An Interesting Case of Fatigue

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Clinical History
A 27-year-old fruit vendor presented to Internal medicine casualty with history of fatiguability for 2 days, acute in onset and gradually progressive that restricted his activities of daily living.

- No h/o fever or night sweats
- No loss of weight or appetite, diarrhoea or vomiting
- No chest pain, dyspnoea on exertion, orthopnoea or PND
- No weakness of limbs/deviation of angle of mouth
- No palpitation or sweating
- No h/o alcohol intake.
- No illicit drug abuse or stressor.

Sleep and appetite normal, occasional alcoholic and smoker

Drug History- No known drug allergies, no h/o drug intake for chronic disease

Examination Findings
- General examination – Normal
- Vitals -stable, a febrile
- Chest-clear, Air entry equal on both sides
- CVS-S1+ S2+ No murmur
- GIT-No organomegaly
- CNS
  - Higher Functions- NORMAL
  - Cranial nerves – NORMAL
  - Motor System
    - Bulk-NORMAL
    - Tone – NORMAL B/L
    - Power-GR 5 IN B/L Upper limb
    - GR 5 IN B/L Lower Limb
  - Reflexes- Superficial and deep all normal
  - B/L flexor plantar
  - Test for coordination- NORMAL
  - ANS- Normal

Past History- No DM, Hypertension, TB, Asthma or recent COVID-19 infection

Family History- 4th child of non-consanguineous marriage
No h/o disease that run-in family

Personal History- Mixed diet, normal bowel and bladder
No signs of meningeal irritation
H/O AND EXAMINATION WISE EVERYTHING –NORMAL
ARRANGED FOR ECG AND SENT ALL ROUTINES….

Investigations
Hb-14.5
Tc-8900
Plt-3.5 L
Na/k- 133/2
Ca- 8.7
Mg-1.5
UA-3.5
TSH-4.83, fT3-0.4, fT4-1.1
COVID-19 rtpcr- NEGATIVE
CXR-NORMAL
USG abdomen-Liver – normal echotexture.
Right kidney-10*8*2
Left kidney -10*4*3
CMD maintained, no abnormalities
ECG

Findings
1. Presence of U wave.
2. Progressive Flattening of T wave.

Provisional Diagnosis
Hypokalemia ? Cause

Further Workup
We retook the history.
1. Revealed h/o 1 episode of acute onset of weakness of B/L upper limbs in 2016
2. Consulted local hospital
3. Given some IV fluids
4. Symptoms relieved in one day….
5. No further workup / No details of treatment available
6. Patient also ignored that as there were no further episodes

Hence we planned to evaluate the cause for hypokalemia and hence his fatigue
Diagnostic Approach for Hypokalemia Workup

- 24hr urine K-82.9 meq/day
- TTKG-9.6
- ABG
- Ph-7.49
- Pco2-41
- Po2-36
- Hco3-32
- So2-95
- K-<2
- Metabolic alkalosis
  - Urine chloride-252meq/l
  - Urine calcium-3mg/dl
- Urine creatinine -64 mg/dl
- Urine ca/cr-0.04 (<0.3)

Clinical Clues
- Hypokalemia
- Metabolic Alkalosis
- Hypocalciuria
- Hypomagnesemia

Diagnosis
- Gitelman Syndrome

Treatment
- Patient was started on Syrup potchlor and Inj KCL
Symptoms of patient improved dramatically
Serial measurements of potassium showed:
- DAY 1 - 2
- DAY 2 - 3.1
- DAY 3 - 3.1
- DAY 4 - 3.5
- DAY 5 - 3.9

Nephrology consultation was sent. Advised to discharge patient on Syrup KMac and to keep patient under follow up.
Patient was counselled and discharged Came for followup and had K levels corrected and fatiguability improved.

Discussion

- Syndrome first described By American nephrologist Hillel J. Gittelman who first identified condition in 1966 after observing a pair of sisters
- familial hypokalaemia-hypomagnesemia syndrome
- characterized by hypokalemic metabolic alkalosis in combination with significant hypomagnesemia and low urinary calcium excretion
- Prevalence: 1 in 40,000
- Symptoms do not appear before the age of six years and the disease is usually diagnosed during adolescence or adulthood.
- Follow AR Pattern of inheritance
- caused by mutations in the solute carrier family 12, member 3, SLC12A3 gene, which encodes the renal thiazide-sensitive sodium-chloride cotransporter NCC that is specifically expressed in the apical membrane of cells in the first part of the distal DCT

Pathology

- disruption of NaCl reabsorption in the DCT
- less NaCl is reabsorbed, more sodium reach in the collecting duct resulting in mild volume contraction
- RAAS activated and increasing renin activity and aldosterone levels.
- Elevated aldosterone levels give rise to increased electrogenic sodium reabsorption in the cortical CD via the ENaC.
- increased secretion of potassium and hydrogen ions, thus resulting in hypokalemia and metabolic alkalosis.
- passive Ca2+ reabsorption in the proximal tubule and reduced abundance of the epithelial Mg2+ channel TRPM6, located in the DCT explains thiazide-induced hypocalciuria and hypomagnesemia.
- thiazides are known to inhibit NCC, and there is phenotypic resemblance between GS and chronic thiazide-treatment.
Presentation

► usually present above six years of age and in many cases the diagnosis is only made at adult age
► tetany, especially during periods of fever or when extra magnesium is lost due to vomiting or diarrhea.
► Paresthesias, especially in the face
► experience severe fatigue interfering with daily activities, while others never complain of tiredness
► suffer from chondrocalcinosis, which is assumed to result from chronic hypomagnesemia.
► It causes swelling, local heat, and tenderness over the affected joints.
► symptoms, such as ataxia, vertigo, and blurred vision have been reported

Differential Diagnosis

1) Type 3 Bartter syndrome (CLCNKB mutation)
2) Primary renal hypomagnesemia
3) Chronic thiazide use
4) Chronic laxative abuse or chronic vomiting

Prognosis

► Excellent long-term prognosis.
► severity of fatigue may seriously hamper some patients in their daily activities
► Progression to renal insufficiency is extremely rare in GS
► One patient who developed chronic renal insufficiency and subsequent progression to ESRD has been reported in literature.

References

1. Orphanet journal of rare diseases.
2. Harrisons principles of Internal Medicine
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