

A case report on a rare combination of Gitelman syndrome and marfanoid body habitus in a young female

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Introduction

We present a unique case report of a young female, who presented with clinical features of severe hypokalemia along with the Marfanoid body habitus. The evaluation of hypokalemia revealed Gitelman syndrome as the possible underlying etiology. The clinical diagnosis of the combination of Gitelman syndrome and marfanoid body habitus is a rare phenomenon that has been reported only once in the literature, to the best of our knowledge. [1] In Gitelman syndrome, the prevalence is 1 in 40,000 people, and males and females are equally affected. The prevalence of Marfan syndrome is 1 in 5000 people.

Case Presentation

A 22-year-old female with marfanoid body habitus presented with generalized body weakness for 02 weeks with predominantly affected bilateral lower limbs. The weakness was worsening over the last 05 days. She denied a history of fever, a preceding history of gastrointestinal or respiratory tract infections, and associated other neurological symptoms. She had no other features to suggest hypo or hyperthyroidism and was not on long-term medications such as steroids or statins. She had no positive family history of Marfan syndrome or myopathies.

Regarding her physical examination, she was thin and tall (BMI of 16.8 kgm⁻²) with characteristic Marfanoid facies including a long narrow face with malar hypoplasia, down-slanting eyes, high arched palate, and micrognathia.

Her height was 158 cm with an arm span of 163 cm but in the context of scoliosis. (Figure 2. A & B). She had arachnodactyly, and positive thumb, and wrist signs. (Figure 3. A, B & C). Her feet were flat. She had lumbar scoliosis. (Figure 2. B). No lens dislocation or cataracts were found. On auscultation, mid systolic click was found which was confirmed as mitral valve prolapse with the echocardiogram and there was no aortic root dilatation.

Following a thorough evaluation, initial differential diagnosis of Guillen Barre syndrome and spinal cord pathologies were clinically excluded.

But notably, on investigation she was found to have severe hypokalemia. She had no recent history of vomiting, diarrhea, or clinical history to support the suspicion of refeeding syndrome. She was not on medications such as diuretics which can cause hypokalemia and there was no obvious cause to suggest redistribution. She had no history of renal calculi and no family history of renal diseases such as chronic kidney disease or polycystic kidney disease. So, in this patient, renal loss of potassium was suspected as there was no evidence to suggest gastrointestinal loss or redistribution and subsequently, it was confirmed biochemically.

She had severe hypokalemia with a value of 1.7 mmol/L and the serum sodium level was normal. Further evaluation confirmed the excessive urinary loss of potassium (urine K⁺ 45 mmol/L). She was normotensive with a blood pressure of 100/60 mmHg. At this point, the most likely tentative diagnosis was type 1 renal tubular acidosis associated with Marfan syndrome. But her arterial blood gas

findings and serum chloride level were against the diagnosis of renal tubular acidosis in the presence of metabolic alkalosis with normal serum chloride.

In further evaluation, she was in a state of hypocalciuric with low urine calcium (mg/dl) to urine creatinine (mg/dl) ratio (0.03) and significantly low 24-hours urinary calcium excretion with

coexisting hypomagnesemia. Her serum creatinine was normal and urinalysis showed no proteinuria. Her ECG showed a significant long QT interval (the corrected QT interval according to the Bazett formula was 745 msec). (Figure 1)

The most likely clinical diagnosis for hypokalemia was Gitelman syndrome.

