Recurrent, refractory hypokalemia as a diagnostic clue to thyrotoxic periodic paralysis in a patient with acute kidney injury and suspected Guillain-Barre syndrome.

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Abstract

Hypokalemia can be multifactorial. When the primary driver of hypokalemia is obvious it is easy to miss other contributing causes that could be vital to optimal patient management and outcomes. Our case report highlights the importance of recognizing recurrent, refractory hypokalemia as a diagnostic clue to thyrotoxic periodic paralysis.

[Category: Case Report]

Recurrent, refractory hypokalemia as a diagnostic clue to thyrotoxic periodic paralysis in a patient with acute kidney injury and suspected Guillain-Barre syndrome.

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Key words: refractory hypokalemia, diagnostic clue, thyrotoxic periodic paralysis, T3 toxicosis, Guillain-Barre syndrome, rhabdomyolysis, acute kidney injury

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Abstract

Hypokalemia can be multifactorial. When the primary driver of hypokalemia is obvious it is easy to miss other contributing causes that could be vital to optimal patient management and outcomes. Our case report highlights the importance of recognizing recurrent, refractory hypokalemia as a diagnostic clue to thyrotoxic periodic paralysis.

Key words: refractory hypokalemia, diagnostic clue, thyrotoxic periodic paralysis, T3 toxicosis, Guillain-Barre syndrome, rhabdomyolysis, acute kidney injury

Introduction: Most cases of thyrotoxic periodic paralysis have been reported in Asian men with the incidence of about 2% in thyrotoxic patients [1]. However, the incidence is reported to be only 0.1 to 0.2% in non-Asian population [2]. A very high degree of clinical suspicion is therefore needed to diagnose thyrotoxic periodic paralysis in non-Asian population. We present a case of thyrotoxic periodic paralysis in a 34y old Caucasian male who presented with clinical features suspicious of Guillain-Barre (GB) syndrome where the finding of severe, recurrent and refractory hypokalemia served as a key diagnostic clue for timely diagnoses and management of thyrotoxic periodic paralysis.

Case report:

Patient is a 34-year-old Caucasian male with a 5-year history of Human immunodeficiency virus (HIV) infection, controlled on anti-retroviral medications, who was admitted to the hospital for fever, nausea, and muscle weakness.

The patient was in his usual state of health until 8 days prior to this admission, when one morning patient began experiencing fever and nausea upon waking up that morning. Patient fell getting out of bed as his legs gave away from profound weakness in both legs which lasted for 15-20 minutes and improved but did not resolve until 3 hours later. He fell once more that morning and developed pins and needle sensation in both legs since then. Five days later when he went to work, he had 2 more episodes of leg weakness with falls similar to the previous falls except for bilateral arm weakness. Patient has a 5-year history of HIV and was taking Efavirenz, Emtricitabine & Tenofovir (Atripla) but had never been treated with a diuretic. Viral load had been undetectable on Atripla and he was never diagnosed with an Acquired immunodeficiency syndrome (AIDS) defining illness. On examination, heart rate was 64 beats/minute, BP 153/74 mmHg, respiratory rate 16 breaths per minute, oxygen saturation 96% on room air. Pupillary reflexes were normal with normal extra ocular movements. Upper extremity strength was 3/5 proximally and 5/5 distally. He had weakness in both hip flexors 2/5, left worse than right, bilateral knee flexion and extension 3/5 but near normal strength 4/5 in both ankles. Bilateral knee reflexes were diminished. Rest of the physical examination was unremarkable. Patient had CKD with baseline creatinine 1.6 mg/dL and normal potassium levels prior. Initial labs on admission to the 1st hospital showed elevated WBC count of 16,000 per microliter, hypokalemia of 1.6 mEq/L, and elevated creatinine of 3.2 mg/dL. He had Lumbar puncture and received single dose Vancomycin and Ceftriazone. He was given IV fluids with 20mEq potassium and transferred to the 2nd hospital for further work-up and management. Electrocardiogram showed normal sinus rhythm. Bedside chest X ray, computerized tomography (CT) head without contrast, CT abdomen and pelvis and magnetic resonance imaging (MRI) of thoracic and lumbar spine were unremarkable. Pertinent labs are summarized in Table 1.

Hospital course:

Because of initial suspicion of Guillian-Barre (GB) syndrome patient was started on intravenous immunoglobulin (IVIG). After 180 mEq of potassium replacement, potassium level was 1.8mEq/L (Table-2). Because of recurrent, refractory hypokalemia in the absence of other identifiable triggers (discussed below), thyrotoxic

periodic paralysis was suspected and T3 toxicosis was found in the thyroid lab panel. Patient had significant improvement in muscle weakness and potassium levels after treatment with methimazole and propranolol in addition to ongoing potassium replacements (Table 2). Tenofovir was stopped. Patient was discharged on Methimazole 20mg twice daily and Propranolol 40mg every 6 hours.

