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Hypokalemic Paralysis Complicated by Concurrent Hyperthyroidism and Hyperaldosternoism: A Case Report

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Patient: Female, 38
Final Diagnosis: Primary hyperaldosteronism
Symptoms: Paralysis
Medication: —
Clinical Procedure: —
Specialty: Nephrology

Objective: Challenging differential diagnosis

Background: Thyrotoxic periodic paralysis (TPP) is commonly observed in patients with acute paralysis and hyperthyroidism. However, there is a possibility of secondary causes of hypokalemia in such a setting.

Case Report: Herein, we present the case of a 38-year-old woman with untreated hypertension and hyperthyroidism. She presented with muscle weakness, nausea, vomiting, and diarrhea since one week. The initial diagnosis was TPP. However, biochemistry tests showed hypokalemia with metabolic alkalosis and renal potassium wasting. Moreover, a suppressed plasma renin level and a high plasma aldosterone level were noted, which was suggestive of primary aldosteronism. Abdominal computed tomography confirmed this diagnosis.

Conclusions: Therefore, it is imperative to consider other causes of hypokalemia (apart from TPP) in a patient with hyperthyroidism but with renal potassium wasting and metabolic alkalosis. This can help avoid delay in diagnosis of the underlying disease.

MeSH Keywords: Hyperaldosteronism • Hypokalemia • Hypokalemic Periodic Paralysis • Thyrotoxicosis

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/901793

Background

Hypokalemic periodic paralysis is a common condition which presents as severe muscle weakness and markedly low serum potassium level. Most commonly affected age group is between15 and 35 years; the incidence tends to decrease with an increase in age [1]. It could be familial and inherited with an autosomal dominant pattern. However, the most common cause is thyrotoxic periodic paralysis (TPP), which is particularly observed among Asians. However, with global population transmigration, an increase in its incidence in Western countries has been reported [2]. Nevertheless, concomitant occurrence of primary hyperaldosteronism (PA) and thyrotoxic nodular goiter is rare and has a similar clinical presentation (hypokalemia), which may lead to delayed diagnosis.

We present our experience of successful early diagnosis in a patient with hypokalemia and thyrotoxicosis, in whom the underlying cause of hypokalemia was PA.

Case Report

A 38-year-old woman with underlying hypertension and untreated hyperthyroidism due to Grave's disease since three years presented to emergency department with chief complaints of general weakness, nausea, vomiting, and diarrhea since one week. She also had palpitations with shortness of breath and insomnia. She experienced three episodes of recurrent paralysis in the past year. There was no history of recent strenuous physical activity, intake of Chinese traditional medicine, or use of diuretics.

On physical examination, the patient was alert, well-oriented with a pulse rate of 96 beats/minute; her blood pressure was 160/88 mm Hg. Her body mass index (BMI) was 23.4 kg/m^2 (height, 166 cm and weight, 64.5 kg). Hand tremors and diffuse enlarged goiter (grade II) were also noted. On neurological examination, there was a generalized decrease in muscle strength (muscle power: grade 4/5 in all four limbs).

Arterial blood gas analysis showed metabolic alkalosis (pH: 7.487; PCO_2: 48.8 mm Hg; and HCO_3: 37.3 mmol/L). Blood biochemistry revealed hypokalemia (K^+: 2.8 mmol/L) and primary hyperthyroidism [TSH <0.0025 uIU/mL (normal range, 0.35–0.49); free T4: 32.04 pmol/L (normal range 9–19); and thyroid peroxidase antibodies: 709 IU/mL (normal range 0–60)].

The initial diagnosis was hypokalemic paralysis caused by hyperthyroidism (TPP). Therefore, non-selective β-blocker (propranolol, 90 mg per day) and propylthiouracil (100 mg per day) therapy was initiated, which led to the resolution of palpitations. Moreover, cautious potassium supplementation was initiated to stabilize her serum potassium level. However, findings of metabolic alkalosis and renal potassium wasting accompanied by a high transtubular potassium gradient of 7.63 on spot urine test did not support the diagnosis of TTP (Table 1). Endocrinological investigations revealed normal cortisol level [333.8 nmol/L (normal range 186.8–630.3)], elevated aldosterone level [1175.8 ng/L (normal range 78–104)], low plasma renin level [1.25 ng/L (normal range 15.7–57.6)], and a high aldosterone/renin level of 940; based on these findings, primary

Table 1. Serum and urine biochemistry at admission.

