Original Article

A Case Series Of Periodic Approach To Hypokalemic Periodic Paralysis - The Paralysis By The Potassium

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Doi: 10.47750/pnr.2022.13.S05.259

Abstract

In day-to-day practice, quadriparesis is one of the most common cases encountered by any practising clinician. Among the causes of quadriparesis, hypokalaemia remains one of the essential causes. Periodic paralysis secondary to hypokalaemia is one of the significant reversible causes, which on appropriate treatment, will completely reverse quadriparesis. This research article is about a series of four uncommon cases with a typical clinical presentation of quadriparesis secondary to hypokalaemia improved with potassium correction. A proper diagnostic approach to hypokalaemia during the initial presentation is necessary for early diagnosis and appropriate management. This article emphasises the importance of understanding the various associated features of quadriparesis, which will yield a diagnostic value.

Keywords: Quadriparesis, Hypokalemia, Periodic Paralysis

INTRODUCTION:

Potassium ion forms the primary cationic constituent of the intracellular component. The tendency to rapidly shift between the intracellular and extracellular compartments and the dynamic movement makes potassium ions vulnerable to changes. Periodic paralysis refers to short-lived, episodic hyporeflexia with or without myotonia.

We report a series of four cases of secondary periodic paralysis, which were brought due to the dysfunction of multiple organ systems like the renal system (Barters syndrome and Gitelman syndrome), endocrine (thyrotoxic periodic paralysis) and autoimmune disorders (Sjogren's syndrome).

CASE 1:

A 42-year-old male presented to the casualty with c/o weakness of bilateral lower limbs for the past three days, which was insidious and progressive in nature. His weakness worsened further to involve the bilateral upper limbs, and he could not ambulate. He also complained of tingling and numbness on and off. He had a significant history of similar complaints six months prior, which improved with treatment.

On clinical examination, the patient was conscious, oriented, and afebrile. His vitals were stable. Systemic examination revealed quadriparesis with a power of 3/5 in all four limbs, diminished deep tendon reflexes, and normal sensory examination. Other system examinations did not show any significant clinical findings. ECG showed normal sinus rhythm with “U” waves in the chest leads with no acute ST/T changes. Serum electrolytes were done, which revealed hypokalemia with a serum potassium of 1.5 meq/l and magnesium of 1.6 meq/l.

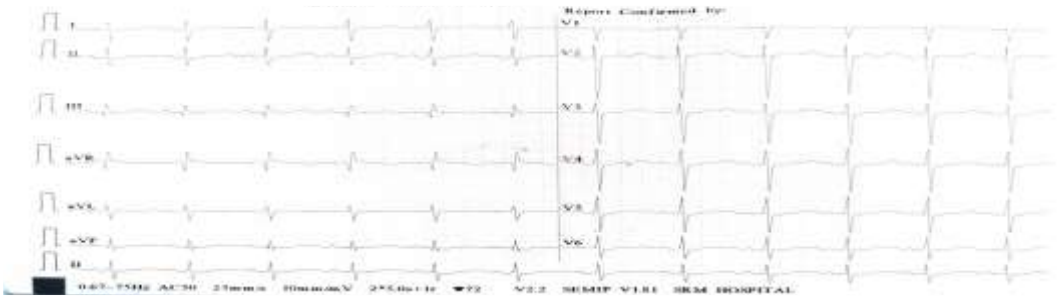

Figure 1: ECG showing sinus rhythm with T wave flattening and “U” waves in chest leads

The patient was further evaluated for hypokalemia after ruling out pseudohypokalemia. Urinary spot potassium was checked and found to be elevated, denoting probable renal cause of potassium loss. His Trans Tubular Potassium Gradient (TTKG) was found to be 12.9. The patient was normovolemic, and ABG showed metabolic acidosis. Urine examination showed urinary chloride levels of >20 with a urinary calcium creatinine ratio of 0.2, making a possible differential diagnosis of loop diuretics or barters syndrome. Since the patient was not on any diuretics, a diagnosis of barters syndrome was made, and he was advised to continue a high-potassium diet with potassium supplementation. He showed significant improvement in power after the normalisation of potassium.

CASE 2:

A 50-year-old female presented to the casualty with complaints of difficulty using both lower limbs for the past two days. It was insidious in onset and was gradually progressive. She had no other complaints, and there was no bowel or bladder incontinence. She had a history of working under the sun for two days. There was no other significant history. She had a history of covid 19 two months before this presentation. On clinical examination, her vitals were stable, and she had a power of 2/5 in both lower limbs with upper limb power of 3/5. Deep tendon reflexes were reduced, and the patient had hypotonia. The sensory system examination was normal. ABG was done, which showed metabolic alkalosis. Serum electrolytes were done, which revealed hypokalemia with potassium of 2.1meq/l.

