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TEACHING FILES (GRAND ROUNDS)

# SEVERE HYPOKALEMIA IN AN ADOLESCENT: UNRAVELING THE MYSTERY OF GITELMAN SYNDROME

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**Clinical Problem:**

A 16 year old female presented in OPD with complaint of severe pain in lower limbs for 2 days, with reduced oral intake and generalized weakness, on presentation she was lethargic, sunken eyes and loss of skin turgor. She was admitted to Inpatient Department for further management. On examination the patient was afebrile, with feeble pulse but normal rate (76/min), RR 24/m, Blood pressure was low (70/50 mm of Hg), 92% O2 Saturation. In anthropometry Height 144 cm (Median height 50$^{th}$ percentile: 155 cm), weight 29 Kg (Median weight 50$^{th}$ percentile: 49 kg), head circumference (46.2 cm), MAC (19.5 cm), Abdominal circumference (46.2 cm), BMI 14 kg/m$^2$(underweight) were not appropriate for age (Failure to thrive). On general examination, the girl was afebrile, with sunken eyes, indicative of severe dehydration, which was further corroborated by the presence of marked hypotonia, diminished skin turgor, and a feeble pulse. She was cooperative with the examination. Skin was cold and dry with notable hyperpigmentation of knuckles. Patient had Sparse and dry hairs with normal distribution, no lymphadenopathy was noted. On respiratory examination, breath sounds were clear and equal bilaterally. The cardiovascular examination found a weak pulse, although her heart rate was normal at 76 beats per minute. Her blood pressure was notably low at 70/50 mmHg. No abnormal heart sounds were detected during the examination. Abdominal examination was soft abdomen with no organomegaly and no tenderness. CNS examination revealed altered mental status, characterized by confusion and disorientation. Her Glasgow Coma Scale score was 11 out of 15, with sub-scores of E4, V4, and M3. Additionally, significant muscle weakness was observed, with notable deficits in strength and tone. Muscle power assessment using the Medical Research Council scale yielded a grade of 2, indicating marked muscle weakness. She was also observed to have characteristic features of claw feet and short toes (Figure 1, 2, 3). Past history revealed episodes of muscle cramps and spasm on and off since 10-12 days.

**Figure 1.** Showing tetany/claw hands.

**Figure 2.** Short 1$^{st}$ toe in feet.

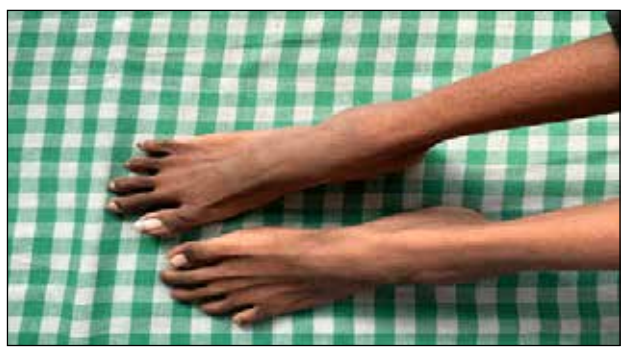

**Figure 3.** Showing tetany/Claw feet.

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**Table 1.** Laboratory findings in IPD.

| | Observed Value | Normal Values |
|---|---|---|
| Sr. Sodium | 134 mmol/L | 135-148 mmol/L |
| Sr. Potassium | 1.95 mmol/L | 3.5-5.3 mmol/L |
| Sr. Calcium | 8.3 mg/dl | 8-11 mg/dl |
| Mangnesium | 1.4 mE/L | 1.31-1.89 mE/L |
| Phosphorus | 1.8 md/dl | 4-7 mg/dl |
| Vitamin B12 | 149 pg/ml | 190-900 pg/ml |
| 25 OH Vit D3 | 8.1 ng/ml | <10 Severe Deficeat |
| 24 hr Urine for potassium | 18 mmol | 25-125 |
| Creatinine | 0.64 mg/dl | 0.8-1.3 mg/dl |
| GFR | 133 mL/min/1.73m | >100 mL/min/1.73m |
| TSH | 8.490 µIU/mL | 0.51-4.3 µIU/mL |
| T3 | 118 ng/dl | 91-217 ng/dl |
| T4 | 11.8 µg/dl | 5.9-13.2 µg/dl |
| Sr. Cortisol | 18.3 µg/dl | 3.7-19.4 µg/dl |
| Sr. ACTH | 21.9 pg/ml | 7.2-63.6 pg/ml |

