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A 13 YEAR OLD GIRL WITH MUSCLE WEAKNESS AND VENTRICULAR TACHYCARDIA

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ABSTRACT

Gitelman's syndrome is characterized by hypokalemia, hypomagnesemia and hypocalciuria. It is an autosomal recessive renal disorder and mostly present with asymptomatic hypokalemia but muscle cramps, dizziness, fatigue, muscle weakness and arrhythmias are the usual presentation. Same is the case with us, young girl presented with multiple symptoms and arrhythmia was worked up for electrolyte imbalance. Long term prognosis in terms of maintaining growth, renal function and life expectancy is excellent. Family screening is important for its early detection and treatment. This needs future genetic studies.

INTRODUCTION

Gitelman's syndrome (GS) is a autosomal recessive renal disorder characterized by hypokalemia, hypomagnesemia and hypocalciuria. As compared to bartter syndrome(BS), patients with GS presents usually at an older age.[1] They often present for workup of isolated, asymptomatic hypokalemia,[1-3] dizziness, fatigue, muscle weakness, cramps, nocturia and polyuria, in whom 90% are subsequently found to be salt wasters.[4] In fatal form they can presents with ventricular arrythmias and rhabdomyelysis due to hypokalaemia. GS is caused by defective NaCl transport in the distal convoluted tubule, and is linked to the gene encoding the thiazide sensitive Na-Cl-cotransporter located on chromosome 16q as compared to BS, have mutations in the transporters in the thick ascending loop of Henle (NKCC2, ROMK, and C1C-Kb).[5,6] Treatment of GS consists of potassium and magnesium salt replacement. Long term prognosis in terms of maintaining growth, renal function and life expectancy is excellent.[7,8]

CASE REPORT

13 years old girl was brought into emergency room in semiconscious condition. According to her mother she was complaining of fever and chills. Her blood pressure was 110 systolic and 65 diastolic with heart rate 87 per minute regular. She was febrile and having Glasgow comma scale (GCS) 13/15. Planters were bilaterally equivocal and power was 2/5 in both lower limbs and 3/5 in both upper limbs. There was pansystolic murmur at apex radiating to left axilla. Rest of the

Table 1: Serum Potassium Level during Hospital Stay

Duration	At arrival	12 hours	24 hours	48 hours	72 hours	7 day	10th day	14th day
Serum K^+(mmol/l)	1.3	1.9	2.2	2.6	2.8	3.1	3.0	3.2

examination was un remarkable.

Her previous records shows that she recently took her own from Punjab Institute of Cardiology Lahore after being treated for infective endocarditis with Gentamicin and Benzyl Penicillin for 28 days. According to her mother she has recurrent problem of lower limbs weakness and periodic paralysis for which she was treated by different family physicians. She was anorexic and vomited multiple times during her travel from Lahore to Peshawar. Her echocardiography shows severe mitral regurgitation with multiple vegetations on mitral valve leaflets.

She was admitted with suspected stroke secondary to embolism as complication of infective endocarditis. Computed tomography of brain was normal. Her investigation serum electrolytes, urea, creatinine, full blood count, ESR, liver function test, CRP and serum calcium were sent immediately. She was monitored in CCU and IV fluids started. Mean while she went into cardiac arrest and ECG shows torsade's de pointes (Figure 1), she was immediately cardioverted with 260 Joules asynchronized. Patient successfully recovered and ECG shows long QT of 0.54 ms. IV calcium gluconate and IV potassium and magnesium were given.

The arterial blood gases shows pH 7.56, $PaCO_2$ 1.8 kPa, PaO_2 15 kPa and bicarbonate 32 mmol/l. Her investigation showed potassium 1.3 mmol/l, calcium 7.2 mg/dl, urea 92 mg/dl, creatinine 1.9 mg/dl and rest of the investigation were normal. IV potassium started and serum electrolytes repeated every four hourly to see response to replacement of potassium. Muscle power improved after potassium replacement to 4/5 in both upper and lower limbs, ECG still showed long QT (Figure 2).

Despite adequate potassium replacement as per protocol her potassium was still 2.6 mmol/l after 48 hours. As a suspicion of refractory hypokalemia her serum magnesium was sent which were low 0.3 mg/dl. We also replaced magnesium intravenously and her condition improved. Her serial potassium is shown in Table 1.

A detailed family history revealed that one of her brother has symptom of nocturia, polyurea ,dizziness and leg cramps while rest of her 5 siblings are normal. Doing the baseline investigation of her brother shows serum potassium of 2.7 mmol/l. Then with probable diagnosis of Barter and Gittleman syndrome serum rennin and aldosterone level were measured and were increased. 24 hours urinary poatassium, sodium, magnesium and calcium, were also measured showed low calcium level and high magnesium, potassium and sodium were high which differentiate Gittleman syndrome from Barter syndrome.

