Hypokalemia Periodic Paralysis in Subtle Thyrotoxicosis with Renal Insufficiency

Indah Sagitaisna Putri[1*], Dadang Herdiana[2], Pipik Ripa'I[2], Miko Galastri[2]

1 Leuwiliang General Hospital, Bogor, Indonesia
2 Department of Internal Medicine, Leuwiliang General Hospital, Bogor, Indonesia

Corresponding Author:
Indah Sagitaisna Putri, MD. Leuwiliang General Hospital, Bogor, Indonesia.
Email: indahsagitaisna18@gmail.com.

ABSTRACT

Hypokalemia is one of the frequently observed electrolyte imbalances in clinical practice. The clinical manifestations range from asymptomatic to significant manifestation, such as paralysis. Here we report a case of 31-years-old female admitted to our emergency department with chief complaint of acute onset of paralysis in lower extremities. Vital signs showed slight tachycardia. The physical examinations were all normal. Motoric examination showed paraparesis in lower extremities with normal sensory function. Upon admission, laboratory tests showed severe hypokalemia (1.5 mmol/L) with renal insufficiency. The patient got hypokalemia corrected with both potassium oral supplementation and potassium infusion. Thyroid function tests showed hyperthyroidism and the diagnosis of thyrotoxic periodic paralytic (TPP) was made. This case report highlights the importance of early diagnosis and prompt treatment of hypocalemia in TPP patient.

Keywords: *Periodic paralysis, hypokalemia, primary hyperthyroidism, subtle thyrotoxicosis*

INTRODUCTION

Hypokalemia stands out as a frequently observed electrolyte imbalance in the field of clinical medicine. The prevalence of hypokalemia varies from 6.7% to 21%.[1-3] The existing guidelines establish the standard range for lower potassium levels as 3.5 to 3.8 mmol/L and for upper levels as 5.0 to 5.5 mmol/L.[4] This abnormality has broad clinical manifestations, from asymptomatic to significant manifestation such as paralysis, called hypokalemia periodic paralysis (HPP).

Hypokalemia periodic paralysis (HPP) is characterized by episodic of flaccid muscle weakness of variable duration and severity with intact sensory functions. The prevalence of HPP is rare, approximately 1 in 1.000 and most of HPP cases identified as sporadic and more prevalent in male, with ratio of 9:1. [5,6] Theoretically, testosterone can increase the activity of the sodium/potassium (Na+/K+) pump resulting in hypokalemia.[7] Most cases of HPP are hereditary, caused by the mutation in either calcium or sodium ion channel. HPP could also occurred secondarily due to thyrotoxicosis, called thyrotoxic periodic paralysis (TPP). TPP is a rare, yet extremely dangerous complication observed in patients with thyrotoxicosis. Any cause of thyrotoxicosis can lead to TPP, including Graves' disease, toxic nodular goiter, solitary toxic nodule, iodine-induced thyrotoxicosis, thyroiditis, xcess exogenous thyroxine use, drug-induced thyrotoxicosis, etc.[9]

Timely identification of hyperthyroidism in patients experiencing hypokalemic paralysis is crucial to administer suitable treatment and prevent the potential danger of rebound hyperkalemia resulting from unnecessary and excessive potassium supplementation. This article presents a scenario involving hypokalemic periodic paralysis caused by asymptomatic hyperthyroidism.

CASE ILLUSTRATION

A female 31 years old was administered to the emergency department (ED) with acute onset of paralysis in bilateral lower extremities. The symptoms occur when she wakes up from sleep. The symptoms were followed by chest tightness and vomiting. A few hours prior to the onset of symptoms, she didn't engage in any excessive physical activity. The patient mentioned that she had consumed fried rice before going to sleep. There was no fever, diarrhea, sore throat, or cough. There were no indications of weight loss, heat intolerance, alterations in bowel habits, or any other symptoms associated with hyperthyroidism reported. She had a history of similar symptoms in the past 2 years. No history of previous illness such as hypertension, diabetes mellitus, hyperthyroidism, or nervous system disease. No family member has similar symptoms.

Upon admission, the patient was alert. Her vital signs; blood pressure (BP) 101/73mmHg, pulse 118 beat per minute, respiratory rate 24 breaths per minute, saturation 98% with three liters of nasal canula, and body temperature of 37°C. During the physical examination, her thyroid appeared to be of regular size and texture. Listening to the thyroid did not reveal any abnormal sounds. There were no signs of bulging eyes (exophthalmos) or changes in the skin. Motoric examination showed paraparesis in lower extremities with normal sensory function. Electrocardiography demonstrated sinus tachycardia (Figure. 1). Chest x-ray showed no abnormalities.

