Gitelman Syndrome: Presenting During Pregnancy with Adverse Foetal Outcome

N Nand¹, AR Deshmukh², R Mathur², V Chauhan², Brijjal²

Abstract

Gitelman syndrome (GS) is a rare autosomal recessive salt-losing tubulopathy. The incidence of Gitelman syndrome is 25 cases in 1 million among western population. This patient presented with loose stool, vomiting and sudden onset quadriparesis. Investigations revealed hypokalaemia, metabolic acidosis, hypomagnesaemia, hypocalciuria, hypermagnesuria. Symptoms and hypokalemia improved after starting oral magnesium and potassium supplements. But the patient again presented with symptomatic hypokalemia and delivered a still born foetus with hydrocephalus. Patient was put on potassium sparing diuretics along with supplements and thereafter, has been asymptomatic. There have been very few case reports on Gitelman syndrome in pregnancy and most of them show favourable outcomes. This is a rare case report of a pregnant female with Gitelman syndrome with foetal loss.

Introduction

Gitelman syndrome (GS) is an autosomal recessive salt-losing tubulopathy caused by a mutation of genes encoding the human sodium chloride co-transporters and magnesium channels in the thiazide-sensitive segments of the distal convoluted tubule. The clinical presentation ranges from mild muscle cramps and salt craving to severe muscle weakness and respiratory paralysis due to severe hypokalaemia. The incidence of Gitelman syndrome is 25 cases in 1 million among western population but data regarding the incidence in Indian population is limited. Till date 24 pregnancies with Gitelman syndrome have been reported with 20 of them having no foetal complications. Here we are presenting a rare case report of a pregnant female with Gitelman syndrome with unfavorable foetal outcome.

Case Summary

A 33 years old primigravida, presented to the emergency in her first trimester i.e 11 weeks of gestation, with history of three episodes of loose stools and vomiting since four days associated with sudden onset, simultaneous weakness in all four limbs of one day duration. There was no preceding history of fever, altered sensorium, progressive weakness, bowel or bladder incontinence or any co-morbid illness. There was no history of similar complaints in the past in the patient or her family and use of drugs including diuretics. There was no history of pica. General examination was unremarkable and her vitals were stable. Motor system examination revealed generalised hypotonia, power of 2/5 in upper limbs and 1/5 in bilateral lower limbs. Reflexes were absent in all four limbs. Examinations for sensory system, cranial nerves, cerebellum, and extrapyramidal system were normal. Other systems were normal on examination.

On laboratory examination complete haemogram, kidney function tests and liver function test, complete urine examination were unremarkable. Venous blood gas analysis showed pH 7.5, bicarbonate 31.7 mmol/L, pCO₂ 42 mm of Hg, sodium 135 meq/L, potassium 1.90 meq/L, chloride 101 meq/L. Electrocardiogram showed prolonged PR interval of 0.24 seconds, prominent U waves and flat t waves. On ultrasound a single live foetus was seen with no gross congenital malformations. In view of hypokalaemia with quadriparesis, hypokalaemic paralysis due gastrointestinal loss was suspected and the patient was given intravenous potassium chloride of (120 meq in 24 hours).

After 24 hours of hospital admission, there was little improvement in symptoms and repeat biochemistry revealed serum pH 7.515, potassium 1.98 meq/L, chloride 101 meq/L. There was persistence of metabolic alkalosis and hypokalaemia, hence we investigated further and the investigation revealed hypomagnesaemia with hypocalciuria and hypermagnesuria. Considering the above biochemical picture in a normotensive patient a diagnosis of Gitelman syndrome was made. Serum magnesium was 1.3 mg/dl (1.3-2.5). On 24 hour urinary electrolyte examination, urine calcium was 98 mg/dl (100-300), sodium 170 meq/day (75-200), potassium 172 meq/day (40-80), chloride 280.12 meq/day (140-250), magnesium 140 mg/day (73-122). Patient was started on magnesium supplements along with potassium and the patients symptoms improved. Blood pH was 7.462, bicarbonate 31.3 mmol/L, potassium 3.8 meq/L, chloride 112 meq/L, (Tables 1 and 2). The presence of hypokalaemia in a normotensive patient suggested the diagnosis of Gitelman syndrome and patient was discharged on oral magnesium and potassium supplements.

