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Hypokalemic Periodic Paralysis-A Case Report

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Abstract: ***It is a rare condition in which patients have severe episodes of muscle weakness concomitant to variations in blood potassium levels. It is an Autosomal dominant Condition. Periodic paralysis are channellopathies caused by mutation in genes encoding ion channels. Hypokalemic periodic paralysis is a diagnosis of Exclusion and recovery of weakness following potassium correction supports the diagnosis. Long term goal of therapy is to avoid attacks, Hence patients should be aware of importance of low carbohydrate diet and consequence of intense exercise.***

Keywords: Hypokalemic Periodic Paralysis (HypoKPP); Autosomal Dominant; Acute Onset Weakness

1. Introduction

Muscular Channelopathies
Muscle membrane excitability is affected in a group of disorders referred to as *Channelopathies*. These disorders are caused by ion channel dysfunction and majority of which are inherited as autosomal dominant trait. These include hypokalemic periodic paralysis, hyperkalemic periodic paralysis, paramyotoniacongenita, myotoniacongenita, potassium aggravated myotonia, and Anderson Tawil syndrome. General features include episodic weakness or stiffness, interictal return to an asymptomatic state and responsiveness to carbonic anhydrase inhibition.

Hypokalemic Periodic Paralysis (HypoKPP)
The prevalence of hypoKPP is approximately 1 per 100,000. This is an autosomal dominant disorder with episodes of limb weakness accompanied by hypokalemia usually begin during adolescence.

HypoKPP Type 1 is the most common form seen in upto 70% of the cases, and is caused by mutation in VGCC gene, CALCL1A3.Approximately 10-20% of cases are HypoKPP Type 2 arising from mutations in Voltage Sensitive Sodium Channel gene SCNA4A. in both forms the mutations lead to abnormal gating current that predisposes muscle to depolarize when potassium levels are low.

2. Case Reports

Case 1:

A 35-year-old male with no past history presented to the emergency department with complaints of cough for 3 days and acute onset muscle weakness in bilateral upper and lower limbs since morning. Patient gives history of more severe weakness in lower limbs than upper limbs noticed in the form of difficulty in getting up from squatting position, climbing stairs and buckling of knees while walking, however only slight difficulty in gripping his chappals. No history of difficulty in swallowing, speech or breathing, diplopia, no history of tingling sensation in limbs, no bladder and bowel symptoms, no history of similar complaints in past or in family.

On examination patient was conscious oriented, PR-110/min, BP-116/80mmHg, RR-20/min, Temperature-afebrile, GRBS-355 mg/dl, CNS examination shows decreased Tone in all 4 limbs, Power in bilateral upper limb was 3/5 and bilateral lower limb was 3/5 and bilateral DTR was +1, bilateral plantar was flexor and other neurological examination was normal. Other system examination was normal.

Investigations at admission is as follows: Serum Potassium-2.2 mEq/L, RBS-321mg/dL, ABG-normal, ECG-sinus tachycardia, u waves present and prolonged PR Interval; Other blood investigations were unremarkable.

Patient was admitted to ICU and started on IV KCL 40mEqin 500 ml NS over 4 hours, Oral KCl three times a day. Repeat potassium after 4 hours was 2.9 mEq/L. After 24 hours potassium was 3.4 mEq/L. Insulin given according to sliding scale. Repeat ECG was normal. There was significant improvement in weakness in bilateral upper and lower limb within 24 hrs.

Case 2:
A 21-year-old male patient presented to emergency medicine department with complaints of acute onset weakness and pain in upper limb and lower limbs. No history of sensory disturbances, bowel or bladder involvement. No history of head/neck trauma, headache, vomiting, blurring of vision, fever. However, patient gives history of strenuous exercise the previous day.

On examination, PR-62/min, BP-130/80mmHg, SpO2-99% at room air, Temperature-99.1F, CNS – Higher mental function-normal, Cranial nerve examination normal, Motor examination-Tone: UL-normal, LL-hypotonia; Power: UL-4/5, LL-2/5; DTR: UL-+1, LL-absent; Plantar: B/L Mute. Other Systems: normal. ECG-Inverted T waves and positive u waves in chest leads.

Investigations: Complete blood count-normal, RFT-WNL, Serum Potassium-2.5mEq/L, CKMB-normal, MRI brain and spine-normal study.