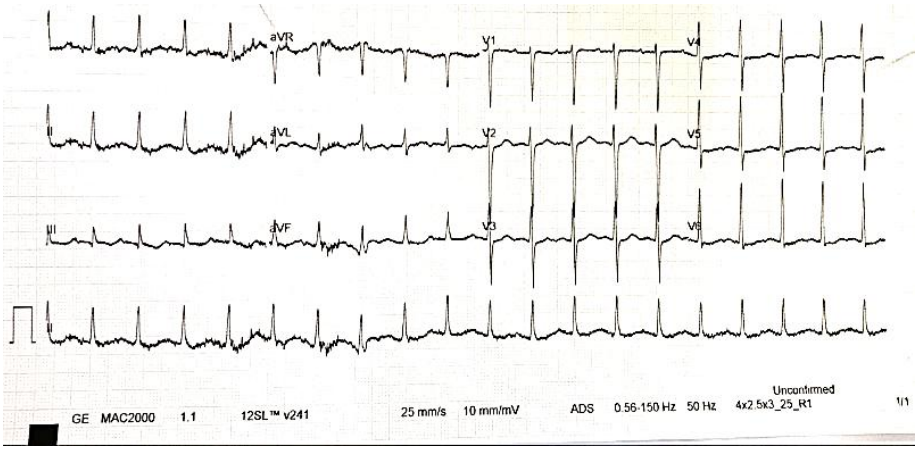

Figure 1. Electrocardiography of the patient upon admission

Complete blood count showed leukocytosis. Biochemical examination showed hyperglycemia, slightly elevated liver enzyme, and azotemia. Electrolyte examination showed severe hypokalemia of 1.5 mmol/L. The details are shown in Table 1.

Table 1. Laboratory Findings Upon Admission

Examination	Normal Range	Result
Blood chemistry		
AST	<35 U/L	56 U/L
ALT	<35 U/L	76 U/L
BUN	10-50 mg/dL	133 mg/dL
Cr	0.45-0.75 mg/dL	2.68 mg/dL
Glucose	70-140 mg/dL	242 mg/dL
Na	135-147 mmol/L	139 mmol/L
K	3.5-5.0 mmol/L	1.5 mmol/L
Cl	95-105 mmol/L	112 mmol/L
Thyroid fuction		
Free T4	10.60-19.40 pmol/L	28.0 pmol/L
TSH	0.40-4.20 mIU/ml	0.1 mIU/ml

AST: aspartate aminotransferase; ALT: alanine aminotransferase; BUN: blood urea nitrogen; Cr: creatinine; Na: natrium; K: potassium; Cl: chloride; TSH: thyroid stimulating hormon

An initial diagnosis of HPP was made. The patient was initially treated with 20 mEq of intravenous potassium chloride (KCl) as well as 25 mEq or oral potassium in ED. Repeat laboratory testing after eight hours showed potassium of 1.5 mmol/L. The administration of potassium replacement was sustained, and the patient was admitted to the intensive care unit. She was given ringer lactate infusion with 50mEq of potassium infusions, antibiotics, and oral potassium supplementation. Serial measurement of serum potassium showed improvement with a level of 3.5 mmol/L on third day and 4.3 mmol/L on fifth day. The thyroid function test indicated primary hyperthyroidism, with a thyroid stimulating hormone (TSH) level below 0.1 mIU/ml and a free thyroxine (T4) level of 28.0 pmol/L. Subsequently, a diagnosis of thyroid periodic paralisys (TPP) was established. The patient was given propranolol 10mg t.i.d as well as methimazole 20 mg once daily.

DISCUSSION

Periodic paralysis refers to a neuromuscular condition linked to dysfunctional muscle ion channels, marked by instances of painless muscle weakness. Most cases are hereditary and follow an autosomal dominant inheritance pattern.[8] Individuals with thyrotoxicosis might occasionally develop hypokalemic periodic paralysis (HPP). Thyrotoxic periodic paralysis (TPP) can occur because of several forms of thyrotoxicosis, but it is most common in Graves' disease. TPP, in contrast to other thyroid disorder, is more common in men and is notably common in Asian populations, with an estimated frequency of roughly 2% in thyrotoxicosis patients.[10]

While the precise mechanism is not fully understood, there is a hypothesis suggesting that individuals with TPP possess an inherent anomaly in their muscle ion channels. This anomaly typically doesn't cause symptoms in individuals with normal thyroid function. Nonetheless, when thyroid hormone levels rise,

they heighten the sensitivity of tissues to beta-adrenergic stimulation. As a result, this amplifies the activity of Na/K-ATPase, leading to the movement of potassium into cells.[11] Excess potassium in the skeletal muscle cells inhibits muscle cell excitability, resulting in weakness. The entry of potassium into muscle cells takes place during the resting phase. This phenomenon could elucidate why patients encounter symptoms during the nighttime or early morning hours while asleep (rest).[12] In this instance, the patient ingested fried rice on the evening prior to the onset of symptoms.

