Case Report

Gitelman Syndrome Presenting with Cerebellar Ataxia and Tetany

Abstract

Gitelman syndrome (GS) is salt-losing tubulopathy characterized by hypokalemia, hypomagnesemia, hypocalciuria, hyperreninemia, hyperaldosteronemia, metabolic alkalosis, and rarely hypocalcemia. Here, we describe the case of a 54-year-old man who presented with cerebellar signs and tetany. On investigation, he was found to have hypokalemia, hypocalcemia, hypomagnesemia, metabolic alkalosis, and high urinary chloride levels. On correction of metabolic parameters, he became asymptomatic. In cases of unexplained recurrent hypokalemia, hypocalcemia and hypomagnesemia, the diagnosis of GS should be considered.

Keywords: *Cerebellar Ataxia, Gitelman syndrome, hypocalcemia, tetany*

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Introduction

Hypokalemia and hypocalcemia are not uncommon clinical problems, and most of the times, the underlying cause can be assessed from a good history and physical examination. It is important to consider the diagnosis of Gitelman syndrome in patients with persistent or recurrent hypocalcemia, hypokalemia, and hypomagnesemia. It was first described by Gitelman *et al*.[1] in 1966. It is a rare autosomal recessive, salt-losing tubulopathy characterized by hypokalemia, metabolic alkalosis with hypomagnesemia, hypocalciuria, and hyperreninemia. Rarely, it may present with hypocalcemia. It is caused by loss of function mutations in the *SLC12A3* gene that encodes the thiazide-sensitive sodium chloride cotransporter (NCC).[2] Its prevalence is 1–10 per 40,000, is more common in Asians, and usually presents in adolescents and adults with mild nonspecific symptoms. Here, we describe a case of GS presenting with cerebellar ataxia and tetany.

A 54-year-old hypertensive gentleman presented with sudden-onset slurred speech, increased involuntary movements, and difficulty in eating and walking for 12 h before presentation. There was no history of fever, loss of consciousness, vomiting, palpitations, headache, trauma, bladder, or bowel complaints. A week before the present complaints, he had acute gastroenteritis and was admitted to a nursing home for 3 days where supportive treatment was instituted but no blood investigations were done. After discharge, he continued to have severe generalized weakness, mild difficulty in walking, mild involuntary movements, and anorexia. Five months before this presentation, he had facial twitching, tingling, and numbness all over the body and generalized weakness and was diagnosed to have thiazide-induced hypokalemia. So, he had been started on potassium supplements, which he had stopped a month back. He had been hypertensive for 3 years, but was taking treatment irregularly. He had never taken any kind of alternative therapy. He had taken the second dose of the Covishield vaccine (adenovirus) a month back. His son had early-onset diabetes, and his parents were hypertensive and dyslipidemic.

On examination, he was conscious and oriented with no focal neurological deficit. He had involuntary movements, dysarthria, and carpopedal spasm of left hand. Gag reflex was weak, there were no signs of meningeal irritation, and planters were equivocal. The rest of the systemic examination was normal. The clinical differentials thought of at this point of time were a cerebrovascular event (atherosclerotic) due to his age and history of hypertension, a viral infection due to the short history, although there had been no fever and/or a metabolic disorder.

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The basic investigations were normal, except for leukocytosis, hypokalemia, hypomagnesemia, and hypocalcemia [Table 1], and so, arterial blood gases were ordered and intravenous broad-spectrum antibiotics, calcium, magnesium, and potassium supplements were started. The arterial blood gas was suggestive of metabolic alkalosis (pH 7.5). Hormonal profile in the form of prostatic specific antigen (PSA), parathyroid hormone, and vitamin D and thyroid function tests were normal; also, autoantibodies (ANA and anti-phospholipid antibodies) were normal. So, an autoimmune disorder affecting the central nervous system (CNS) was ruled out.

Based on a low urinary calcium/creatinine ratio (0.2 mg/mg), a normal urinary magnesium and potassium, high plasma renin (>500 µIU/ml), and high urinary chloride (83 mEq/l) levels, a diagnosis of GS was made. Genetic sequencing was not done due to financial constraints. After 12 h of admission, as the magnesium, calcium, and potassium deficiencies were corrected, the involuntary movements stopped and ataxia improved. As dysarthria and mild dysphagia persisted, magnetic resonance imaging (MRI) of the brain and neck with angiography (could not be done earlier due to his involuntary movements) was done and it showed subacute infarct in the cerebellar vermis [Figure 1a] with complete absence of V1, V2, and V3 segments of the left vertebral artery. With the treatment offered, the patient improved symptomatically over the next 4 days. On discharge, the patient still had mild dysarthria and ataxia, while the potassium, magnesium, and calcium levels were in the normal range. After 1 week, and 3 months of discharge, on follow-up, the patient was asymptomatic and the potassium, magnesium, and calcium levels were normal. A repeat MRI of the brain after 3 months was normal [Figure 1b].

