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Case Report

Internal Medicine Section

Hypokalaemic Periodic Paralysis in a Patient with Rheumatoid Arthritis: A Case Report

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ABSTRACT

Periodic skeletal muscle weakness in Hypokalaemic Periodic Paralysis (HPP) can lead to respiratory muscle failure and mortality. This muscle weakness is caused by decrease in serum potassium levels (<3.5 mmol/dL), which can be either primary or secondary. The present case report describes an unusual presentation of HPP in a 37-year-old female with known Rheumatoid Arthritis (RA), who complained of sudden-onset quadriparesis. Upon evaluation, the patient was diagnosed with hypokalaemia, and treatment for this condition resulted in marked improvement of the paresis. While there are several deadly neuromuscular causes of quadriparesis, dyselectrolytaemia should be evaluated and treated, especially in patients with autoimmune diseases. In such patients, hypokalaemia could be due to medications such as corticosteroids or immunosuppressants like methotrexate, or as a result of underlying renal tubular acidosis. The present report adds to the scant literature on the association between RA and HPP through detailed clinical examination, laboratory investigations, and successful management with potassium supplementation.

Keywords: Autoimmune diseases, Electrolyte imbalance, Immunosuppressants

CASE REPORT

A 37-year-old female presented to the Emergency Department with sudden-onset weakness affecting both upper and lower limbs, which she noticed upon waking three hours earlier. The weakness was neither ascending nor descending in nature and was not associated with autonomic dysfunction or paresthesia. Throughout the day, her weakness progressed without associated respiratory symptoms such as dyspnoea or breathlessness at rest, or gastrointestinal symptoms such as fever or diarrhoea, rendering her unable to stand or perform routine activities by evening. She denied any past medical history of hypertension, asthma, tuberculosis, or other co-morbidities and there was no history suggestive of trauma. She has a one-year history of RA, confirmed by an RA factor of 25 U/L and an anticyclic citrullinated antibody level of 42 U. She had been on a multidrug regimen for one month, consisting of Tab. Prednisolone 40 mg OD, Tab. Hydroxychloroquine (HCQ) 200 mg OD, and Tab. Methotrexate 7.5 mg once a week, along with folic acid 5 mg OD, due to general joint pain and morning stiffness characteristic of her RA. She had no history of addiction, and her sleep pattern was reported as normal. There was no relevant family history reported.

Upon examination, the patient presented with stable vital signs, including a respiratory rate of 16 breaths per minute, single breath counts lasting 22 seconds, and a single breath-holding time of 30 seconds, along with an oxygen saturation of 98% on room air [Table/Fig-1]. Additionally, her blood pressure measured 130/90 mmHg, and her pulse was 95 beats per minute. Neurologically, the patient remained alert and oriented, achieving a Glasgow Coma Scale score of E4V5M6. An asymmetric reduction in muscle strength was noted in both upper and lower limbs, reflected by a Medical Research Council (MRC) scale score of 1/5 in the right upper limb, 3/5 in the right lower limb, and 2/5 in both upper and lower limbs on the left side, with intact sensation, no paresthesia, and normal deep tendon reflexes [Table/Fig-2]. Cardiovascular examination revealed regular heart sounds without murmurs, while respiratory assessment demonstrated clear breath sounds bilaterally. Abdominal examination yielded normal findings, devoid of tenderness, organomegaly, or masses. The musculoskeletal evaluation revealed generalised joint tenderness, consistent with the patient's history of RA, without notable swelling or deformities. An Electrocardiogram (ECG) was also performed [Table/Fig-3], revealing a normal sinus rhythm with U waves in leads V2-V6 and a prolonged QTc interval, highlighting the cardiac implications of hypokalaemia. The patient also reported normal bowel and bladder function.

