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Hypokalemic periodic paralysis in subclinical hyperthyroidism: A case report

Eunike Vania Christabel*[1], Onggo Williyanto[1]

[1]Panti Wilasa Citarum Hospital, Semarang, Indonesia

Case Report

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***Corresponding author:**
eunikevania@gmail.com

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ABSTRACT

Hypokalemia is a common electrolyte abnormality often encountered in daily practice. While mild hypokalemia often asymptomatic, moderate-to-severe hypokalemia usually manifested as significant symptoms such as muscle weakness. In this paper, we presented a case of 23-years-old male coming to our emergency department because of muscle weakness in all his four limbs when he woke up in the morning. Physical examinations were all within normal limit, except that his muscle strength decreased in all four extremities. Laboratory measures showed severe hypokalemia (1.9 mmol/L), hence patient was treated with potassium infusions. During hospitalization, thyroid function tests revealed hyperthyroidism. Therefore, in patient with paralysis, in which laboratory finding showed hypokalemia, hyperthyroidism should be considered as one of the potential diagnosis especially in younger patient, even in patient without previous history of hyperthyroidism. Merely treating hypokalemia in patient with underlying hyperthyroidism could be a dangerous boomerang.

Hipokalemia merupakan salah satu kelainan elektrolit yang sering dijumpai dalam praktek sehari-hari. Hipokalemia ringan sering kali tidak menunjukkan gejala, akan tetapi hipokalemia sedang hingga berat dapat menyebabkan gejala yang signifikan seperti kelemahan otot. Dalam tulisan ini, kami mempresentasikan kasus seorang laki-laki berusia 23 tahun yang datang ke unit gawat darurat kami dengan keluhan kelemahan otot di keempat anggota tubuh saat bangun pagi. Pada pemeriksaan fisik tidak didapatkan kelainan, kecuali kekuatan otot yang menurun pada keempat ekstremitas. Hasil pemeriksaan laboratorium menunjukkan hipokalemia berat (1,9 mmol/L), sehingga pasien diterapi dengan infus kalium. Selama rawat inap, tes fungsi tiroid menunjukkan adanya hipertiroid. Jadi, pada pasien dengan paralisis ekstremitas, dimana hasil laboratorium menunjukkan hipokalemia, hipertiroid harus selalu dipikirkan sebagai salah satu diagnosis diferensial terutama pada pasien usia muda, meskipun pasien tidak memiliki riwayat hipertiroid sebelumnya. Tanpa mengatasi hipertiroid yang mendasari terjadinya hipokalemia tersebut, pemberian terapi kalium dapat menjadi bumerang yang berbahaya.

INTRODUCTION

Hypokalemia is the most common electrolyte abnormality encountered in daily practice.[1] It occurs in over 20% hospitalized patients, although only quarter showed significant clinical manifestation, such as muscle paralysis.[1–3] The fundamental pathophysiology of hypokalemia can be divided into excessive loss through kidney or gastrointestinal tract, increasing intracellular shift, or reduced potassium intake.[3–5] However, it is often appear as part of another underlying condition. The most common cause of

hypokalemia is excessive loss through kidney due to diuretic therapy.[6] Rarely, hypokalemia may also be caused by hyperthyroidism. Merely treating hypokalemia without solving the underlying diseases could be fatal due to potential rebound hyperkalemia.[7] Hence, treatment of hypokalemia should not only be focused on overcoming the emergency of hypokalemia, but also to treat the cause appropriately.

While mild hypokalemia often show no symptom, moderate-to-severe hypokalemia may exhibit significant symptoms, such as muscle weakness. In fact, muscle weakness is an uncommon symptom indicating for hyperthyroidism. In this paper, we presented a case of hypokalemic periodic paralysis due to asymptomatic hyperthyroidism.