Table 1: Baseline investigations on admission

	On admission	Normal range
Hemoglobin	15.5	13-16.5 g/dl
TLC	17,000/mm^3	4000-10,000/mm^3
DLC	79/15/1/5	
ESR	19	mm/1st hour
CRP	<0.5	<1.0 mg/dl
S. creatinine	0.9 mg/dl	
RBS	92 mg/dl	
S. calcium	8.0 mEq	
Ionized calcium	0.98	1.1-1.5 mmol/l
S. magnesium	0.5	1.6-2.3 mg/dl
S. potassium	3.2	3.5-5.1 mmol/l
S. sodium	142	137-145 mmol/l
S. chloride	98.4	98-107 mmol/l
S. proteins	7.2	6.3-8.2 g/dl
S. albumin	4.08	3.5-5.0 g/dl
S. globulin	3.19	2.3-3.5 g/dl
ALT	30	10-50 IU/l
Urine routine	Normal	
Urine chloride	83 mmol/l	
ABG		
pH	7.5	7.35-7.45
pCO_2	41.5	32.0-48.0 mmHg
pO_2	72.9	83-108 mmHg
TCO_2	29.8	23-27 mmol/l
Bicarbonate	28.6	21-27 mmol/l
Base excess	+4.6	(−2) to (+3)
O2 saturation	93%	95%–99%
PTH	35.4	15-68 pg/ml
Vitamin D	100	30-100 ng/ml
PSA	0.87	0-4 ng/ml
Urine calcium/creatinine ratio	0.2	<0.26 mg/mg

Discussion

GS is a salt-losing tubulopathy characterized by hypokalemia, metabolic alkalosis with hypomagnesemia, hypocalciuria, and hyperreninemia. There are several case reports wherein GS was diagnosed in patients presenting with persistent hypokalemia,[3,4] sudden quadriparesis,[5] unresponsive tetany,[6] and severe hypocalcemia with periodic paralysis.[7] Our patient also presented with involuntary movements, ataxia, carpopedal spasm, and was then detected to have metabolic alkalosis with hypokalemia, hypocalcemia, and hypomagnesemia. He showed dramatic improvement with correction of the deficiencies [Table 2]. Even though hypocalcemia is rare in GS, it has been reported by Desai *et al*. and Pantanetti *et al*.[6,7] as a presenting feature. It is important to consider the diagnosis of GS in patients with unexplained and recurrent hypocalcemia which might be associated with hypokalemia. The cause of hypocalcemia, in

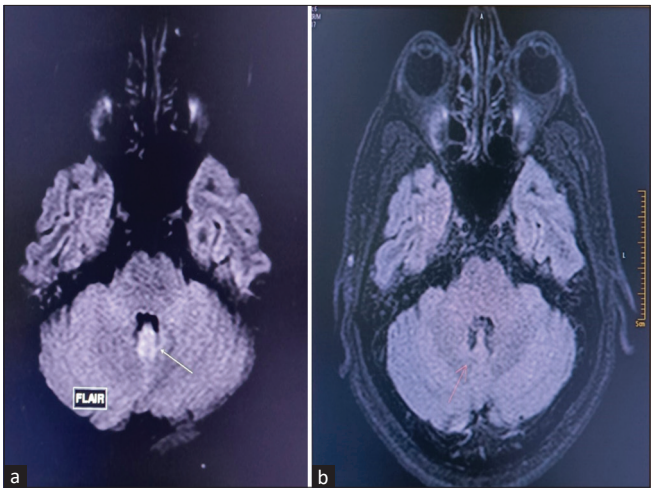

Figure 1: MRI (brain) flair image (a) showing the subacute infarct in cerebellar vermis (marked by the pointer). (b) Repeat scan after 3 months is normal. MRI = magnetic resonance imaging

Table 2: Serial monitoring of laboratory investigations of potassium, magnesium and calcium

	20/5	21/5	22/5	23/5	24/5	31/5	2/7
TLC (6000-10,000/mm^3)	17,000		15,000		11,000	10600	7000
DLC	79/15/1/5		85/7/1/4	79/14/3/4	79/14/3/4	75/21/2/2	76/20/2/2
S. potassium (3.5-5.1 mmol/l)		3.23	3.92	3.6	4.3	3.5	3.8
S. magnesium (1.5-2.3 mg/dl)	0.5	1.4		1.9		2.5	1.9
S. calcium (8.4-10.2 mg/dl)	8.0		8.75	7.62		10	9.2
Ionized calcium (1.10-1.5 mmol/l)	0.98	1.18		1.15	1.15		1.2

spite of hypocalciuria in GS, is postulated to be due to *hypomagnesemia*-induced impaired synthesis, secretion of PTH, end-organ resistance to PTH and vitamin D. Tetany is due to hypomagnesemia. It can be differentiated from enteral loss of potassium by high urinary chloride levels, as was seen in our patient. Usually, this syndrome can be unmasked after excessive vomiting or gastroenteritis, as was seen in our patient. Management includes liberal salt intake with oral magnesium and potassium supplements.[3] Potassium-sparing diuretics, ACEI, and ARBs have been used occasionally. There is limited data on the long-term consequences of the syndrome, such as chondrocalcinosis, chronic kidney disease, secondary hypertension, and cardiac arrythmias, due to its rarity, and a close follow-up is necessary to look for these. Certain drugs like proton pump inhibitors, antimicrobials like aminoglycosides, antiretrovirals, amphotericin, thiazides, xanthine, verapamil, and insulin in high doses with glucose need to be avoided or should be used with caution.[2]

Our patient responded well to potassium, magnesium, and calcium correction. He also had cerebellar infarcts, which could be secondary to hypomagnesemia and may be a part of new entity called *hypomagnesemia-induced cerebellar syndrome*.[8] There are case reports of severe hypomagnesemia causing cerebellar ataxia with hyperintensities on MRI, which is reversible on correction of magnesium levels, as was seen in our patient.[8-10] It is postulated that the low magnesium levels may cause vascular endothelial dysregulation and cerebral edema, similar to rapid rises in blood pressure seen in posterior reversible encephalopathy syndrome or eclampsia.[9,10]

In conclusion, GS, though rare, should be considered in patients with a combination of unexplained persistent hypokalemia, tetany, and cerebellar ataxia. It may rarely present with hypocalcemia. Also, magnesium levels should be checked in all cases of cerebellar ataxias, as the newly described hypomagnesemia-induced cerebellar syndrome should not be missed.

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Conflicts of interest

There are no conflicts of interest.

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