GITELMAN'S SYNDROME PRESENTED WITH TETANY: A CASE REPORT

Md. Zahid Alam, AMB Safdar, Shabnam Jahan Hoque, Rownak Jahan Tamanna, Rowsan Ara and MM Zahurul Alam Khan

Department of Cardiology, Bangladesh Institute of Research & Rehabilitation in Diabetes Endocrine and Metabolic Disorders (BIRDEM)

Abstract

Gitelman's syndrome is an autosomal recessive disorder caused by a defect of the thiazide-sensitive sodium chloride co-transporter at the distal tubule, characterized by hypomagnesemia, hypokalemic alkalosis and hypocalciuria. We report a case of Gitlman's syndrome in a 44 years old female patient who presented with generalized muscle weakness and carpal spasm and characteristic electrolyte abnormalities. This condition is sometimes confused with Bartter's syndrome.

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Key words: Gitelman's syndrome, tetany

Introduction

Gitelman's syndrome is an autosomal recessive disorders with characteristic metabolic abnormalities which are hypokalemia, metabolic alkalosis, hyperreninemia, hyperplasia of the juxtaglomerular apparatus, hyperaldosteronism and in some patients, hypomagnesemia.[1-3] It is usually confused with Bartter's syndrome and primary hyperaldosteronism. However, Gitelman's syndrome is usually not present until adulthood and has hypocalciuria which are opposite features of Bartter's syndrome. Gitelman's syndrome also differs from primary hyperaldosteronism in two ways – the patients are not hypertensive and the plasma renin activity is increased which is not suppressed by aldosterone induced volume expansion.[4,5] The estimated prevalence is approximately 1 per 40,000.[6] It is often not diagnosed until late childhood or even adulthood.[2] The dominant features are fatigue, weakness, muscle cramp, polyuria and nocturia.[4,7,8] Here we report a case of Gitelman's syndrome presented with tetany.

Case report

A 44 years old female was admitted to our hospital with complaints of fever for one month and vomiting for 15 days. She was normotensive, and a known case of type 2 diabetes mellitus for 14 years and was on premixed insulin for 10 years. She denied any form of self-medication, surreptitious diuretic and laxative abuse. There was no history of persistent vomiting, diarrhea, chest pains and exacerbation of weakness by exertion or after heavy carbohydrate meal. Family history was unremarkable. After four days of hospital admission, she developed carpal spasm and increased generalized weakness.

On examination, she was clinically euvolemic with normal skin turgor and no peripheral edema. Carpal spasm was present with positive Chvostek's sign. The blood pressure was 110/70 mmHg and pulse rate was 84/ minute. Apart from mildly reduced ankle jerks there was no other neurological deficit or proximal muscle weakness. ECG showed prolong QT interval with hypokalemic changes. Laboratory investigations showed low serum potassium (2.4 meq/L), sodium (119 meq), chloride (75 meq/L), magnesium (0.4 mmol/L) and calcium (6.8 mg/dl). Serum bicarbonate was 28 meq/L while serum urea and creatinine were 12 mg/ dl and 0.8 mg/ dl respectively. Blood pH was 7.50. The urinary calcium was subnormal at 18 mg/24 hour

Address for Correspondence:

Dr. Md. Zahid Alam, Junior consultant, Department of Cardiology (Room: 813), BIRDEM Hospital, 122 Kazi Nazrul Islam Avenue, Shahbagh, Dhaka-1000, email: ilazybear@yahoo.com

while on intravenous calcium supplementation (normal range 250 - 300 mg/24 hour in a high Ca^{2+} supplement). Urine sodium was 117 mmol/24 hour (40-220 mmol), potassium 22 mmol/24 hour (25-150 mmol) and chloride 115 mmol/24 hour (110-250 mmol). Urine specific gravity and urine osmolality were normal. Thyroid function tests (FT3, FT4, TSH), serum parathyroid and cortisol levels were normal. Ultrasound of the abdomen did not reveal any abnormality. Patient was treated with electrolyte supplement. But she did not recover from hypokalemia until spironolactone (100mg twice daily) was started. Based on the above features, the case was diagnosed as Gitleman's syndrome.

Discussion

Gitelman's syndrome is an inherited disorder of sodium chloride transport channel of distal renal tubules characterized by hypomagnesemia, hypokalemia and hypocalciuria. The diagnosis is usually made on the basis of clinical and biochemical findings. Patients are frequently asymptomatic or may present with transient episodes of weakness, abdominal pain, constipation, vomiting, fever and tetany. Prolonged disease free intervals may result in delay in diagnosis until adulthood.[9] The outstanding biochemical findings in Gitelman's syndrome are hypomagnesemia and hypocalciuria. Hypokalemia and mild to moderate metabolic alkalosis are usually present but their presence is not necessary to establish the diagnosis. Urinary calcium in affected patients is usually below 2.0 mg/kg body weight per day and the urine calcium/ creatinine is less than 0.1.[10] Though Gitelman's syndrome is unlikely to present with tetany as in our case, there are reports of such unusual presentation earlier.[11-13] In our case we could not do plasma renin level to distinguish it from primary hyperaldosteronism as the test was not available in the country. However, the characteristics clinical and biochemical features and correction of hypokalemia with the addition of spironolactone suggest our case as Gitelman's syndrome. Adult onset and documentation of hypocalciuria help to differentiate it from Bartter's syndrome.