Discussion:

AKI due to Tenofovir nephrotoxicity was the primary driver of hypokalemia in our patient evidenced by transtubular potassium gradient (TTKG) of 9. However with refractoriness to therapy based on the calculated potassium deficit, non-renal etiology was suspected.

The intracellular compartment holds 98% of total potassium in the human body and only about 60 mmol of potassium fills the extracellular potassium pool [3]. The usual daily requirement is approximately 1 mEq per kilogram. Potassium deficit can be calculated by the formula: K deficit (in mEq) = (Knormal lower limit - Kmeasured) × kg body weight x 0.4. In our patient, if we consider the lowest potassium of 1.7 mEq/L and weight of 71 kg, potassium replacement dose in the 1st 24-hour would be 121.4 mEq. Potassium level after 180 mEq of potassium replacement within 24h in the 2nd hospital was 1.8 (additional 20mEq was given in 1st hospital making the total to 200mEq; see Table-2). The case had an absence of reported instigating factors associated with hypokalemia such as primary hyperaldosteronism, hypomagnesemia, hyperglycemia, vitamin B12 therapy, insulin therapy, bicarbonate therapy, β2-adrenergic agonist therapy. Refractory hypokalemia presenting as muscle weakness would include thyrotoxic periodic paralysis in the differential diagnosis. The patient's thyroid hormone levels were consistent with primary hyperthyroidism as the thyroid stimulating hormone (TSH) level was below the reference range and free triiodothyronine (fT3) level elevated. The T3 toxicosis likely led to thyrotoxic periodic paralysis precipitating recurrent hypokalemia in the case. Notably patient's free thyroxine level was not elevated (Table-1).

Muscle weakness in thyrotoxic periodic paralysis is a medical emergency and acute hypokalemia correlates with the severity of paralysis [4] Thyroid hormones are known to increase the expression and activity of Na+/K+-ATPase [3]. It is estimated that if all the Na+/K+-ATPase pumps in the skeletal muscles are activated to their maximum potential, then the entire extracellular potassium pool (approximately 60mmol) may be taken up into the muscle cells within 25 seconds [5]. Exercising muscles release potassium and cause vasodilation [6]. In thyrotoxic periodic paralysis, the potassium is redistributed to intracellular compartment, predisposing to hypokalemia and rhabdomyolysis. In our patient, the T3 toxicosis lead to hyperactivity of Na+/K+-ATPase pumps leading to transcellular potassium shift, causing severe, recurrent, refractory acute hypokalemia. As expected with thyrotoxic periodic paralysis, the patient did not respond to potassium replacements in excess of the calculated potassium deficit. Potassium levels eventually normalized with introduction of methimazole, an agent that inhibits the enzyme thyroperoxidase which decreases thyroid hormone synthesis [7].

Conclusion:

In many cases, hypokalemia can be multifactorial. When potassium replacements exceed the calculated deficit values by wide margin and with suboptimal correction of potassium, secondary causes should be entertained.

Persistent, refractory hypokalemia associated with muscle weakness should prompt suspicion for thyrotoxic periodic paralysis. In suspected cases, appropriate testing should include the measurement of free T3 levels along with a free thyroxine and TSH so that T3 toxicosis is not missed.

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Table 1: Sequential laboratory data

Variable

Variable

Treatment	On Admission to 2nd hospital	10 hours after admission	24 hours after admission	35 hours after admission	48h after admission	84h after admission
Cumulative Potassium replacement (mEq)¥ and corresponding Serum Potassium levels (mEq/L)	2.3	60 1.7	180 2.01.8	304.2 2.32.8	358.2 3.13.7	594.6 3.83.43.94.03.9
Cumulative Phosphorus replacement (mmol)\euro			46		92	170
IV Calcium replacement					3g	
Methimazole 20mg PO Q8H cumulative				1 dose =20mg	2 doses =40mg	6 doses =120mg
Propranolol 40mg PO 6h				2 doses =60mg	4 doses = 160mg	8 doses=320mg
IVIG 10% (25g) cumulative		1 dose	2 doses		3 doses	3 doses
Vitamin B12 1000mcg PO (cumulative)					1 dose	2 doses
Cholecalciferol PO (cumulative)				50,000 iu	51, 000 iu	52,000 iu
Ceftriaxone IV 2g Q24h (cumulative)	1 dose		2 doses			
Doxycycline 100mg Q24h (cumulative)		1 dose		2 doses		

¥: Combined potassium replacement in the form of IV KCl. PO KCl, IV potassium phosphate (Kphos) and oral potassium phosphate-sodium phosphate (Neutra-phos)

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