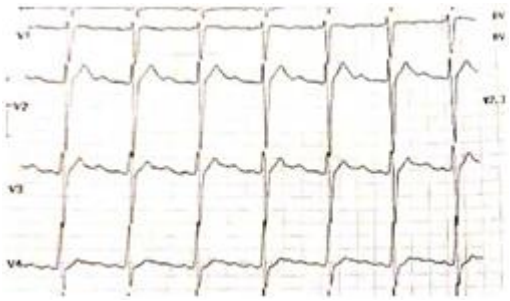
Patient was admitted and started on IV KCl infusion 40mEq/L over 3-4hours, oral potassium administration. Patient noticed improvement in weakness within 48hours

and Repeat S. Potassium was 4.1mEq/L and ECG changes were reversed.

Case 3:
A 32-year-old male patient was brought to the casualty with complaints of fever for 1 day, acute onset of lower limb weakness since 1 day, history of vomiting 3 to 4 episodes present. No history of numbness/tingling sensation of limbs, no history of bowel or bladder involvement, no history of progression of weakness, no history of difficulty in speech/ swallowing/ breathing. No history of loose stools. History of trekking the previous day present.

On examination, PR-87/min, BP-110/80mmHg, SpO2-99% at room air, Temperature-afebrile, CNS – Higher mental function-normal, Cranial nerve examination normal, Motor examination-Tone: UL-normal, LL-hypotonia; Power: UL-5/5, LL-3/5; DTR: UL-+1, LL-absent; Plantar: B/L Mute. Other Systems: normal. ECG-prolonged PR interval, positive u waves in chest leads.

Investigations: Complete blood count-normal, RFT-WNL, Serum Potassium-2.9mEq/L, CSF analysis-Normal, MRI brain and spine-normal study.



Patient was admitted and started on IV KCl infusion 20mEq/L over 4hours, oral potassium administration. Patient noticed improvement in weakness within 10 hours, however, ECG changes persisted and hence oral potassium administration was continued. The next day S. Potassium was 3.7mEq/L and ECG changes were reversed.

3. Discussion

Hypokalemic periodic paralysis is an autosomal dominant disorder with onset in adolescence. Males are more affected because of decreased penetrance in females. Attacks usually occur in the morning and is often triggered either by the ingestion of carbohydrate load and hish salt intake the previous night or rest following the strenuous exercise.

Generalised muscle weakness and reduced or absent tendon reflexes are characteristic. Weakness usually affects proximal limb muscles more than the distal. Sensory changes, fatigue or a feeling of heaviness or aching in the legs or back may herald the weakness. However, during the attacks level of consciousness and sensation is preserved. Ocular, bulbar and respiratory muscles are less likely to be affected. The frequency, length and severity of attacks may vary but typically resolves within 24 hours. Patients usually recover full strength although may develop severe disabling proximal lower extremity weakness as a late complication.

Pathophysiology
HypoKPP is caused by mutations in the voltage sensitive, skeletal muscle calcium channel gene, CALCL1A3. This channel functions as the voltage sensor of the ryanodine receptor and plays an important role in Excitation-Contraction coupling in skeletal muscle. Some 10-20% have mutations in voltage sensitive sodium channel gene SCN4A. These mutations allow a leak current to pass through the Gating Pore at resting membrane potentials, bypassing the central channel pore and leading to inappropriate muscle fibre depolarisation and consequent channel and action potential failure.

Diagnosis
An accurate clinical history is mainstay for the diagnosis because observation of attacks is unusual and patients are often normal between attacks. Low serum potassium level during an attack, excluding secondary causes establishes the diagnosis. Electrocardiogram changes includes increased PR interval, prolonged QT interval, flattened T waves, prominent u waves. Other diagnostic tests include electromyogram, muscle biopsy, genetic testing and provocative tests. EMG may demonstrate decreased action potential amplitudes during the attacks and may show electrical silence in severely weak muscles. However, in between attacks, the EMG and routine NCS are normal.

Treatment
Holistic approach to treatment includes lifestyle modifications, dietary changes, acute and long-term pharmacological intervention. Patient should be made aware of the importance of low carbohydrate, low sodium diet and the consequences of intense exercise.

Acute Attack: Potassium administrations can reverse severe attacks of weakness. Oral KCl 0.2-0.4 mmol/kg can be given every 30 min. IV therapy is necessary when there is swallowing problems or vomiting is present.

The long-term goal of therapy is to avoid attacks. Prophylactic administrations of carbonic anhydrase inhibitors like acetazolamide or dichlorphenamide effectively reduce the frequency of attacks. Potassium sparing diuretics or angiotensin converting enzyme inhibitors may also be of prophylactic benefit in patients with normal renal function in whom other conservative measures are insufficient.

4. Conclusion

Hypokalemic Periodic Paralysis is a relatively uncommon but potentially life threatening disorder wherein prompt identification and appropriate treatment can reverse the weakness and protect against the development of permanent myopathy.

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