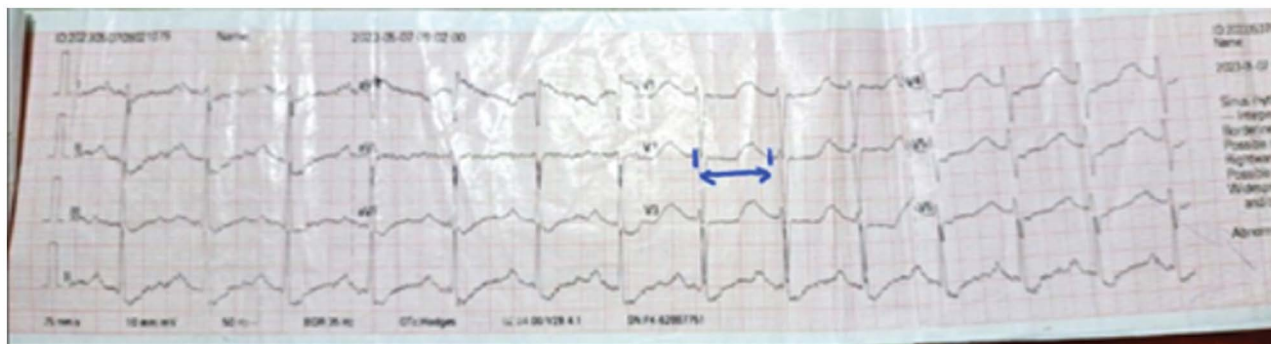


Figure 1 : ECG showing long QT

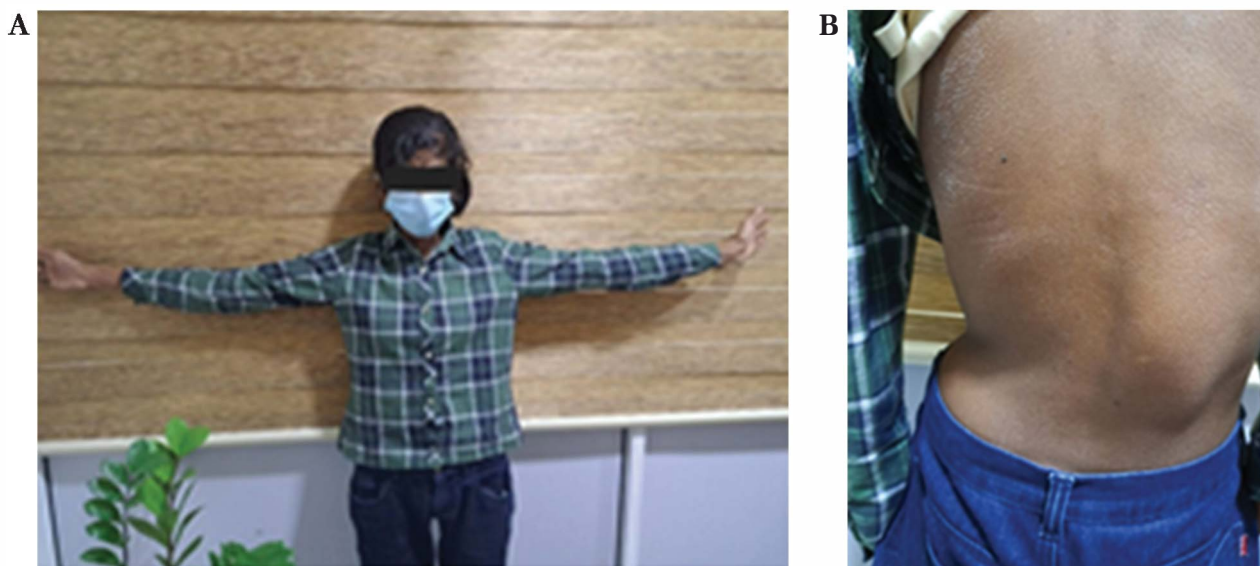


Figure 2 : A. Arms span > Height B. Scoliosis in the lumbar spine

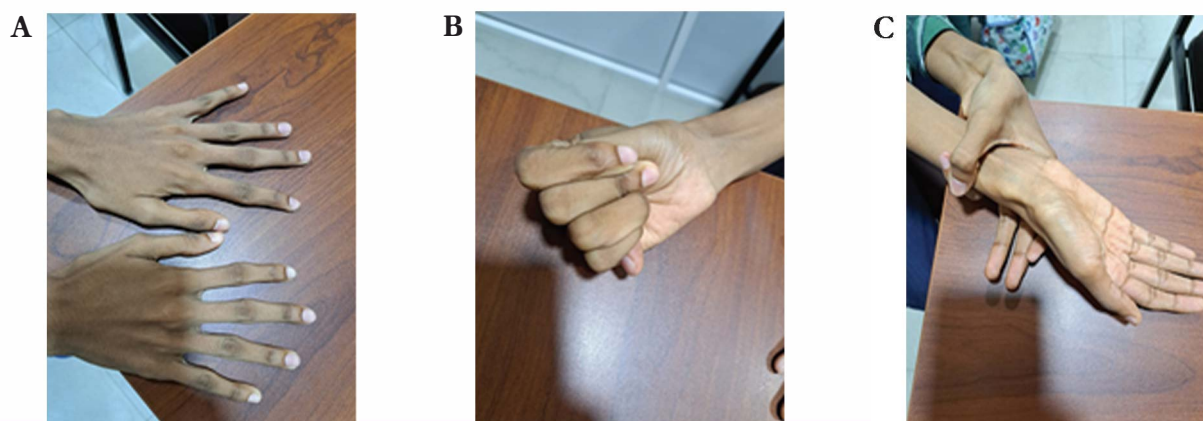


Figure 3 : A. Arachnodactyly (Spider fingers) B. Positive thumb sign (Steinberg sign)
C. Positive wrist sign (Walker sign)