She was started on replacement of large doses of magnesium and potasium orally and advised to avoid consumption of heavy amounts of lemon juices and tea because the may aggravate hypokalemia. Mean while her blood culture yielded staph aureus and was started on Vancomycin and Ampicillin IV for 6 weeks. After 15 days the patient was afebrile, appetite improved and was generally well. Repeated echocardiography showed regressed vegetation. After 6 weeks of completion of treatment of infective endocarditis patient was discharged and advised to take potassium and magnesium regularly. Patient was also referred to cardiovascular surgeon for mitral valve replacement.

DISCUSSION

Bartter syndrome and Gitelman syndrome usually presents with complaints of constipation, fatigue, dizziness, muscle cramps and weakness, secondary to chronic hypokalemia.[8,9] But our patient present with bilateral leg weakness because of severe hypokalaemia which then went to cardiac arrest, which was successfully cardioverted. The biochemical features of both these syndromes include hypokalemic, hypochloremic metabolic, high plasma renin activity and high aldosterone concentration.[8-10]

Although the chronic hypokalemia may be mild but it can be aggravated by diarrhea or vomiting precipitating prolonged QT interval, rhabdomyolysis, paralysis, cardiac arrhythmia, syncope and sudden death.[11] Our patient present with

Figure 1: ECG showing Torsade's De Pointes

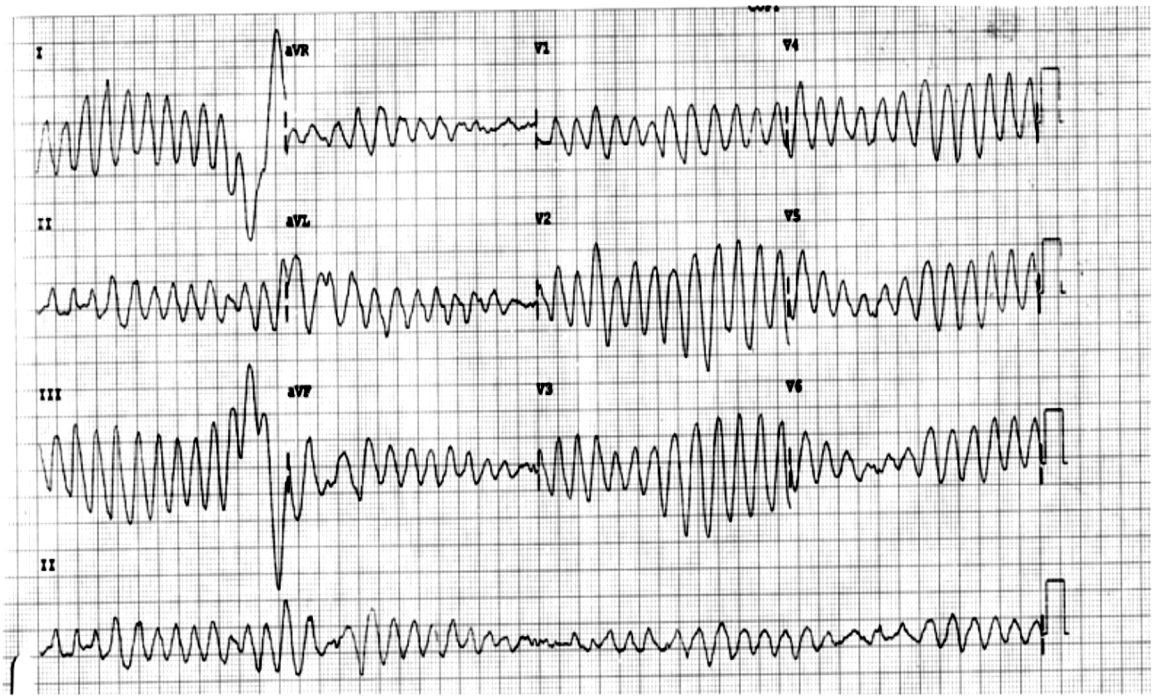
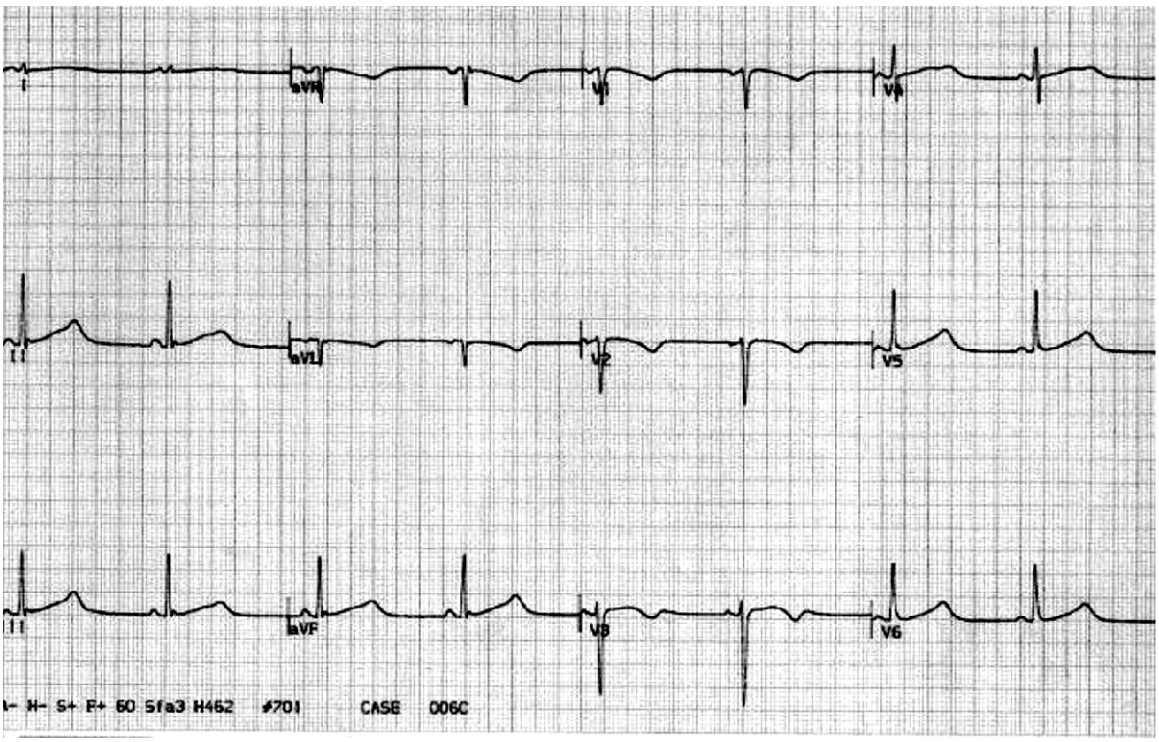