CASE DESCRIPTION

A 23-year-old Asian male came to the emergency department with chief complaint of sudden onset weakness in all four limbs. Patient felt this symptom when he woke up in the morning. He was unable to get up from bed, not even to lift his legs from bed or to lift his hand above shoulder. He denied any history of trauma or fever. He had no palpitations, chest pain, nor shortness of breath. Patient had no history of similar complaint and no history of other diseases, such as diabetes, hypertension, or mental illness. He also had no family history of diseases. He denied any use of medications or substance abuse.

Patient was alert. Blood pressure was 137/86 mmHg, pulse rate was 62 regular beats per minute, non-labored breathing 16 times per minute, temperature was 36.8°C, and oxygen saturation was 98% on room air. General physical examinations were unremarkable. No signs of exophthalmos, palpable neck masses, no crackles or wheezing on lung auscultation. Neurological examination showed that patient was alert and oriented. Cranial nerves were intact. No facial asymmetry. Upper and lower extremities had no deformity or atrophy, but showing flaccid paralysis. Muscle strength was 2/5 on all upper and lower extremities. Higher mental function and sensory systems were all within normal limit. No cerebellar signs and no meningeal signs. Upper motor neuron examinations were intact.

Electrocardiogram examination (ECG) showed sinus bradycardia with prominent U-waves. Chest radiograph and computerized tomography scan (CT-scan) of the brain revealed no abnormalities. On laboratory examination, complete blood count, liver function test, and renal function test were normal. Potassium level was 1.9 mmol/L (reference range 3.5-5.0 mmol/L), sodium 139.1 mmol/L (reference range 135.0-147.0 mmol/L), calcium 9.0 mmol/L (reference range 8.8-10.3 mmol/L), and magnesium 1.6 mmol/L (reference range 1.8-3.0 mmol/L). Due to severe hypokalemia and ECG abnormality, patient was treated with 100 mEq potassium infusions over 24 hours. During hospitalization, twenty-four-hours urine potassium level was normal. Thyroid function test showed thyroid stimulating hormone (TSH) 0.01 mIU/L (reference range 0.3-4.5 mIU/L) and free thyroxine (FT_4) 6.90 pmol/L (reference range 1.15-2.21 pmol/L).

Patient was treated with methimazole, propranolol, and oral potassium supplements. He responded well and was discharged after 5 days. One month after hospitalization, he visited our outpatient clinic for follow up. Thyroid marker and serum electrolyte were normal and no other episodes of weakness.

DISCUSSION

This paper presented a case of hypokalemic periodic paralysis in patient with previously subclinical hyperthyroidism. Hypokalemia is a common electrolyte abnormality. Patients with mild hypokalemia often show no symptoms. However, moderate-to-severe hypokalemia, as in our patient, may demonstrate muscle pain, cramping, constipation, and even paralysis.[1,3] Hypokalemic paralysis usually displayed flaccid characteristic and occurs during rest or during bed at night, although it is also

possible to appear during physical activities.[8] Patients will complaint weakness involving lower extremities more than upper extremities, preceded with myalgia. Attacks are often precipitated by certain behavior or diet that alter potassium level, such as vigorous physical activity, excessive carbohydrate consumption, alcohol, insulin or epinephrine use, trauma, cold temperature, infection, menstruation, and psychological stress.[9] Other neurologic functions will otherwise be normal. Patients are conscious, normal mental state, no respiratory, ocular, or bulbar muscle involvement, intact sensory function and cranial nerve. However, symptoms of severe hypokalemia (less than 2.0 mmol/L) may become nonspecific and respiratory muscle may also become weak.[10]

Hypokalemia mostly presented as a sign to an underlying condition, so it is crucial and strongly required to differentiate the potential diagnosis of hypokalemia. Figure 1 showed an algorithm that could possibly be used in daily practice when encountering patients with hypokalemia. In our case, our patient has no history of diarrhea, no history of renal diseases, no history of reduced intake, and no history of medication use. Laboratory test also showed normal renal function test. Hence, we began to look for potential causes that are due to transcellular shift. With normal ECG and normal head CT scan, one potential cause is thyrotoxicosis. Ultimately, laboratory test showed hyperthyroidism.

