at the same time to maintain the patient's serum potassium at about 3.0mmol/L and serum magnesium at about 0.8mmol/L. Obstetric ultrasound during hospitalization indicated normal fetal development, and the patient was discharged from hospital after her condition improved.

Conclusions: The clinical manifestations of GS are non-specific, and there is a lack of evidence-based treatment guidelines for pregnant GS patients, so multidisciplinary management of pregnant GS women is essential. Treatment should be cautious and individual, and the electrolytes should be closely monitored to avoid complications caused by electrolyte disturbance and strive to obtain a good maternal and fetal outcome.

Background

Gitelman syndrome (GS) is an autosomal recessive inherited salt-losing tubulopathy[1]. The cause of GS is a loss-of-function mutation in the gene SLC12A3 encoding the thiazide-sensitive sodium-chloride cotransporter (NCCT) protein located in the distal renal tubules, which leads to abnormalities in the structure and/or function of NCCT, resulting in a series of pathophysiological changes and clinical manifestations caused by the disturbance of sodium chloride reabsorption in renal tubules, such as hypovolemia, the activation of renin-angiotensin-aldosterone system, hypokalemia, and metabolic alkalosis[2]. The majority of GS patients present mild and nonspecific symptoms during adolescence or adulthood. Common clinical manifestations are associated with electrolyte abnormalities, such as muscle weakness, salt craving and

Tetany. However, the phenotype of GS is highly variable and links to the quality of life. Diagnosis of GS is based on the clinical symptoms, biochemical abnormalities (normal/low blood pressure, metabolic alkalosis, hypomagnesemia, hypocalciuria and increased activity of renin-angiotensin-aldosterone system) and genetic test Here we are presenting a rare case report of a pregnant female with Gitelman syndrome.

Case Presentation

A 26-year-old woman who at 16 weeks of pregnancy was admitted to the gynaecology department complaining of intermittent nausea and vomiting for 1.5 months, and she was transferred to the intensive care unit due to severe hypokalemia. Her vital signs and physical examination were normal, but biochemical analysis revealed metabolic alkalosis with hypokalemia based on the following values: blood gas analysis: PH 7.53, PO_2 87mmHg, PCO_2 32mmHg, HCO_3^- 27mmol/L, BE 4.0mmol/L, serum potassium level was 1.83 mmol/L (normal range: 3.5–5.3 mmol/L), chlorine was 96.7mmol/L (normal range: 99-110mmol/L), and serum magnesium level was 0.26mmol/L (normal range: 0.74-1.02mmol/L). She received intravenous replacement of 1 g/h KCl, 12.5g/w $MgSO_4$. Within 1 week of treatment, serum potassium and magnesium levels increased to 3.5 mmol/L and 0.6mmol/L, respectively.

Such a large amount of potassium supplements leaded us to wonder, was it just the increase in the demand for potassium during pregnancy and the excessive loss of potassium due to hyperemesis gravidarum causing such severe hypokalemia? Therefore, we consulted the relevant literature, and further laboratory examinations were carried out. The 24-hour urinalysis showed that calcium was 0.94mmol/24hour, significantly lower than the normal range of 2.5–7.5 mmol/24 hour. Whole blood DNA sequencing revealed 2 heterozygous mutations in the SLC12A3 gene (c.179C□T p.T60M and c.1077C□G p.N359K). Additionally, heterozygous mutation (c.179C□T) was found in her mother, and heterozygous mutation (c.1077C□G) in SLC12A3 gene was found in her father. The patient was eventually diagnosed with Gitelman syndrome. In terms of treatment, the amount of potassium supplementation was gradually reduced, and magnesium supplementation was intermittently provided at the same time to maintain the patient's serum potassium at about 3.0mmol/L and serum magnesium at about 0.8mmol/L. Obstetric ultrasound during hospitalization indicated normal fetal development, and the patient was discharged from hospital after her condition improved.

