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Original Research Paper

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COMMON PRESENTATION OF A RARE SYNDROME

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ABSTRACT Gitelman's syndrome is an autosomal recessive syndrome presenting primarily with renal tubular hypokalemic metabolic alkalosis with hypocalciuria and hypomagnesemia .

KEYWORDS : Hypocalciuria, hypokalemia, Bartter's syndrome

INTRODUCTION

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 38 year old female with no co morbidities was apparently normal till February 2021, when she developed sudden onset weakness of bilateral upper and lower limbs (lower limbs>upper limbs) associated with difficulty in standing and generalized fatigue & weakness. There was no history of difficulty in lifting the hands over the head, difficulty in neck lifting, dyspnea, dysphagia, dysphonia, bladder and bowel disturbances (no diarrhea, vomiting, fever, seizures, headache, respiratory, gastrointestinal symptoms, and prior to the development of symptoms Taken with these complaints to our hospital, found to have potassium of 2.0, received inj. KCL for 4 days, after which the weakness recovered completely. She took potassium chloride syrup for 2 weeks and improved. There was no history of exacerbation of weakness by exertion or after heavy carbohydrate meal in both the episodes. There was no history of vomiting or diarrhea before the onset of symptoms. No h/o chest pain, palpitation, SOB, h/o dryness of mouth, eyes or dysphagia, malar rash, hyperpigmentation, polyuria, loss of appetite, loss of weight, paroxysms of sweating, Raynauds phenomenon. There was a history of cholecystectomy in past. There was no history of previous co morbidities or similar family history or parental consanguinity any other significant history. Patient was not on diuretic therapy. She presented with similar complaints in November 2021. Potassium 2.1, improved with inj. KCl followed by oral potassium supplementation.

On examination, she was found to be conscious, oriented, hemodynamically stable and no systemic abnormalities. Deep tendon reflexes were normal bilaterally. Power was 4+/5 in bilateral upper limbs and 5/5 in bilateral lower limbs.

On examination, the blood pressure was 130/86 mmHg and pulse rate was 74 per minute. There was neither neurological deficit nor proximal muscle weakness. ECG showed normal sinus rhythm. Laboratory investigations showed following results- Serum potassium 2.1 mEq/L (Normal range 3.5-5 mEq/L), serum sodium-140 mEq (136-145 mEq), serum chloride-101 mEq/L (96-106 mEq), serum bicarbonate18 mEq/L(24-28), serum magnesium-1.5 mg/dl (1.8-2.4 mg/dl), serum urea-30mg/dl, serum creatinine-1.1 mg/ dl, blood pH-7.56(7.35-7.45). Interpretation of the 24 hr urine electrolytes sent after stopping potassium supplementation showed urine potassium to creatinine ratio(PCR) of 80mEq/g with corresponding serum K of 2.1.The urinary calcium was lesser than normal at 1.6 m mols/24 hour (2.5-7.5 mmols). Urine sodium was 84.59 mmol/24 hour (40-220 mmols), urine potassium 30.15 mmols/24 hour (25-150 mmols), urine chloride 116.45 mmols/24 hour (110-250 mmols), and urine magnesium 39 mg/24 hour (1.2-29.2 mg). Urine specific gravity and urine osmolality were normal. Renal loss was suspected. Transtubular pottasium gradient (TTKG) was >4. Blood pressure remained in low normal range and venous blood gas analysis (VBG) was showing metabolic alkalosis. As the24 hr urine chloride was increased (116.45 mmols/24 hr) and urine calcium creatinine ratio was 0.11, it was suggestive of renal loss with increased distal potassium secretion with loss of potassium and chloride in urine. She also had polyuria with 24 hr urine volume of more than 3litres. ANA was negative, Thyroid function test and Serum cortisol levels were normal. Schirmer's test was negative. Serum osmolality was 299.4mOsm/kg and urine osmolality was 232mOsm/kg.USG abdomen was suggestive of mild hepatomegaly.

In view of hypokalemia, with renal loss of potassium and chloride with polyuria and absence of hypercalciuria, renal tubulopathy was suspected and a diagnosis of Gitelman syndrome was kept clinically, however she needs genetic study for confirmation.

Patient was treated with iv KCL followed by oral potassium supplementation. Empirically, Indomethacin 25 mg twice daily was started and stopped after one month. Patient symptoms resolved with the treatment. She was discharged with advice to continue oral potassium and magnesium supplement and get genetic analysis done. She is currently symptom free and normokalemic on OPD follow up.

DISCUSSION

Gitelman's syndrome, also referred as familial hypokalemia-hypomagnesemia, is an autosomal recessive salt–losing renal tubulopathy that is characterized by hypomagnesemia, hypocalciuria and secondary aldosteronism, which is responsible for hypokalemia and metabolic alkalosis. 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. In some cases Gitelman's syndrome is found incidentally on investigation for other symptoms.[1]

Rodriguez-Soriano et al[4] first suggested that hypocalciuria may distinguish 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 increased 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] Gitelman syndrome and Bartter syndrome are rare inherited tubulopathies and should be suspected in patients with renal pattern of hypokalemic alkalosis with hypomagnesemia .All Gitelman's syndrome patients should be encouraged to maintain a high-sodium and high potassium diet along with lifelong supplementation of magnesium.Cardiac work-up should be offered to screen for risk factors of cardiac arrhythmias. Genetic counselling should be offered to all diagnosed cases of Gitelman's and Bartter's syndromes.

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