Figure 2: ECG showing Long QT Syndrome



weakness of all limbs because of aggrevated hypokalaemia by vomiting which last into cardiac arrest because of cardiac arrythmias. Alcohol abuse, cocaine or other drug abuse can also precipitate life-threatening arrhythmia.[11] Prompt electrolyte balance and fluid replacement, oral potassium supplementation, potassium sparing diuretics, cyclo-oxygenase inhibitors and renin-angiotensin inhibitors become life-saving in such emergencies.[11]

Finally in familial cases, both conditions are conveyed by autosomal recessive transmission.[10,12] This also support our case because one of the brother of the patient was also affected. The site of defect is at the distal convoluted tubule (DCT) in Gitelman syndrome. Gitelman syndrome is usually associated with less severe failure to thrive and the growth retardation is usually milder as compare to barrter syndrome. Gitelman symptoms are similar to thiazide diuretic-abusers with salt wasting.[13,14]

Indeed, Gitelman patients are mostly asymptomatic. They often present for workup of isolated asymptomatic hypokalemia,[13] Chronic hypokalemia may give rise to interstitial nephritis. Noncompliance with potassium chloride supplementation and other therapy is very important issue in long-term follow-up of these patients. Urinary calcium excretion is important because it distinguishes between the two syndromes.[10] In contrast to the hypocalciuria of Gitelman syndrome, Bartter patients are often documented to have hypercalciuria which differentiate the two. This finding was evident in our case and has differentiated it from Bartter syndrome.

The molecular defects of chloride reabsorption in Bart ter syndrome[1-3] and Gitelman syndrome[3] originate at different sites of the nephron. The transport defects for Bartter syndrome are at the TAL of the loop of Henle and for Gitelman syndrome at the DCT, respectively. Gitelman syndrome[15] is due to defective NaCl-cotransporter (NCCT) at the DCT which is encoded by the SLC12A3 gene. Significantly, the abnormal mutation of the NCCT protein in DCT is also expressed in blood mononuclear cells,[15] which are easily accessible for the study. Measurement of urinary chloride excretion can help to distinguish between renal and non-renal causes of chloride loss.[7]

Distinguishing between Bartter and Gitelman syndromes is not always straightforward due to phenotypic variance of the two syndrome. Genetic diagnosis is now possible, but there are several limitations including lack of general availability, cost and absence of "hot spot" mutations along the gene. The gitelman syndrome patients are thiazide diuretics resistant for fractional excretion of chloride.[5,6] So this can be utilized for differentiation among the two syndrome but this is contraindicated in small children because of severe hypovolumia.

In conclusion Gitelman's syndrome is not a straightforward diagnosis due to its phenotypic variance with Barter's syndrome. It is a rare disease but still exists. Family screening is really important which needs further genetic studies.

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