The patient was started on potassium correction, following which her weakness improved. Pseudohypokalemia was ruled out, and further workup for hypokalemia was initiated. She had urinary potassium loss of 20meq/l, and TTKG was elevated. The urinary calcium and creatinine ratio was <0.15, which denoted a possibility of Gitelman syndrome as the patient was not on any diuretics.

CASE 3:

A 22-year-old male came to the hospital complaining of weakness in all four limbs for the past three days. He had an acute presentation with weakness involving the lower limbs first, rapidly progressing to involve the upper limbs within 24 hours. There was no sensory involvement or bowel and bladder involvement. The patient had a history of significant weight loss of around 5 kgs over the past two months, along with a history of palpitations. There was no history of similar complaints in the past.

On examination, the patient was conscious and oriented. He had tachycardia of 121 beats per minute. Neurological examination revealed reduced power in all four limbs, with 3/5 in lower limbs and 4+/5 in upper limbs. Deep tendon reflexes were depressed.

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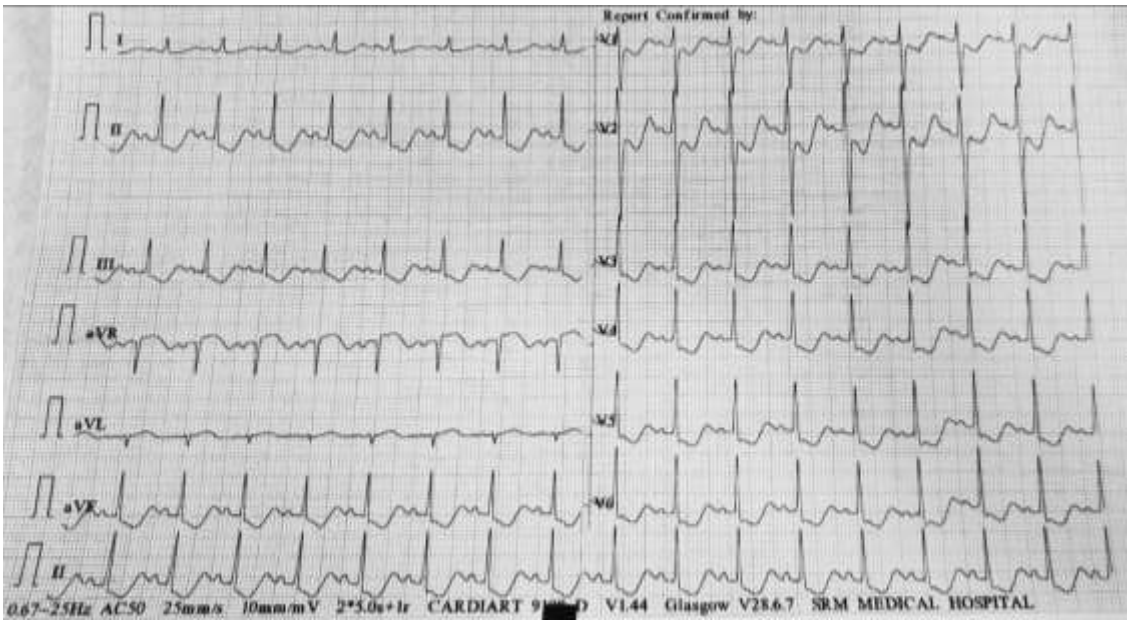

Figure 2: ECG showing sinus tachycardia with "U" waves in chest leads

ECG showed sinus tachycardia, ST depression and "u" waves. Blood investigations revealed hypokalemia with normal renal and liver parameters. History of weight loss, palpitation and sinus tachycardia provoked us to investigate for possible aetiology of hyperthyroidism. TFT showed reduced TSH and elevated T3 and T4 values, denoting hyperthyroidism. USG neck revealed diffuse enlargement of the gland with increased vascularity. Following the correction of potassium, the patient improved. He was started on carbimazole and beta blockers for the treatment of thyrotoxicosis.

