Gitelman’s syndrome

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Gitelman’s syndrome is primarily renal tubular hypokalemic metabolic alkalosis with hypocalciuria and magnesium deficiency, a benign disorder, inherited as autosomal recessive traits.

Key words: Hypocalciuria, hypokalemia, Bartter’s syndrome

Introduction

Classic Bartter’s syndrome is primary renal tubular hypokalemic metabolic alkalosis with normocalciuria or hypercalciuria, a severe disorder and Gitelman’s syndrome is primary renal tubular hypokalemic metabolic alkalosis with hypocalciuria and magnesium deficiency, a benign disorder.[1] It has been suggested that the antenatal and classic Bartter’s syndrome and Gitelman’s syndrome represent distinct variants of primary renal tubular hypokalemic metabolic alkalosis and are easily distinguished on the basis of urinary calcium levels.[2] The Gitelman’s syndrome present during adolescence or adulthood, inherited as autosomal recessive traits. The dominant features are fatigue, weakness, hypocalciuria, hypomagnesemia with hypermagnesuria and normal prostaglandin production. We report here a patient who presented with features of Gitelman’s syndrome.[3]

Case Report

A 57 years old female was admitted to our hospital with complaints of generalized weakness, fatigue, palpitation and vomiting since 2 weeks. Patient was on treatment for hypertension and coronary artery disease with amlodipine, nitrates and atenolol. There was past history of bronchial asthma with 2-3 attacks per year, for which she was not on regular treatment. Diabetes mellitus was diagnosed during laboratory evaluation, which is controlled with dietary restriction. Patient was not on diuretic therapy. There was no history of exacerbation of weakness by exertion or after heavy carbohydrate meal. No other family member had similar illness and there was no history of parental consanguinity.

On examination, the blood pressure was 160/96 mmHg and pulse rate was 78 per minute. There was neither neurological deficit nor proximal muscle weakness. ECG showed ischemic changes. Laboratory investigations showed following results- Serum potassium 2.7 mEq/L (Normal range 3.5-5 mEq/L), serum sodium-119.6 mEq (136-145 mEq), serum chloride-83 mEq/L (96-106 mEq), serum bicarbonate-18 mEq/L(24-28), serum magnesium-1.3 mg/dl (1.8-2.4 mg/dl), serum urea-38 mg/dl, serum creatinine-1.4 mg/dl, blood pH-7.58 (7.35-7.45). The urinary calcium was subnormal at 1.2 m mols/24 hour (2.5-7.5 mmols). Urine sodium is 79.75 mmol/24 hour (40-220 mmols), urine potassium 26.12 mmols/24 hour (25-150 mmols), urine chloride 123.75 mmols/24 hour (110-250 mmols), urine magnesium 44 mg/24 hour (1.2-29.2 mg). Urine specific gravity and urine osmolality were normal. Thyroid function tests (T3, T4, TSH) and serum cortisol levels were normal. Ultrasound of the abdomen did not reveal any abnormality.

Patient was treated with oral magnesium and potassium supplementation. Indomethacin 25 mg twice daily was given empirically and stopped after one month. Patient symptoms resolved quickly as the treatment continued. She was discharged with advice to continue oral potassium and magnesium supplements. She remains symptom free and normokalemic after one year of follow up.

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**Discussion**

Antenatal Bartter’s syndrome, classical Bartter’s syndrome and Gitelman’s syndrome are the three phenotypes of Bartter’s syndrome that have now been recognized. Mutations in several renal tubule transport protein have been shown to be responsible for this syndromes. In Gitelman’s syndrome, mutations have been found in the thiazide sensitive Nacl transporter. The reduced sodium reabsorption in the distal convoluted tubule leads to volume depletion and hypokalemia, though not as severe as would result from a lesion in the loop of Henle. Loss of activity of the thiazide sensitive transport increases tubule calcium reabsorption, leading to the classic finding of hypocalciuria in Gitelman’s syndrome.[3] In our patient, diagnosis of Gitelman’s syndrome was based on clinical findings and laboratory investigation findings like hypocalciuria, hypokalemia, hypermagnesuria, low serum sodium, low serum bicarbonate and alkalosis. Although rarely required for diagnosis, renal biopsy reveals hyperplasia of the juxta glomerular apparatus and prominence of medullary interstitial cells, with variable degrees of interstitial fibrosis.[3]

Patients with Gitelman’s syndrome do not have symptoms throughout infancy and preschool years other than some febrile seizures, a common disturbance in this age group. In some cases Gitelman’s syndrome is found by chance because of measurement of serum electrolytes for other reason.[1] Chronic vomiting may be a differential diagnosis for Gitelman’s syndrome, which can be easily diagnosed by low urine chloride concentration.[3] Our patient also presented with vomiting.

Rodriguez-Soriano et al[4] were the first to suggest that hypocalciuria may be useful in distinguishing the Gitelman’s syndrome from classic Bartter’s syndrome. It is less certain whether changes in calcium excretion provide insight into the renal tubular pathophysiology of these syndromes. The greater urinary calcium excretion in patients with classic Bartter’s syndrome is consistent with impaired reabsorption in the ascending limb of loop of Henle. Alternatively the hypocalciuria of Gitelman’s syndrome suggests the involvement of the distal convoluted tubule, where reduced chloride absorption is associated with augmented calcium absorption.[2] Our patient also had hypermagnesuria. Our current understanding of tubular function does not easily explain the dissociation between calcium and magnesium excretion in these disorder. The thick ascending limb of loop of Henle is the major site of magnesium reabsorption, where the reabsorption thought to parallel the reabsorption of calcium. Consequently involvement of thick ascending limb would be expected to promote severe magnesium wasting, which is not usually present in classic Bartter’s syndrome. Paradoxically in Gitelman’s syndrome there is more consistent and severe magnesium wasting, which would not be expected from a tubular defect limited to the distal convoluted tubule. These considerations suggest the possibility of an additional tubular defect in the Gitelman’s syndrome that contributes to magnesium wasting.[2]

Potassium and magnesium supplements are needed in Gitelman’s syndrome. Prostaglandin synthetase inhibitors are of no benefit in Gitelman’s syndrome.[3] The presence or absence of sodium wasting has important therapeutic implications. Increased delivery of sodium to the distal nephron increases potassium excretion. In sodium wasting or in patients supplemented with sodium in the diet, the augmented potassium excretion will require a large quantity of potassium supplementation and potassium sparing diuretics to maintain the plasma potassium level within the normal range. In the absence of sodium wasting, more modest amounts of potassium supplementation with or without potassium sparing diuretics may be required.[5]

**References**