However, the exact quantity of carbohydrates consumed is not specified. Consuming a high-carbohydrate diet serves as a trigger for TPP.[13] Hyperinsulinemia contributes to the escalation of Na/K-ATPase activity and the inhibition of potassium efflux from muscle cells.[14] The patient refutes experiencing any emotional stress stemming from work or family matters. Emotional factors such as stress and trauma can act as triggers for TPP, with stress potentially influencing hormonal responses. Catecholamines impact the activity of Na/K-ATPase and hinder the outward movement of potassium by suppressing the function of inward-rectifying potassium channels.[15,16]

TPP presents as temporary occurrences of painless muscle weakness while maintaining intact consciousness. These episodes generally endure for several hours to a few days. The muscle weakness is widespread, yet frequently more prominent in proximal muscles. Episodes can be intensified by the consumption of high-carbohydrate foods, physical activity, stress, infections, anesthesia, or exposure to extreme temperatures.[17] Less frequent symptoms encompass myalgia, diminished or absent reflexes (hyporeflexia or areflexia), as well as concurrent hyperthyroid manifestations like rapid heart rate (tachycardia). Tachycardia was noted at presentation in one series, differentiating these patients from those with familial HPP.[18]

Electrocardiogram (ECG) changes are common during a TPP attack. These include ST depression, sinus tachycardia, and U waves, as well as those that are not consistently associated with hypokalemia: an elevated higher heart rate, abnormal PR interval, higher QRS voltage, and first-degree atrioventricular (AV) block.[19,20] Severe arrhythmias such as sinus arrest, second-degree AV block, ventricular fibrillation, and ventricular tachycardia are rarely occurred but are documented.[21]

Typically, the degree of hypokalemia corresponds to the severity of weakness. Laboratory findings include an increase in serum thyroxine (T4) and a decrease in thyrotropin levels (TSH). There have been reports of patients with elevated T3 levels but normal T4 levels.[22] Creatine levels may be normal, but they have been found to be mildly elevated in two-thirds of patients.[23]

TPP should be detected when a patient has paralysis accompanied by hypokalemia and hyperthyroidism. Other causes of acute paralysis, such as myasthenic crisis, botulism, Guillain-Barre syndrome, acute myelopathy, and acute thyrotoxic myopathy, should be separated from TPP. In this situation, the patient exhibited normal cranial nerve function, ruling out myasthenic crisis or botulism. Her weakness was diffused, with no rising trend that would indicate Guillain-Barre disease. Her absence of discomfort and non-dermatomal distribution were also inconsistent with acute thyrotoxic myopathy or acute myelopathy. Other causes of hypokalemia should be differentiated. Initial 24-hours urine potassium level helps to differentiate between two broad groups, renal-loss related or non-renal-loss.

Based on previous reports, almost 50% of TPP patients had only subtle symptoms of thyrotoxicosis, albeit without systematic assessment.[24,25] Study reported by Chang et al[17] showed that only 17% of TPP patients had toxic thyrotoxicosis (Wayne Score >19), supporting the notion that most TPP patients have equivocal symptoms. In this report, our patient also had subtle symptoms of thyrotoxicosis.

The primary treatment for TPP is potassium administration. Although oral potassium chloride is the favored method, intravenous potassium is suitable for those with

difficulty swallowing. As per a recommended protocol, an oral dosage of 30 milliequivalents is advised at intervals of 15 to 30 minutes until serum potassium levels return to normal.[26] Previous review recommended to no potassium replacement more than 90 meq in 24 hours to avoid overcorrection.[27] Given the frequent occurrence of rebound hyperkalemia, meticulous tracking of serum potassium levels and continuous cardiac monitoring are essential precautions.

For case where potassium replacement proves unresponsive, intravenous propranolol might be beneficial in counteracting the surplus beta-adrenergic stimulation responsible for the potassium shift into cells. Propranolol is also advised to be used in the treatment for TPP. Propranolol is a non-selective beta blocker and works by the mechanism of preventing the intracellular shift of potassium and phosphate, it does this by diminishing the hyper-adrenergic stimulation of Na+/K+-ATPase.[28-30] Treatment for the cause of thyrotoxicosis is important. This could be through using anti-thyroid medications, radioiodine therapy and thyroidectomy in Graves' disease and toxic nodules. Long-term TPP prevention involves restoring euthyroid status and avoiding the trigger factors, such as excessive activity, high-carbohydrate meals, and alcohol consumption.

CONCLUSION

In conclusion, timely identification, and intervention in cases of TPP held significance in averting severe cardiac complications. To avoid rebound hyperkalemia, potassium replenishment was performed in stages accompanied by continuous monitoring. Therefore, the ultimate treatment aimed to achieve a euthyroid state, thereby preventing recurring attacks.

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