Table 1 : Summary of investigations

Investigations	Results	Reference range
Serum electrolytes		
Na ⁺	140 mmol/L	135-145 mmol/L
K ⁺	1.7 mmol/L	3.5-5.5 mmol/L
Cl ⁻	102 mmol/L	95-105 mmol/L
Mg ²⁺	0.51 mmol/L	0.7-1.0 mmol/L
Ionized Ca ²⁺	1.16 mmol/L	1.15-1.33 mmol/L
Serum creatinine	66 micromol/L	70-115 micromol/L
Arterial blood gas Analysis	PH- 7.51	7.36-7.44
Urine K ⁺	45 mmol/L	<20 mmol/L
Urine Ca ²⁺	0.40 mg/dl	
Urine creatinine	15.80 mg/dl	
Urine calcium to urine creatinine ratio	0.03	<0.14
24hour urinary calcium excretion	<< 2.99 mmol/day	2.99- 68.61 mmol/day

Despite the presence of marfanoid body habitus, the criteria to diagnose Marfan syndrome were not met according to the revised Ghent criteria.

Therefore, finally, the patient was diagnosed with Gitelman syndrome with marfanoid body habitus.

She was managed symptomatically with the replacement of electrolytes with initial intravenous (IV) slow infusion of KCl and correction of magnesium with IV magnesium sulfate followed by oral supplements. She was not started on potassium-sparing diuretics such as spironolactone or amiloride as her potassium was normalized with the initial treatment. She was also advised on non-pharmacological management including intake of potassium-rich fruits and vegetables.

Her muscle weakness improved gradually to her normal functional status and she didn't develop complications such as arrhythmias and respiratory paralysis during the course of illness.

Discussion

The combination of Gitelman syndrome and Marfanoid body habitus is a rare occurrence. Gitelman syndrome is an autosomal recessively inherited renal tubular disorder with SLC12A3 mutation in chromosome 16q, causing excessive

urinary loss of potassium. Marfan syndrome is an autosomal dominant connective tissue disorder caused by variant mutations in the fibrillin-1 gene in chromosome 15q. Marfanoid body habitus refers to the physical features resembling Marfan syndrome. The aortic root dilatation and the ectopia lentis are the first and second hallmark features of Marfan syndrome respectively [4]. And also, as it is being inherited in an autosomal dominant pattern, family history can be positive. Marfan syndrome-associated hypokalemia due to type 1 renal tubular acidosis has been described well in the literature [2,3]. But our patient did not meet the criteria to diagnose either type 1 renal tubular acidosis or Marfan syndrome. Instead, she had a Marfanoid phenotype. The Marfanoid features include dysmorphic facial features such as dolichocephaly, malar hypoplasia, micrognathia, high arched and narrow palate with dental crowding and other system involvement. The physical examination may include thin and tall in stature, arachnodactyly, positive wrist and thumb sign, pectus deformities, scoliosis, flat feet and joint hypermobility. There can be cardiac, respiratory and skin manifestations as well. In the presence of Marfanoid features with unmet criteria to diagnose Marfan syndrome according to the 2010 Revised Ghent criteria, the differentiation of these two conditions can be done. According to the Revised Ghent criteria, her systemic score was 8 (wrist and thumb sign-3, plain pes planus-1, scoliosis-1, facial

features-1, skin striae-1, mitral valve prolapses -1) which indicated major systemic involvement (≥ 7)

The findings of hypokalemia due to urinary loss of potassium in a young patient with normal blood pressure, metabolic alkalosis, hypocalciuria and hypomagnesemia is suggestive of the diagnosis of Gitelman syndrome [9]. To confirm the diagnosis, though genetic testing is essential, in most settings, it cannot be performed due to cost and unavailability.

Conclusion

Hypokalemia due to urinary loss of potassium in the context of Marfanoid body habitus should raise awareness of the possibilities of Marfan syndrome with type 1 renal tubular acidosis and Gitelman syndrome with Marfanoid body habitus. In the presence of Marfanoid body habitus, it is always necessary to evaluate further for the complications as same as for Marfan syndrome.

Consent

Consent was given by the patient for this case report.

Conflicts of interests

The authors have no conflict of interest to declare.

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