CASE 4:

A 25-year-old female presented to the emergency with c/o difficulty using both upper and lower limbs for the past 16 days. Her quadriparesis was insidious in onset and progressive in nature. She did not give any history of vomiting, diarrhoea, chest pain or palpitations. She gave a history of dryness of eyes in the past, for which she is on topical lubricant. There was a history of

playing football for 4 hours under sunlight a day before the incident. She had a history of similar episodes twice in the past six months. She gave a family history of her mother having similar complaints.

Clinical examination revealed stable vitals with ABG showing metabolic acidosis. CNS examination revealed the power of 2/5 in all four limbs with normal higher mental function. She also had depressed reflexes with the mute plantar and insignificant sensory examination.

Serum potassium was found to be 1.7meq/l. The patient was started on potassium correction and the patient's clinical condition improved. Further workup was done for hypokalemia which revealed urinary potassium loss (22meq/l) with elevated TTKG and normal anion gap, indicating a probable renal tubular acidosis. Since the patient had dry eyes and positive family history, we evaluated the patient for autoimmune disease. It revealed ANA positivity in high titers with immunofluorescence showing a granular pattern.

S.NO	Antigen	Intensity	Class
1	SS-A native (60 kDa) (SSA)	68	+++
2	Ro-52 recombinant (52)	104	+++
3	SS-B(SSB)	3	O
4	PCNA	3	O
5	Control (Co)	85	+++

Table 1: Autoantibody profile

An entire autoimmune panel was done, which revealed SS-A native (60 kDa) positivity along with Rho-52 recombinant (52) positivity. The patient was provisionally diagnosed with Sjogren's syndrome and was started on treatment.

DISCUSSION:

Evaluation of Hypokalaemia periodic paralysis begins in the emergency room. Clinical suspicion with good history is the first step in diagnosing hypokalaemia. Quadriparesis is suspected when patients present with flaccid weakness, which is acute in onset involving proximal muscles with decreased or normal deep tendon reflexes.

History involves enquiring about symptoms of diarrhoea, vomiting, fever, past medication use and family history. Analysis of the neurological system plays a vital role in evaluating quadriparesis. ABG forms an integral part of the investigation.