Discussion And Conclusions

There have been very few case reports on Gitelman syndrome in pregnancy, and most of them show favourable outcomes[3–5], but there are also reports of adverse consequences of the fetus[6]. In this case, the patient suffered from hyperemesis gravidarum, which could lead to a decrease in serum potassium level. Moreover, increased demand for potassium in the body during pregnancy further exacerbated hypokalemia[7, 8]. The above conditions can easily lead to missed diagnosis of GS. Therefore, for hypokalemia that is difficult to correct, it is necessary to be alert to the possibility of GS, and further examinations such as serum magnesium and 24-hour urinary electrolytes should be tested. Finally, genetic testing can be performed to confirm the diagnosis. In terms of treatment, potassium and magnesium supplementation is essential[8]. When potassium supplementation is insufficient, potassium-sparing diuretics are an option, such as spironolactone, which is a category C drug in pregnancy, but it has been reported to use it in pregnant GS patients without apparent complications[9, 10]. In patients who have failed spironolactone treatment, other potassium-sparing drugs, such as eplerenone and amiloride,

can be selected as class B drugs during pregnancy[11, 12]. GS patients can hardly achieve the normalization of electrolytes, especially in pregnant women with GS, and Basu et al. suggested that serum potassium do not need to reach normal levels in pregnant patients with GS, the principle of treatment is to prevent convulsions and spasms during childbirth[13]. In our patient, oral potassium supplementation can maintain blood potassium at 3.0 mmol/L, and there is no clinical manifestation of hypokalemia.

In short, there is a lack of evidence-based treatment guidelines for pregnant GS patients, and the clinical manifestations of GS are non-specific, from no obvious symptoms to fatigue, muscle spasms, convulsions, limb paralysis, etc. Other rare manifestations include rhabdomyolysis and arrhythmia and sudden death[14], so multidisciplinary management of pregnant GS women is essential. Treatment should be cautious and individual, and the electrolytes should be closely monitored to avoid complications caused by electrolyte disturbance and strive to obtain a good maternal and fetal outcome.

Abbreviations

GS
Gitelman syndrome
NCCT
thiazide-sensitive sodium-chloride cotransporter

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent for publication of the clinical details was obtained from the patient.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

FFH, NL, and DZ participated in the treatment of this patient and were involved in the development of the conclusions. FFH wrote the first draft with assistance from NL and DZ edited the final draft. All authors had read and approved the final manuscript.

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References

1. Gitelman HJ, Graham JB, Welt LG. A new familial disorder characterized by hypokalemia and Hypomagnesemia[J]. Transactions of the Association of American Physicians. 1966;79:221–35.
2. Nakhoul F, Nakhoul N, Dorman E, et al. Gitelman's syndrome: a pathophysiological and clinical update[J]. Endocrine. 2012;41(1):53–7.
3. Kenny LC. Gitelman's syndrome in pregnancy: case report and review of the literature[J]. Nephrology Dialysis Transplantation. 2010;25(4):1338–40.
4. Etik S, Basaran NC, Ozisik L, et al. Gitelman Syndrome Diagnosed in a Woman in the Second Trimester of Pregnancy[J]. 2019.
5. de Bustros A, Aleppo G, Zikos D. Hypokalemia in Pregnancy: Clue to Gitelman Syndrome[J]. Endocrinologist. 2001;11(6):447–50.
6. Nand N, Deshmukh AR, Mathur R, et al. Gitelman Syndrome: Presenting During Pregnancy with Adverse Foetal Outcome[J]. J Assoc Physicians India. 2016;64(10):104–5.
7. Haan JD, Geers T, Berghout A. Gitelman syndrome in pregnancy[J]. international journal of gynaecology obstetrics the official organ of the international federation of gynaecology obstetrics. 2008;103(1):0–71.
8. Talaulikar GS, Falk MC. Outcome of Pregnancy in a Patient with Gitelman Syndrome: A Case Report[J]. Nephron Physiology. 2005;101(2):35–8.
9. Groves TD, Corenblum B. Spironolactone therapy during human pregnancy[J]. American Journal of Obstetrics Gynecology. 1995;172(5):1655–6.
10. Arriba GD, Sánchez-Heras M, Basterrechea MA. Gitelman syndrome during pregnancy: a therapeutic challenge[J]. Archives of Gynecology Obstetrics. 2009;280(5):807–9.
11. Morton A, Panitz B, Bush A. Eplerenone for Gitelman syndrome in pregnancy. [J] Nephrology. 2011;16(3):349–9.
12. Mascetti L, Bettinelli A, Simonetti GD, et al. Pregnancy in Inherited Hypokalemic Salt-Losing Renal Tubular Disorder[J]. Obstetrics Gynecology. 2011;117(2):p..art 2):512–6.
13. Basu A, Dillon RDS, Taylor R, et al. Is normalisation of serum potassium and magnesium always necessary in Gitelman Syndrome for a successful obstetric outcome?[J]. Bjog An International Journal of Obstetrics Gynaecology. 2004;111(6):630–4.
14. Knoers NV, Levtchenko EN. Gitelman syndrome. Orphanet Journal of Rare Diseases. 2008;3:22.