These symptoms led us to perform various Laboratory evaluations which showed normal BSL (91 mg/dl), however serum electrolyte revealed hypokalemia, and hyponatremia as Na- 134 mmol/L, K 1.95 mmol/L and ionic Ca 0.98 mmol/L. CBC with Hb 13.5, WBC 8.4x103/ul, RBC 5.87x106/ul, PLT 302x103/ul, ESR 12 mm/Hr, SGPT 63.6 U/L, CRP 8.6 mg/L, PBS normocytic normochromic. To address the severe hypokalemia, we promptly administered potassium corrections and monitored electrolyte panel. Despite correction On Day 2nd, patient's potassium levels remained significantly low; and low calcium levels were also detected. This persistence of electrolyte imbalances, combined with the emergence of low calcium levels, indicated a potential underlying issue requiring further investigation. To better comprehend the patient's condition and identify possible underlying causes, we ordered additional comprehensive tests, including assessments of calcium, magnesium, phosphorus, Vitamin B12, 25-Hydroxy Vitamin D3.On Day 2nd investigations revealed calcium at 8.3 mg/dl, magnesium at 1.4 mEq/L, and phosphorus at 1.8 mg/dl. Vitamin B12 and 25-hydroxy vitamin D3 levels were also assessed, revealing values of 149 pg/ml and 8.1 ng/ml, respectively. Morning Electrolytes were Na 138.3 mmol/L K 2.49 mmol/L, Ca 0.95 mmol/L. ECG finding suggested ST depression & Abnormal T wave due to Electrolyte imbalance and Prolonged QT interval (QTC>495mS) with increased risk of arrhythmia. Evening Electrolytes were Na 137 mmol/L K 2.3 mmol/L, Ca 0.98 mmol/L. On Day 3rd A 24-hour urine test was performed to evaluate potassium excretion, which was found to be 18 mmol. Renal function was assessed with creatinine and glomerular filtration rate (GFR) yielding values of 0.64 mg/dl and 133 mL/min/1.73m, respectively. Morning Electrolytes were Na 138 mmol/L K 2.20 mmol/L, Ca 1.02 mmol/L. USG (abdo-pelvis) was within normal limits. On Day 4th Keeping in mind failure to thrive, Renal profiles and 24 Urine values, thyroid profile, Sr Cortisol & ACTH were evaluated (Table 1). By examining these parameters, we aimed to develop a more detailed understanding of the patient's electrolyte imbalances and create an effective treatment plan to address the root causes of their condition. Thyroid function was evaluated through thyroid-stimulating hormone (TSH), triiodothyronine (T3), and thyroxine (T4) measurements, which revealed values of 8.49 µIU/mL, 118 ng/dl, and 11.8 µg/dl, respectively. Hormonal assays were also conducted, showing cortisol levels of 18.3 µg/dl and adrenocorticotropic hormone (ACTH) levels of 21.9 pg/ml. ABG report revealed that the patient exhibits alkalosis (pH 7.478) with concurrent respiratory alkalosis (PCO2 25.4 mmHg) and compensatory metabolic acidosis (HCO3- 18.8 mmol/L). Base deficit was present as BE (ecf) of - 4.7 mmol/L. Electrolyte disturbances in ABG include hypokalemia (K+ 2.4 mmol/L), hypocalcemia (Ca++ 0.86 mmol/L), and hyperchloremia (Cl- 113 mmol/L), with normonatremia.

*So why Hypokalemia, Hypomagnesemia, hypotonia, low BP, FTT with low D3, B12 levels and increased GFR are associated with?*