The tubular defect in sodium chloride transport is thought to initiate initial salt loss leading to mild volume depletion and activation of the renin-angiotensin-aldosterone system. The combination of hyperaldosteronism and increased distal flow, due to the reabsorptive defect, enhance potassium and hydrogen secretion at the secretory sites in the collecting tubules leading to hypokalemia and metabolic alkalosis. Because of the tendency to renal salt wasting, patients with Gitelman's syndrome have a lower blood pressure than that seen in the general population.[14,15] The hypocalciuria of Gitelman's syndrome suggests the involvement of the distal convoluted tubule, where reduced chloride absorption is associated with augmented calcium absorption.[16]

Regarding treatment, the tubular defect in Gitelman's syndrome cannot be corrected, thus, treatment is aimed at minimizing the effects of aldosterone production. So along with potassium and magnesium supplementation, administration of spironolactone is necessary and yields good result. In fact, our case did not recover from hypokalemia until spironolactone was started. 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 (ie extra table salt), 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.[17] Therefore, our case indicates that Gitleman's syndrome may present atypically with tetany.

References

1. Stein JH. The pathogenetic spectrum of Bartter's syndrome. *Kidney Int* 1985; **28**: 85.
2. Bettinelli A, Bianchett MG, Girardin E, Caringella A, Cecconi M, Appiani AC, *et al*. Use of calcium excretion values to distinguish two forms of primary renal tubular hypokalemic alkalosis: *Bartter's and Gitelman's syndrome. J Pediatr* 1992; **120**: 38-43.
3. Kurtz I. Molecular pathogenesis of Bartter's and Gitelman's syndromes. *Kidney Int* 1998; **54**: 1396.
4. Brenner RM, Brenner BM. Disorders of the kidney and urinary tract. In: Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL Editors. Harrison's Principles of Medicine, 15th ed. McGraw-Hill: NewYork 2001; 1601-2.
5. Umami V, Oktavia D, Kunmartini S, Wibisana D, Siregar P. Diagnosis and Clinical Approach in

Gitelman's Syndrome. *Acta Med Indones* 2011; **43**(1): 53-8.

6. Foo JW, O'Roak JN. Rare independent mutations in renal salt handling genes contribute to blood pressure variation. *Nat Genet* 2008; **40**: 592.
7. Monnens L, Bindels R, Grunfeld JP. Gitelman syndrome comes of age (editorial). *Nephrol Dial Transplant* 1998; **13**: 1617.
8. Cruz DN, Simon DB, Nelson-Williams C, *et al*. Mutations in the Na-Cl cotransporter reduce blood pressure in humans. *Hypertension* 2001; **37**: 1458.
9. Barakat AJ, Rennert OM. Gitelman's syndrome (familial hypokalemia- hypomagnesemia). *J Nephrol* 2001; **14**: 43-7.
10. Geven WB, Willem JL, Schroder CH. Study of the pathophysiology of Bartter/Gitelman's syndrome. Attempt of classification-role of renal magnesium depletion. *Magnesium Bull* 1994; **16**: 29-36.
11. Nakamura A, Shimizu C, Nagai S. A rare case of Gitelman's syndrome presenting with hypocalcemia and osteopenia. *J Endocrinol Invest* 2005; **28**: 464-8.
12. Ran XW, Wang C, Dai F. A case of Gitelman's syndrome presenting with severe hypocalcaemia and hypokalemic periodic paralysis. *Sichuan Da Xue Xue Bao Yi Xue Ban* 2005; **36**: 583-7.
13. Al-Ali N, Al-Sayed A, Ramadan A. A Case of Gitelman's Syndrome Presenting with Hypocalcemia. *Kuwait Medical Journal* 2008; **40**(1): 67-9.
14. Jamison RL, Ross JC, Kempson RL. Surreptitious diuretic ingestion and pseudo-Bartter's syndrome. *Am J Med* 1982; **73**: 142.
15. Fujita T, Ando K, Sato Y. Independent roles of prostaglandins and the renin-angiotensin system in abnormal vascular reactivity in Bartter's syndrome. *Am J Med* 1982; **73**: 71.
16. Giteman HJ. Hypokalemia, hypomagnesemia and alkalosis: Arose is a rose- or is it? *J Pediatr* 1992; **120**: 79-80.
17. Robson WL, Arbus GS, Balfe JW. Bartter's syndrome. *Am J Dis Child* 1979; **133**: 636-8.