Gitelman's Syndrome – A Case Report

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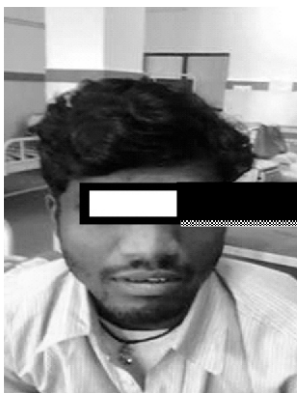
INTRODUCTION

Gitelman syndrome (GS) , also referred to as familial hypokalemia-hypomagnesemia, is an autosomal recessive salt-losing renal tubulopathy that is characterized by hypomagnesaemia, hypocalcaemia and secondary aldosteronism, which is responsible for hypokalemia and metabolic alkalosis (1). The prevalence is estimated at ~25 per million and accordingly, the prevalence of heterozygotes is approximately 1% in Caucasian populations, making it one of the most frequently inherited renal tubular disorders. It is also known as the "milder" form of Barter's syndrome, as patients with GS are usually diagnosed in adulthood during routine investigation. Symptoms reported in the literature range from asymptomatic, to mild symptoms of cramps and fatigue, to severe manifestations such as tetany, paralysis, and rhabdomyolysis (2). Here we report a classical case of Gitelman's Syndrome.

CASE SUMMARY

A 25 year old male patient presented with complaints of generalized weakness of all four limbs, cramps and malaise since 2 days along with stiffness of hands and abnormal posturing of hands. There were h/o similar complaints 3-4 times in the past. There was no h/o fever, headache, vomiting or loose motions. No h/o cranial nerve or bowel or bladder involvement.



PATIENT

TETANY

On examination his Pulse- 60/min, BP-90/60mmHg. Trousseau's sign and chvostek's sign were positive. On systemic examination abdomen was soft, no organomegaly; chest was clear and heart sounds were normal. Neurologically he was conscious, co-operative, higher functions were normal and there was no cranial nerve palsy. Power was 4/5 in all 4 limbs, DTR were sluggish in upper limbs and absent in lower limbs. Plantars were bilateral flexor. There was no sensory loss or s/o cerebellar involvement.

On investigating him, Hb was 10.5 gm%, TLC was 7400/cmm, S.creat was 0.8, Na- 133mmol/L, K-1.2 mmol/L, Ca-8.2 mmol/L and Mg-1.2 mmol/L. Urinary Na -156 mmol/L, K-30.1 mmol/L, Ca-25 mmol/L, Mg-2.25 mmol/L. ABG revealed pH 7.54, HCO3 -26. ECG showed sinus bradycardia, a prolonged QT interval along with U waves.

Patient was treated with only potassium supplements (both IV and oral) , aldosterone antagonists along with magnesium supplements.

DISCUSSION

Episodic weakness beginning after age 25 is almost never due to primary periodic paralysis(3). Gitelman syndrome (GS) after 'Hillel Gitelman' is an autosomal-recessive renal tubular disorder characterized by hypokalemia, hypomagnesaemia, hypocalcaemia, metabolic alkalosis, secondary hyperreninemic aldosteronism, and low blood pressure(1,5,6). GS patients are usually diagnosed relatively late, because malaise, low blood pressure, hypokalemia, hypocalcaemia, and hypomagnesaemia are difficult to categorize clinically. Inactivating mutations in the SLC12A3 gene encoding the thiazide-sensitive sodium chloride co transporter (NCCT) cause GS(5). Most are missense mutations substituting conserved amino acid

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residues within putative functional domains of NCCT, whereas nonsense, frameshift, and splice site defects and gene rearrangements are less frequent. GS is clinically variable (men are more severely affected than women), and the combination of mutations present in each allele may determine phenotype variability(6).

Defective functioning of NCC results in inhibition of sodium-chloride reabsorption across the apical membrane across the DCT, causing increased delivery of sodium and chloride to the collecting duct causing mild volume contraction. The reduced vascular volume stimulates the rennin-angiotensin system, increasing rennin and aldosterone. Subsequent aldosterone stimulated sodium absorption via the epithelial sodium channel, which is accompanied by potassium and hydrogen secretion results in hypokalemia and metabolic alkalosis. In addition the lower entry of sodium-chloride into the DCT cells accompanied by a continue efflux of chloride at the basolateral membrane is assumed to cause hyperpolarisation of the cells, which in turn stimulates the entry of calcium at the apical membrane through an epithelial calcium channel resulting in hypocalcaemia(7). Though the exact mechanism of hypomagnesaemia is unknown, there is evidence of apoptosis of DCT cells in SLC12A3 knockout mice. Since both NCC and the putative magnesium transport channels are located here, the death of the DCT cells would result in loss of active magnesium reabsorption as well. This would explain the renal loss of magnesium(8).

Our patient had hypokalemic metabolic alkalosis along with hypocalcaemia and hypomagnesaemia. He responded to treatment with potassium and magnesium supplements.

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