In emergency setting, first goal is to prevent potentially life-threatening event. Severe hypokalemia could disturb cardiac conduction and respiratory muscle and is therefore requires immediate treatment. Severe hypokalemia, symptomatic hypokalemia, acute onset, ECG changes, and presence of comorbid diseases are indications for urgent treatment.[4] Potassium replacement could be administered

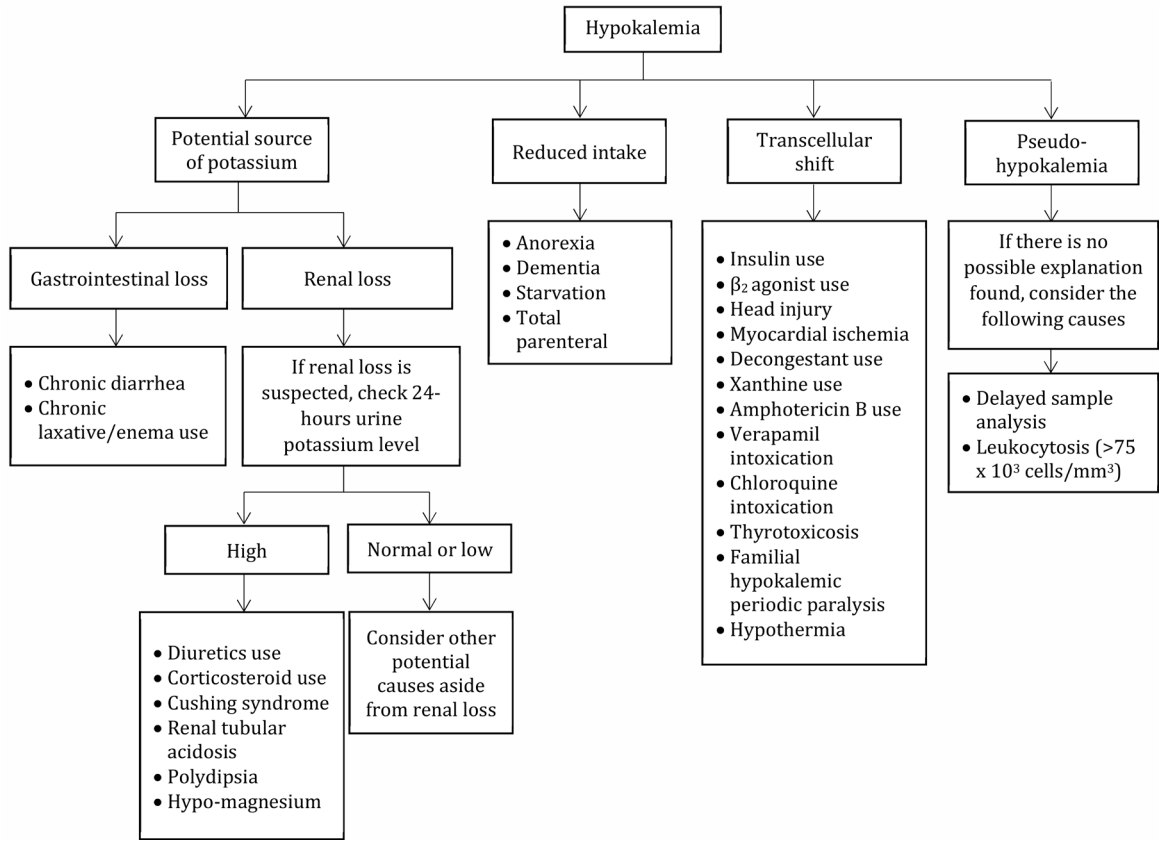

Figure 1. Algorithm of possible potential diagnosis of hypokalemi

intravenously or orally, but physicians should always aware of rebound hyperkalemia, especially at high speed rate.[1,4,11] This adverse event should be particularly emphasized because hyperkalemia in hospitalized patients mostly resulted from potassium supplementation.[1]

