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Gitelman's Syndrome –A Rare Case Report

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ABSTRACT

Gitelman's syndrome is primarily renal tubular hypokalemic metabolic alkalosis with hypocalciuria and magnesium deficiency, a benign disorder, inherited as autosomal recessive traits.We report a2 years old male admitted in our hospital with complaints of vomiting for 2 days, increased thirst and urination for 2 days. No other family member had similar illness and there was no history of parental consanguinity.On examination, the blood pressure was 76/60 mmHg and pulse rate was 136 per minute. Patient was dehydrated and hypothermic. Sensorium was normal. Systemic examination was within normal limit.Laboratory investigationshowed hypocalciuria, hypokalemia, hypermagnesuria, low serum sodium, high serum bicarbonate and metabolic alkalosis.All these findings confirmed the diagnosis of a rare Gitelman's syndrome.

KEYWORDS Hypocalciuria, hypokalemia, gitelman'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 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 History-

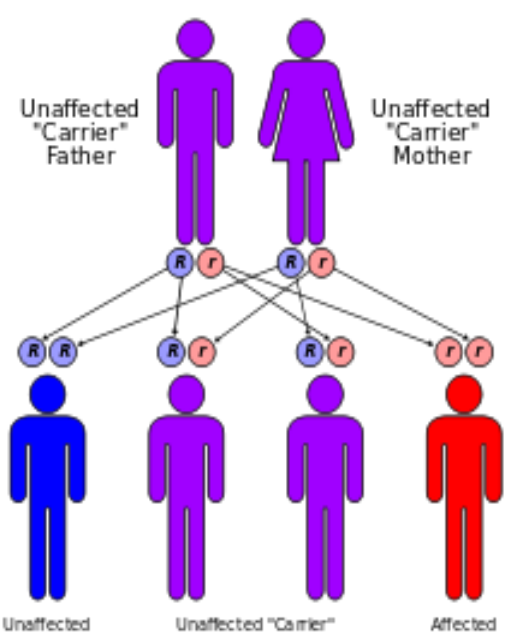
A 2 years old male was admitted in our hospital with complaints of vomiting for 2 days, increased thirst and urination for 2 days. No other family member had similar illness and there was no history of parental consanguinity.

On examination, the blood pressure was 76/60 mmHg and pulse rate was 136 per minute. Patient was dehydrated and hypothermic. Sensorium was normal. Systemic examination was within normal limit. Laboratory investigation findings were, serum potassium - 1.2 mEq/L (normal range 3.5-5 mEq/L), serum sodium-140 mEq/L (136-145 mEq/L), serum chloride - 102 mEq/L (96-106 mEq/L), serum bicarbonate 30 mEq/L(24-28 mEq/L), serum magnesium-1.2 mg/dl (1.8-2.4 mg/dl), serum urea- 18.4 mg/dl, serum creatinine- 0.03 mg/ dl. In ABG the pH was 7.55 (7.35-7.45). The urinary calcium was subnormal - 1.2 mmols/24 hours (2.5-7.5 mmols). Urine chloride was 90 mmols/24 hours (110-250 mmols), urine magnesium- 42 mg/24 hour (1.2-29.2 mg). Specific gravity and osmolarity of urine were normal. Serum aldosteron level was 462.02 (25-315).

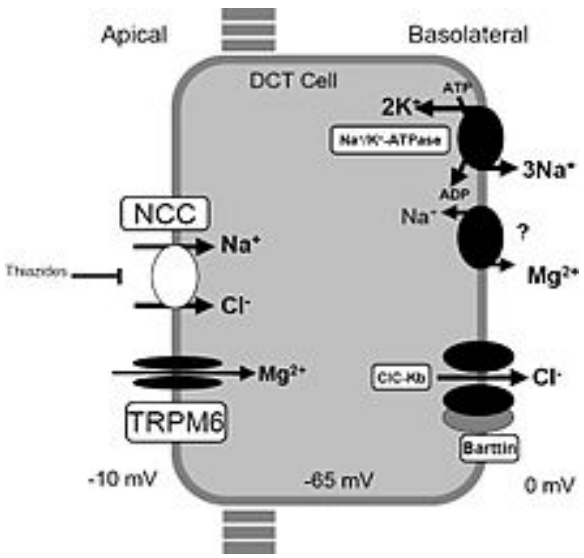
Patient was treated with oral magnesium and potassium supplementation. Indomethacin was given empirically and stopped after one month. Patient symptoms resolved quickly as the treatment continued. He was discharged with advice to continue oral potassium and magnesium supplements. He remains symptom free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

Discussion

Gitelman's syndrome is a benign disorder, inherited as autosomal recessive traits.



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 reabsortion, leading to the classic finding of hypocalciuria in Gitelman's syndrome.[3]



[A model of transport mechanisms in thedistal convoluted tubule.]

Sodium-chloride (NaCl) enters the cell via the apical thiazide-sensitive NCC and leaves the cell through the basolateral Cl- channel (ClC-Kb), and the Na+/K+-ATPase. Indicated also are the recently identified magnesium channel TRPM6 in the apical membrane, and a putative Na/Mg exchanger in the basolateral membrane. These transport mechanisms play a role in familial hypokalemia-hypomagnesemia or Gitelman's syndrome.

In our patient, diagnosis of Gitelman's syndrome was based on clinical findings and laboratory investigation findings like hypocalciuria, hypokalemia, hypermagnesuria, low serum sodium, serum bicarbonate and alkalosis. Although rarely required for diagnosis, renal biopsy reveals hyperplasia of 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]

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