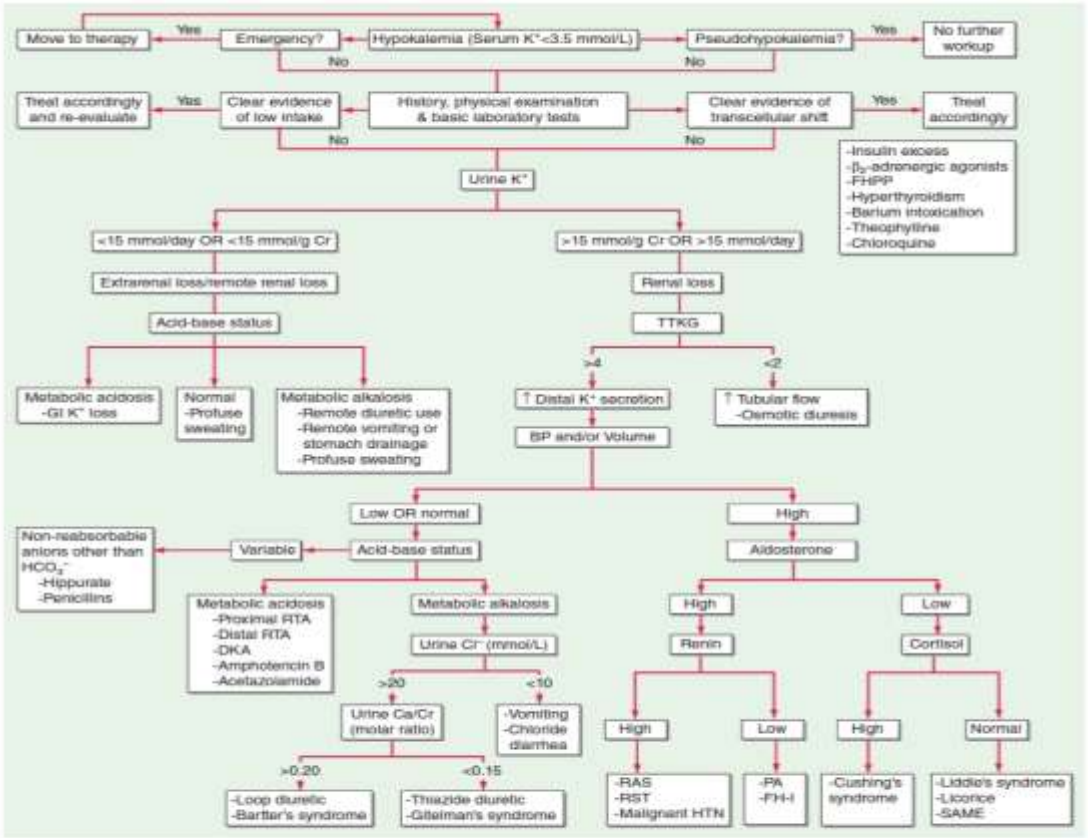

FIGURE 49-7 The diagnostic approach to hypokalemia. See text for details. AME, apparent mineralocorticoid excess; BP, blood pressure; CCD, cortical collecting duct; DKA, diabetic ketoacidosis; FH-I, familial hyperaldosteronism type I; FHPP, familial hypokalemic periodic paralysis; GI, gastrointestinal; GRA, glucocorticoid remediable aldosteronism; HTN, hypertension; PA, primary aldosteronism; RAS, renal artery stenosis; RST, renin-secreting tumor; RTA, renal tubular acidosis; SAME, syndrome of apparent mineralocorticoid excess; TTKG, transtubular potassium gradient. *(Used with permission from DB Mount, K Zandi-Nejad K: Disorders of potassium balance, in Brenner and Rector's The Kidney, 8th ed, BM Brenner [ed]. Philadelphia, W.B. Saunders & Company, 2008, pp 547–587.)*

Figure 3: Approach to hypokalaemia

When there is an established family history of hypokalaemia, periodic paralysis, and a low serum potassium level during a typical attack of weakness establishes the diagnosis and no further diagnostic investigations are needed.
Evaluation of the secondary causes of hypokalaemia paralysis is warranted only during the initial presentation. These include a thyroid function test (TSH, T3, T4 level) to rule out hyperthyroidism and an ECG, which may show the feature of Anderson syndrome, prolonged QT interval[1], apart from U waves.
In primary hypokalaemia periodic paralysis, serum potassium levels usually remain normal after or between attacks. A low serum potassium level between episodes usually represents a secondary cause of hypokalaemia, such as in distal renal tubular acidosis[2]. Further diagnostic options include genetic, provocative, and electromyography (EMG).

OUR CASE SERIES OF PERIODIC PARALYSIS SECONDARY TO HYPOKALEMIA :

- CASE 1: Barters syndromes
- CASE 2: Gitelman syndrome
- CASE 3: Thyrotoxic periodic paralysis
- CASE 4: Sjogren's syndrome

BARTERS SYNDROME:

Barters syndrome is inherited in an autosomal recessive pattern. The mechanism of hypokalaemia in barters syndrome is salt-losing tubulopathy. It is mainly characterised by metabolic alkalosis, hypokalaemia, hypochloraemia and normal blood pressure[3]. Our patient presented with quadriparesis due to hypokalaemia with a potassium of 1.5meq/l. In the further evaluation of hypokalaemia, he had metabolic alkalosis and normal blood pressure. The presence of hypertension increases potassium excretion via the tubules resulting in hypokalaemia. The absence of hypertension rules out mineralocorticoid excess states like hyperaldosteronism, Cushing's syndrome, and Liddle's syndrome[4].
With evidence of urinary loss of potassium with normal volume status and alkalosis, we evaluated the patient with urinary calcium creatine ratio, revealing the presence of Barters syndrome.
Hence when a presentation of periodic paralysis secondary to hypokalaemia is present, prompt suspicion of salt-losing tubulopathy is necessary to evaluate the cause of hypokalaemia.

GITELMAN'S SYNDROME:

Gitelman syndrome is also an autosomal recessive disease like Barters syndrome[5]. Loss of function mutation occurs in the sodium chloride co-transporter in the distal tubules. Loss of water, chloride, and sodium occurs, which triggers RAAS activation by a negative feedback mechanism.
More sodium is transported to the collecting ducts, where it is reabsorbed under the influence of aldosterone. The release and loss of potassium and hydrogen ions in the urine result in hypokalaemia and metabolic alkalosis[6]. Our patient had a similar presentation with hypokalaemia and metabolic alkalosis.
Additionally, this condition results in a dysfunction of the associated TRPM6 channel, which affects magnesium reabsorption [7]. As a result, magnesium is also excreted in the urine. Urinary magnesium values in our patient were elevated, and the patient had hypomagnesemia. Magnesium correction was done for him, along with potassium.
Hypomagnesemia leads to improper parathyroid hormone secretion[8], which leads to hypocalcemia. Gitelman syndrome, unlike Bartter, does not result in hypercalciuria. Thiazide diuretics also exert their effects on the NCCT channel, causing hypokalaemia. We ruled out thiazide usage.
Muscle weakness, tetany, weariness, and palpitations are symptoms related to low serum potassium and magnesium levels[9]. Clinically, Gitelman syndrome is less severe when compared to Bartter syndrome[10]. Our patient had a history of working under the hot sun for two days, which would have precipitated hypokalaemia.
Reports of sudden cardiac fatalities have been made in Gitelman syndrome. A diagnosis could be challenging, but it is crucial, given its rarity. Understanding the serum and urine biochemical picture is essential to identify it from a broad differential diagnosis.