After patient becomes stable, etiology of hypokalemia should be evaluated. Hypokalemia is usually chronic and is part of another underlying condition.[1] It could be due to excessive loss, reduced intake, or intracellular shift.[3–5,12] Best way to measure potassium loss through urinary tract is by measuring 24-hours urine potassium level. If potassium excretion is high, physician should evaluate any differential diagnoses related to renal loss. If potassium excretion is low or normal, as in our case, gastrointestinal loss or intracellular shift should be evaluated.[3,4,12] In our case, patient complained no vomiting or diarrhea prior to weakness. Therefore, we thought of any factors that could contribute to intracellular shift of potassium.

One of the possible causes that could alter potassium shifting in young male is hyperthyroidism. Hyperthyroid and thyrotoxicosis is common, but its presentation as thyrotoxicosis periodic paralysis (TPP) is rare. When remain undiagnosed, TPP can occur repeatedly and become potentially lethal if respiratory and cardiac muscle are affected.[3] TPP is mostly seen in Asian male usually at their 4th-5th decade of life,13 although several cases on other ethnics were also reported.[6,14]

The three hallmark of TPP are abrupt onset of hypokalemia, hyperthyroidism, and paralysis. Although its pathophysiology is unclear, but thyroid hormone promotes sodium–potassium adenosine triphosphatase (Na/K-ATP) channel to mediate cellular uptake of potassium ions, which leads to intracellular shift of potassium rather than depletion of potassium.[11,13] While in normal condition potassium is mainly found in the intracellular compartment of skeletal muscle, thyroid hormone may induce the channel to actively pump potassium from extracellular fluid into the cell. Thyroid hormone is also known able to stimulate adrenergic response and insulin release, which also stimulate the activity of Na/K-ATP channel.[12] The effect of insulin toward Na/K-ATP channel explains why TPP may occur after carbohydrate-rich meals. Physical exercise will release potassium to extracellular, whereas resting will promote influx of potassium to intracellular space. That is why TPP usually occurs during rest and not during exercise. The diurnal variation of potassium in which potassium influx tend to occur at night explains why TPP tend to occur during bed time.[6]

However, severity of thyrotoxicosis does not related to the manifestation of paralysis.[12] As seen in our case, the patient did not show any other signs and symptoms of thyrotoxicosis and he did not have any history of hyperthyroidism, episodes of paralysis, or family history of hyperthyroidism. Although many conditions could activate Na/K-ATP channel to transport potassium, this factors alone will not results to hypokalemic paralysis in the majority of patients because to maintain potassium homeostasis the body will also increase outward potassium flow. Therefore, only if outward flow is also affected will hypokalemic paralysis occurs and that is why incidence of hypokalemic paralysis is rare.

Recent studies showed that genetic mutation of Potassium Inwardly Rectifying Channel Subfamily J Member 18 (KCNJ18) genes were associated with hypokalemic paralysis. This gene encodes inwardly rectifying potassium channel, namely Kir2.6, which plays a vital role in maintaining potassium balance.[15] Mutation of this gene will lead to decrease potassium outflow. This genetic mutation also explains why certain ethnics are more susceptible to TPP rather than other ethnics.[12]

Treatment of hypokalemic periodic paralysis in hyperthyroid patient includes replacing hypokalemia, correcting hyperthyroid state, and preventing further shift of potassium using beta-blocker agents. Physicians should be aware that paralysis is curable once the patient reaches normal thyroid level.

CONCLUSION

Hypokalemia often appear as part of another underlying condition, such as hyperthyroidism. Accurately diagnosing hypokalemia in patient with unknown previous history could be challenging, but merely treating hypokalemia in patient with underlying diseases could be potentially fatal. Early recognition of hyperthyroid in hypokalemic paralysis patient is important in order to provide appropriate treatment and avoid risk of rebound hyperkalemia from excessive unrequired potassium replacement.

CONFLICT OF INTEREST

Author declares no potential conflict of interest.

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