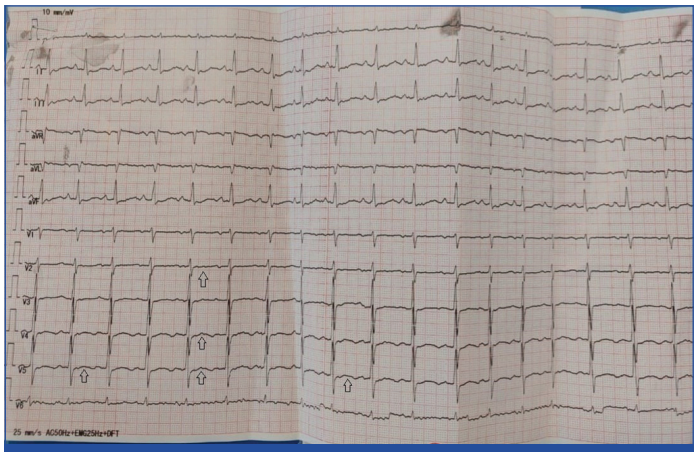
Parameters	Findings	Normal range
Respiratory rate	16 breaths per minute	12-20 breaths per minute
SpO_2 (on room air)	98%	95-100%
Blood pressure	130/90 mmHg	90/60-120/80 mmHg
Pulse	95 beats per minute	60-100 beats per minute
Glasgow coma scale	E4V5M6	Total score: 15
Random blood sugar level	193 mg/dL	200 mg/dL
Pupil size and reactivity	Bilaterally equal (3 mm) and reactive	2-4 mm, reactive
Potassium level	1.8 mmol/L	3.5-5.0 mmol/L
White blood cell count	14,600 cells/µL (cause unknown, probably related to the underlying chronic nature of RA)	4,000-11,000 cells/µL
Haemoglobin	11.2 g/dL	12-15.5 g/dL (female)
Liver and kidney functions	Normal (except for electrolyte imbalance)	-
ECG findings	U waves in leads V2-V6, Prolonged QTc interval of 537 ms	Normal sinus rhythm, QTc interval 350-450 ms
Magnesium	1.1 mg/dL	1.7-2.2 mg/dl
Thyroid Function Test (TSH)	5.46 mIU/L	0.465-4.68 mIU/L
Thyroid function test FT3 & FT4	FT3 5.61 pg/mL FT4 1.68 ng/dL	FT3: 2.77-5.27 pg/mL FT4: 0.78-2.19 ng/dL

[Table/Fig-1]: Characteristics of study patient and laboratory parameters with hypokalaemia.
FT: Free Triiodothyronine

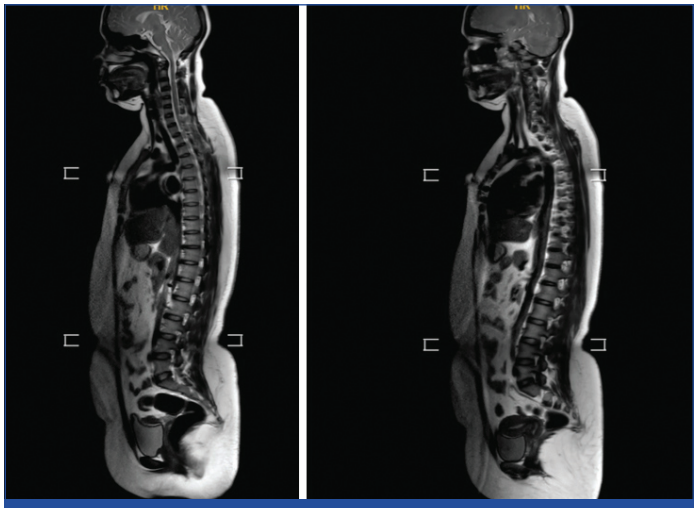
Laboratory results were significant for severe hypokalaemia (potassium level of 1.8 mmol/L), an elevated white blood cell count of 14,600 cells/µL, and a random blood sugar level of 193 mg/dL. Liver and kidney function tests were normal [Table/Fig-1]. Both brain and spinal Magnetic Resonance Imaging (MRI) scans were normal

Test	Right	Left
Tone	Normotonia	Normotonia
Power upper limbs	1/5	2/5
Power lower limbs	3/5	2/5
Reflexes	++	++
Sensory (fine and course touch, vibrations)	Normal	normal
Cerebellar	N/A	N/A
Nystagmus	-	-
Plantar	Flexor	Flexor
Signs of meningitis	Kernig sign and neck rigidity absent	
Paresthesia	Absent in B/L upper and lower limbs	