Patient remained asymptomatic till next 3 months and she presented again with numbness in bilateral lower limbs and bleeding per vaginum. On examination there was severe pallor and rest of the examination was unremarkable. On investigation patient’s complete haemogram showed haemoglobin of 8.2 gm/dl, blood pH 7.497, bicarbonate 35.2 meq/L, potassium 1.69 meq/L and chloride 102 meq/L. On ultrasound foetal heart sound was present and mild ventriculomegaly was present. Patient

¹Senior Professor and Unit Head, ²Resident, Dept. of Medicine, Pt. B. D. Sharma, Post Graduate Institute of Medical Sciences, Rohtak, Haryana

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delivered at 23 weeks of gestation, it was a still birth and there was no other maternal complication. Thorough examination revealed no maternal risk factor except short stature and post-partum examination of the foetus revealed hydrocephalus which was in accordance with the ventriculomegaly seen on foetal ultrasound. Patient was started on intravenous potassium and magnesium supplements. Patients clinical and biochemical picture improved and serum potassium was 3.8 meq/L after 48 hours. Patient was discharged on oral spironolactone 25 mg twice daily, syrup potassium chloride 30 ml thrice daily and magnesium hydroxide 50 mg twice daily.

**Discussion**

In 1966, Gitelman et al. described a familial disorder consisting of hypokalemia, hypomagnesemia, hypocalciuria and metabolic alkalosis. Later the defect was found to be mutation in SCL12A3, thiazide sensitive sodium chloride co-transporter in distal convoluted tubule (DCT), with autosomal recessive inheritance. The prevalence of GS is estimated to range around 25 cases per 1 million Caucasian subjects is ~1% in the Caucasian population. There have been very few case reports on Gitelman syndrome in pregnancy and most of them show favourable outcomes. Till date, 24 cases of pregnancy with Gitelman syndrome have been reported with 20 of them having no foetal complications.

Precipitating causes usually are mild diarrhoea, vomiting and pregnancy as was seen in our case. In pregnancy the increased demand for magnesium and potassium and increased urinary loss create a perfect milieu for precipitation of severe symptomatic hypokalaemia. Diagnosis is usually made by characteristic finding of hypokalaemia, hypomagnesaemia with metabolic alkalosis and hypocalciuria, hypermagnesuria in 24 hours urinary samples. Confirmation of diagnosis can only be made by genetic analysis and detection of the mutation in SCL12A3 gene.

Barter syndrome is another rare autosomal recessive disorder which presents with hypokalaemia with metabolic alkalosis. Even though the biochemical picture is similar hypomagnesaemia and hypocalciuria are absent. It is important for physicians to keep in mind to rule out other more common causes of hypokalaemia with metabolic alkalosis like vomiting, diarrhoea and diuretic abuse before considering such rare causes.

Most of the case reports show no adverse foetal outcomes. In a cohort study of 50 patients with GS, 20 of whom gave birth, seven had complicated pregnancies. These complications included dehydration, the need for intravenous potassium and/or magnesium administration, severe cramping, Sheehan’s syndrome, gestational diabetes, miscarriages in the first trimester, premature delivery, polyhydramnios, preeclampsia and placental abruption. Other than fluid deficit and electrolyte imbalance, it remains unclear whether any of these complications were related to GS. Our patient presented twice with symptomatic hypokalaemia and had adverse foetal outcome during the second admission. The presence of ventriculomegaly and hydrocephalus in the foetus and absence of any obstetric complication implies that the foetal death could be due to the metabolic complications of Gitelman syndrome.

**Conclusion**

It has to be kept in mind that high index of suspicion is required for the diagnosis of Gitelman syndrome followed by vigilant monitoring and aggressive management for better maternal and foetal outcome.

**References**