

GITELMAN SYNDROME AND PREGNANCY- A RARE CASE REPORT

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HOW TO CITE THIS ARTICLE: Sibiy V, Barua RK, Yuvaraja K. Gitelman syndrome and pregnancy- A rare case report. J. Evid. Based Med. Healthc. 2017; 4(76), 4501-4502. DOI: 10.18410/jebmh/2017/897

PRESENTATION OF CASE

A 22 years old G2 P1 D1 came with complaints of shivering of both upper limb and lower limb. She was diagnosed with Gitelman syndrome in previous pregnancy. Previous was a preterm delivery due to polyhydramnios and the baby died at 12 days of life due to some congenital malformation of heart. In previous pregnancy, patient presented with paralysis at 6 months of gestation and was treated conservatively by correcting the electrolytes level. In the present pregnancy, patient had persistent hypokalaemia and hypomagnesaemia, which was treated. Anomaly scan was done. No gross anomaly was detected. Patient is symptomatically better and she is continuing her pregnancy, hope better outcome since GS has no adverse effect on pregnancy.

DIFFERENTIAL DIAGNOSES

- Bartter syndrome (especially type III).
- Pseudo-Bartter/Gitelman syndrome.

CLINICAL DIAGNOSIS

Patient was diagnosed with Gitelman syndrome in previous pregnancy. Gitelman was diagnosed by hypokalaemia (1.4 mEq), hypomagnesaemia (1.1 mg/dL), hypocalciuria and metabolic alkalosis (blood pH - 7.52) and was treated conservatively. Patient had persistent hypokalaemia around 2.6 mEq and hypomagnesaemia with serum magnesium of about 1.4 mg/dL, blood ph-7.51 in the present pregnancy. Nephrologist opinion was sought and the patient was managed conservatively by correcting the electrolytes level.

DISCUSSION OF MANAGEMENT

Gitelman syndrome was first described in 1966 by Gitelman et al. Gitelman Syndrome (GS), also referred to as familial hypokalaemia-hypomagnesaemia is an autosomal recessive condition characterised by hypokalaemic, metabolic alkalosis in combination with significant hypomagnesaemia and low urinary calcium excretion.¹

It is one of the most frequent inherited renal tubular disorders. In the majority of cases, symptoms do not appear before the age of six years. Unlike Bartter syndrome that presents in the neonatal period and childhood up to 5 yrs. of age, GS is usually diagnosed during adolescence or adulthood.²

Transient periods of muscle weakness/paralysis are the commonest symptom seen in GS patients. Cramp and tetany occurs with fever or in hypomagnesaemia.³ Paraesthesias especially in the face, occurs frequently.

Some patients are completely asymptomatic except for the appearance of chondrocalcinosis at adult age that causes swelling, local heat and tenderness over the affected joints.

Blood pressure in GS patients is lower than that in the general population.⁴ Sudden cardiac arrest has been reported occasionally. In general, growth is normal, but can be delayed in those GS patients with severe hypokalaemia and hypomagnesaemia.

GS is transmitted as an autosomal recessive trait. Mutations in SLC12A3 gene on chromosome 16, which encodes the thiazide-sensitive NaCl Cotransporter (NCCT) are found in the majority of GS patients. This NCCT is located in the distal convoluted tubule.⁴ At present, more than 140 different NCCT mutations throughout the whole protein have been identified. In a small minority of GS patients, mutations in the CLCNKB gene encodes a protein necessary for the chloride channel ClC-Kb have been identified.

Impaired sodium chloride reabsorption leads to mild volume depletion and activation of the Renin-Angiotensin-Aldosterone (RAAS) axis. The combination of secondary hyperaldosteronism and increased distal flow, increases potassium and hydrogen secretion. Raised aldosterone levels increase electrogenic sodium reabsorption in the CCD via the epithelial sodium channel ENaC and maintain salt homeostasis at the expense of an increased secretion of potassium and hydrogen ions and an attendant hypokalaemia with metabolic alkalosis.⁵

Though common causes for hypokalaemia in pregnancy is dilution, increased foetal demands diarrhoea and hyperemesis gravidarum, GS an infrequent cause should also be considered.⁴

Diagnosis is based on the clinical symptoms and biochemical abnormalities (hypokalaemia, metabolic alkalosis, hypomagnesaemia and hypocalciuria).

Bartter syndrome (especially type III) is the most important genetic disorder to consider in the differential diagnosis of GS.⁶ As GS is an autosomal recessive disorder, the risk of transmission to the children 25%, hence genetic counseling is important.⁷ Antenatal diagnosis for GS is

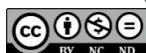
Financial or Other, Competing Interest: None.

Submission 22-08-2017, Peer Review 02-09-2017,

Acceptance 14-09-2017, Published 21-09-2017.

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DOI: 10.18410/jebmh/2017/897



technically feasible, but not advised because of the good prognosis in the majority of patients.

The management of GS is symptomatic and electrolyte imbalance is corrected by initial daily dose of magnesium chloride is 3 mmol/m²/24 hrs. or 4-5 mg/kg/24 hrs. This dose should be divided in 3-4 administrations to avoid diarrhoea and has to be adjusted according to serum magnesium levels. In case of vomiting, the dose usually has to be increased. In case of acute tetany, 20% MgCl₂ should be administered intravenously (0.1 mmol/mg/kg per dose) and can be repeated every 6 hours.⁷

If symptomatic hypokalaemia is not corrected by MgCl₂ administration, it can be treated by drugs that antagonise the activity of aldosterone or block the sodium channel ENaC in the collecting duct. Combination of amiloride (5-10 mg/1.73 m²/day) with KCl (1-3 mmol/kg/day divided in 3-4 doses) is preferred. Amiloride should be started with caution in order to avoid hypotension.⁷

Complaints related to chondrocalcinosis (mainly pseudogout attacks) are caused by the deposition of calcium pyrophosphate dehydrate crystals in synovium and the synovial fluid due to low magnesium level. Chondrocalcinosis can be reduced by Mg²⁺ supplementation.³ The symptoms are acute arthropathy and can be controlled by Nonsteroidal Anti-Inflammatory Drugs (NSAID), joint surgery is generally not required.

Growth and puberty delay in some patients with severe GS can be corrected by adequate magnesium and K⁺ supplementation and a growth-promoting effect of indomethacin was also reported in GS patients.⁷ Sudden cardiac death can occur in GS patients, hence cardiac workup is recommended to screen for cardiac arrhythmias.⁸ All patients with GS are encouraged to maintain a high-sodium and high-potassium diet.

Mode of delivery in GS is determined by obstetric indication. During labour, electrolytes level should be measured every 4-6 hours in order to minimise the risk of electrolyte imbalance. In postpartum period, electrolyte level should be repeated at least once a week.⁹ In case of

caesarean section, regional anaesthetic technique is preferred.¹⁰

In conclusion, pregnancy with Gitelman's syndrome presents with challenges in management of electrolyte imbalance, which may be very difficult. Multidisciplinary team including obstetricians, nephrologist, endocrinologists, anaesthetists, neonatologists and geneticists is of paramount importance for good obstetric and neonatal outcomes.

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