THYROTOXIC PERIODIC PARALYSIS:

Thyrotoxic periodic paralysis constitutes a significant cause of a reversible form of periodic paralysis[11]. It is one of the common causes of acquired periodic paralysis. TPP affects more males with a male: female ratio of 20:1. Our patient (case 3), a young 24-year-old male, presented with weakness of limbs. The typical age of onset is second to fourth decades[12].
The pathogenesis of TPP is an elevated Na^+-K^+ ATPase(sodium-potassium) activity caused by elevated thyroid hormone, hyperadrenergic activity, hyperinsulinemia, and high androgen levels [13].
Clinical features of TPP are similar to those of familial periodic paralysis, with few patients presenting with tachycardia and palpitation history. Our patient had a history of palpitations in the past but was not evaluated for it.
Although Graves disease is the most common cause of hyperthyroidism[14], other causes of thyrotoxicosis, including exogenous thyroid hormone administration, can induce TPP. Our patient did not have any history of ingestion of thyroid supplements. Although hypokalaemia is commonly encountered in thyrotoxic periodic paralysis, normal potassium can also be expected[15].
Although antithyroid treatment is the most definitive treatment for TPP, acute cases like our patients require potassium correction to prevent cardiac arrhythmias and other complications.

SJOGRENS SYNDROME:

Sjogren's syndrome is a chronic, multisystem autoimmune illness that causes exocrine gland dysfunction[19]. It has a female preponderance with a female-to-male majority of 9:1.

Common presentations include dry eyes, dry mouth, and enlargement of salivary glands. However, renal involvement in Sjogren is not an uncommon presentation. Sjogren's syndrome is suspected based on clinical characteristics. Although plasma renin activity is decreased and aldosterone levels are higher, the aldosterone-renin ratio is often lower than in cases of primary aldosteronism brought on by an aldosterone-secreting adenoma.

Type 1 distal RTA is Sjogren's syndrome's most common renal involvement [20]. This can result in potassium loss leading to hypokalaemia.

Our patient presented with periodic paralysis with quadriparesis as the initial presentation. Sudden life-threatening muscle paralysis due to hypokalaemia is a severe clinical consequence of distal RTA [21,22]. Furter ABG showed metabolic acidosis and hypomagnesemia.

In SS, xerostomia and keratoconjunctivitis sicca are symptoms of chronic inflammation brought on by lymphocytic infiltration of the salivary and lacrimal glands and the deposition of many types of autoantibodies, primarily anti-SS-A (anti-Ro) and anti-SS-B (anti-La)[23]. Further workup showed anti-SSA and ro-52 positivity for our patient.

Treating hypokalaemia paralysis associated with renal tubular acidosis requires correcting hypokalaemia and treating the primary cause. Treatment of Sjogren's involves steroids and disease-modifying drugs[24].

Our patient was started on intravenous potassium correction, after which her weakness improved. She was also started on prednisolone and hydroxychloroquine.

CONCLUSION:

Early recognition is crucial and lifesaving in periodic paralysis secondary to hypokalemia. Good clinical history and systematic evaluation can help us in identifying the etiology. This case series of periodic paralysis secondary to hypokalemia signifies the importance of evaluating the various causes of hypokalemia.

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DECLARATION:

Ethical committee approval:

Ethical clearance was not required.

Declaration of patient consent:

The authors certify that appropriate patient consent was obtained.

AVAILABILITY OF DATA AND MATERIALS

The data is available in our texts and images and publicly available in the General Medicine department of SRM Medical college hospital and research centre through communication with the corresponding author.

Financial support and sponsorship:

Nil.

Conflicts of interest:

The authors certify that there are no conflicts of interest.

ACKNOWLEDGEMENT:

Not applicable