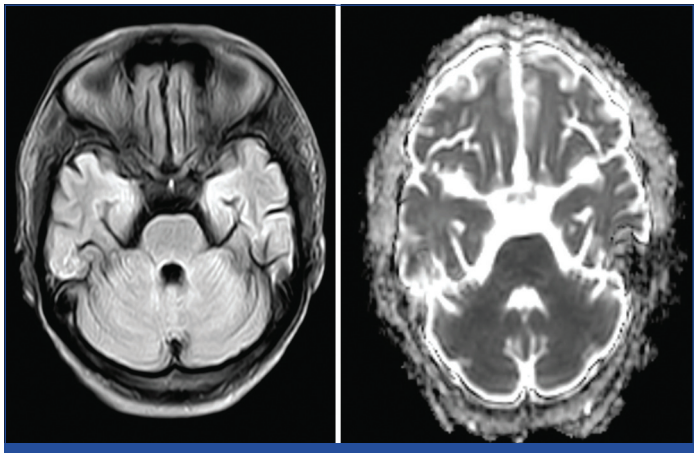
[Table/Fig-2]: Neurological assessment of the patient.



[Table/Fig-3]: The ECG revealed a normal sinus rhythm with U waves in leads V2-V6 and a prolonged QTc interval as shown in [Table/Fig-5], highlighting the cardiac implications of hypokalaemia



[Table/Fig-4]: MRI whole spine screening.



[Table/Fig-5]: MRI brain.

[Table/Fig-4,5], ruling out central nervous system and cervical spine pathology. A detailed central and peripheral nervous system examination was performed.

The provisional diagnosis for the patient was HPP secondary to an electrolyte imbalance. Diagnostic tests for RA, such as Rheumatoid Factor (RF) and anti-Cyclic Citrullinated Peptide (anti-CCP) antibody tests, were conducted along with routine blood tests, liver function tests, kidney function tests, thyroid function tests, and magnesium and potassium blood tests. Since there is no evidence of trauma, cervical trauma has been ruled out. Additionally, the patient's normal bowel and bladder function, intact sensory sensation, absence of fever and paresthesia, normal reflexes, and lack of autonomic dysfunction exclude Guillain-Barré syndrome and transverse myelitis. These conditions were considered and systematically evaluated based on clinical presentation, laboratory findings, and imaging results. Given the overall clinical picture, HPP was the most likely diagnosis.

Immediate treatment for hypokalaemia included intravenous potassium chloride (60 mEq) mixed with magnesium sulfate (2 g) in 500 mL of Ringer's Lactate over four hours, under continuous cardiac monitoring, and electrolyte reassessment to avoid hyperkalemia from overcorrection. Intravenous optineuron (a multivitamin formulation) in 100 mL of normal saline, Ondansetron (4 mg i.v.) for nausea, inj. Paracetamol 1g SOS, and 10% calcium gluconate (10 mL i.v.) over 10 minutes to counter potential adverse cardiac events of hypokalaemia, along with maintenance i.v. fluids at 80 ml/hour. She was admitted to the neurology Intensive Care Unit (ICU) for three days, and treatment was continued. During her stay in the ICU, she underwent continuous limb physiotherapy, and the patient's muscle power improved significantly to 3/5 in all four limbs. Her potassium level on the 3rd day of the ICU was 3.3 mmol/L. After three days, she was shifted to the neurology ward, where syrup kesol TDS was started to maintain potassium levels, along with i.v. optineuron, i.v. ondansetron 4 mg BD, i.v. pantoprazole 40 mg OD, and i.v. paracetamol 1g SOS. After two days, her muscle power improved to 4/5 in all four limbs.