**Discussion:**

The patient showed signs of muscle weakness and fatigue, likely caused by critically low potassium levels hypokalemia. Muscle cramps and spasms also occurred due to hypophosphatemia and hypokalemia. The patient’s Hypomagnesemia and Hypocalcaemia led to muscle twitching. The patient experienced excessive urination and thirst, likely due to impaired kidney function and an imbalance of acids and bases

in the blood. This imbalance, combined with electrolyte disturbances, caused persistent fatigue, weakness, and lethargy. The patient's blood pressure was low, due to impaired kidney function and electrolyte imbalances. Additionally, the patient was at risk of developing brittle bones and fractures due to disrupted calcium and magnesium metabolism. The patient was also diagnosed with Rickets, due to low vitamin D levels and impaired calcium metabolism. Despite electrolyte disturbances, the patient's adrenal gland function appeared normal, as indicated by normal hormone levels. Electrolyte imbalances include hyponatremia, hypophosphatemia, and low urinary potassium excretion, contributing to muscle weakness, fatigue, and cardiac arrhythmias. The patient was treated with multiple potassium correction till normal serum potassium level is achieved. Gitelman Syndrome is a rare autosomal recessive disorder caused by mutation in SLC12A3 gene leading to impaired salt re-absorption in the distal convoluted tubule.[1] Characterized by hypokalemic metabolic alkalosis, low urinary calcium levels, and magnesium deficiency[2,3], this condition typically manifests during late childhood or early adulthood. Gitelman Syndrome is particularly a defect in the apical thiazide sensitive sodium chloride cotransporter (NCCT) in the distal tubules.[4] The laboratory findings presented exhibit a characteristic profile of electrolyte and metabolic disturbances, aligning with the diagnostic criteria for Gitelman Syndrome, a rare genetic disorder. A prominent feature of this condition is the severe potassium deficiency, with a serum potassium level of 1.95 mmol/L; which accompanied by a notable magnesium deficiency, with a serum magnesium level of 1.4 mEq/L. The observed low calcium level of 8.3 mg/dl, in conjunction with normal renal function, suggests impaired urinary calcium excretion, a hallmark feature of Gitelman Syndrome. Furthermore, the presence of respiratory alkalosis , as indicated by the ABG report showing compensated metabolic acidosis hypokalemia, and hypomagnesemia, is consistent with this condition.[5] Normal renal function is supported by a serum creatinine level of 0.64 mg/dl and an elevated glomerular filtration rate (GFR) of 133 mL/min/1.73m$^2$. Additionally, the severe deficiency of 25-OH vitamin D3, with a level of 8.1 ng/ml, aligns with the expected biochemical profile of Gitelman Syndrome. Electrolyte imbalances, including hyponatremia, hypophosphatemia, and low urinary potassium excretion, are also characteristic of this condition. Thyroid function tests revealed an elevated thyroid-stimulating hormone (TSH) level of 8.490 µIU/mL, with normal triiodothyronine (T3) and thyroxine (T4) levels, suggesting subclinical hypothyroidism. Although thyroid dysfunction is not a characteristic feature of Gitelman Syndrome, it can occur in patients with this condition, possibly due to electrolyte imbalances. Adrenocorticotropic hormone (ACTH) levels in Gitelman Syndrome patients often fall within normal ranges or are slightly elevated. The observed ACTH value of 21.9 pg/mL aligns with this trend, suggesting that normal ACTH levels do not preclude a diagnosis of Gitelman Syndrome. Instead, diagnosis relies on a comprehensive evaluation of clinical presentation, electrolyte imbalances. Furthermore, stress triggered by electrolyte disturbances or other complications may influence ACTH levels, although this stress response does not necessarily translate to elevated ACTH levels. In terms of cortisol regulation, Gitelman Syndrome typically spares adrenal function, leading to expected normal cortisol levels. Cortisol production is regulated by the hypothalamic-pituitary-adrenal (HPA) axis, the hypothalamic-pituitary-adrenal (HPA) axis remains intact in Gitelman Syndrome, ensuring that patients' adrenal glands respond appropriately to stress, maintaining normal cortisol levels. In summary, the laboratory findings presented are consistent with Gitelman Syndrome, characterized by FTT adolescent with severe hypokalemia, hypomagnesemia, impaired urinary calcium excretion, and metabolic alkalosis, along with supporting features such as normal kidney function, low vitamin D levels, normal ACTH levels, and electrolyte imbalances. The patient was given discharge on Vitamin D, Magnesium and Thyroxine Orally after she had recovered from hypokalemia. Hypokalemia can be a complex condition to treat when it's associated with a genetic syndrome, such as Gitelman or Bartter syndrome. The presence of an underlying genetic defect or physiological imbalance often makes it difficult to completely cure hypokalemia. Hypokalemia associated with a syndrome can be considered a manageable condition, rather than one that can be completely cured.

**Compliance with ethical standards**

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**Conflict of Interest:** None

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