Upon discharge, the patient was prescribed oral medications, Tab. Dimox 250 BD, Syrup Kesol TDS, Tab. Supradyn OD, Tab. prednisolone 30 mg OD, Tab. Methotrexate 7.5 mg once a week, with Tab. folic acid 5 mg OD, Tab. Leflunomide 100 mg OD for three days then 20 mg OD. She was advised to follow-up in the Neurology Outpatient Department after one week for close monitoring of her electrolyte levels and neurological status. During the follow-up visit, the patient was oriented to time, place, and person and was compliant with her medications. On examination, power in all her limbs was 5/5, and her potassium level was 4.0 mmol/L.

DISCUSSION

The HPP is a rare neuromuscular disorder characterised by episodes of muscle weakness or paralysis associated with low blood potassium levels [1]. These episodes typically last hours to days and often begin in adolescence or early adulthood. HPP is predominantly familial with mutations in genes encoding sodium or calcium channels in muscle cells leading to abnormal ion fluxes during attacks [2]. Secondary causes of hypokalaemia, such as thyroid disease, renal tubular acidosis, and drug-induced disturbances, can closely mimic the clinical presentation of HPP [3]. The pathophysiology of HPP centres around the dysfunctional ion channels in skeletal muscle cells. These channels are crucial for muscle contraction and relaxation. Mutations in the SCN4A gene (encoding the voltage-gated sodium channel Nav1.4) or the CACNA1S gene (encoding the calcium channel Cav1.1) disrupt normal muscle cell polarisation, leading to an inability to respond to nerve impulses [4]. This dysfunction results in the episodic muscle

weakness or paralysis characteristic of HPP. During an episode, affected individuals may experience profound muscle weakness, typically sparing the respiratory and cardiac muscles, hence not usually life-threatening but significantly impairing quality of life [5,6]. Epidemiologically, HPP is a rare disorder with an estimated prevalence of 1 in 100,000 [1]. The condition has a higher incidence in males compared to females and often presents in the second decade of life [7,8].

Management strategies for HPP focus on early treatment of such occurrences, prevention of future episodes, and management of any underlying cause. The management involves oral or intravenous potassium supplementation, carefully monitored to avoid hyperkalemia. Apart from that, preventive measures include lifestyle modifications, avoiding known triggers, and pharmacotherapy with carbonic anhydrase inhibitors or potassium-sparing diuretics to stabilise serum potassium levels [1,9].

The RA is a chronic autoimmune disorder causing synovial joint inflammation, pain, swelling, and potential joint damage if untreated, affecting about 1% of the global population, predominantly females [9,10]. Its aetiology involves genetic predisposition, environmental factors, and immune system dysregulation, characterised by autoantibody production targeting joint tissues, though its pathogenesis remains incompletely elucidated [10,11]. For instance, autoimmune conditions like Sjögren's syndrome and systemic lupus erythematosus have been associated with renal tubular acidosis, a condition that can lead to hypokalaemia [12,13].

The diagnostic process in the present case highlights the complexity of distinguishing between different causes of acute paralysis. Initially, considering Guillain-Barré syndrome and cervical spine trauma, among others, underscores the clinical complexity. Symptom resolution with potassium supplementation confirmed HPP, aligning with prior studies like Statland JM et al., and Levitt JO emphasising thorough history-taking and laboratory investigations in diagnosing HPP, especially when secondary to non hereditary causes [14,15].

Therapeutically, the management of this patient with intravenous potassium chloride and magnesium sulfate, followed by careful monitoring, signifies the recommended approach for HPP. Comparing the present case to previous studies, the rarity of HPP secondary to RA becomes evident. While numerous cases in the literature describe HPP in the context of thyrotoxicosis or as a hereditary condition, reports linking it to RA are not noted [13,15]. The present report appears to be the first of its kind, making it essential for diagnosticians to maintain a high index of suspicion in patients with autoimmune disorders presenting with para/quadriparesis.

CONCLUSION(S)

The case explores the rare association between RA and HPP in a 37-year-old female patient with sudden quadriparesis, shedding light on potential links between autoimmune disorders and electrolyte imbalances. It emphasises through diagnostics, and highlights the importance of early detection of dyselectrolytaemia in autoimmune disorders and a high index of suspicion in identifying and managing HPP. The authors recommend that further studies be performed to identify the implications for clinical care and further research into the pathophysiology of the same.

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