Parameter	Value
Plasma (reference range)	
pH (7.35–7.45)	7.48
Bicarbonate (22–24 mmol/L)	37.3*
BUN (2.4–8.9 mmol/L)	2.49
Creatinine (44.2–203.3 µmol/L)	35.3
Na^+ (136–145 mmol/L)	133
K^+ (3.5–5.0 mmol/L)	2.8*
Cl^- (98–107 mmol/L)	100
Ca^{++} (2.18–2.58 mmol/L)	2.45
Phosphate (0.8–1.5 mmol/l)	1.06
Magnesium (0.78–1.10 mmol/L)	0.82
Osmolality (285–295 mOsm/kg)	283
Spot urine	
pH	7.0
UUN (mmol/L)	674
Creatinine (µmol/L)	7160
Na^+ (mmol/L)	31
K^+ (mmol/L)	42
Cl^- (mmol/L)	40
Ca^{++} (mmol/L)	4.8
Phosphate (mmol/L)	32.4
Magnesium (mmol/L)	4.9
Osmolality (300–900 mOsm/kg)	556
TTKG (<3b)**	7.63
K^+/Cr (mmol/mmol) [<(2b)]**	5.8
Ca^{++}/Phosphate (mmol/mmol)	0.14

* Indicates abnormal values; ** indicates reference range for normal renal response to hypokalemia. BUN – blood urea nitrogen; UUN – urine urea nitrogen; TTKG – transtubular K^+ gradient.

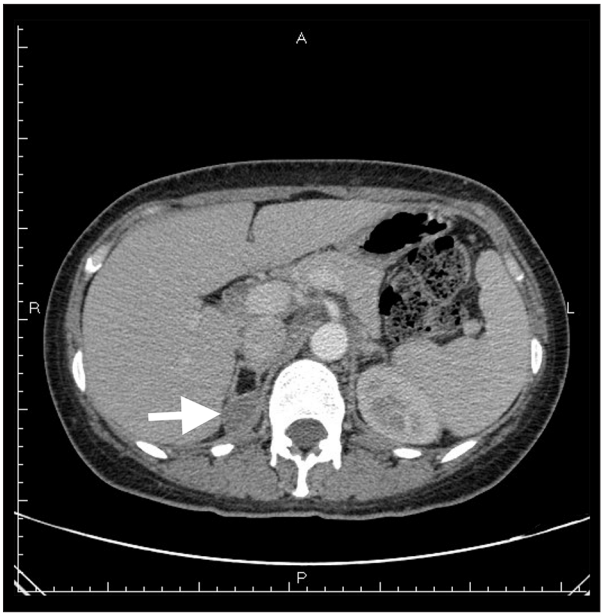

Figure 1. Contrast-enhanced abdominal CT showing a mass lesion (30 mm) on the left adrenal gland (arrow).

hyperaldosternoism was highly suspected. It was verified on contrast-enhanced abdominal computed tomography, which showed a right adrenal gland tumor of approximately 30 mm in dimension (Figure 1).

Based on the diagnosis of hypertension and hypokalemia due to primary aldosteronism, we prescribed her spironolactone (25 mg per day) and sevikar® (amlodipine plus olmesartan medoxomil, 5 mg/20 mg per day) for blood pressure control. She was discharged with corrected serum potassium levels and blood pressure. However, hypokalemia (K^+: 2.4 mmol/L) was again noted seven days later. Therefore, laparoscopic adrenalectomy was performed one month later. Histopathological examination of the surgical specimen showed cortical adenoma. Postoperatively, her blood pressure and serum potassium levels were maintained within the normal range on oral propylthiouracil (100 mg per day).

Discussion

Hypokalemia is one of the most frequently encountered fluid and electrolyte abnormalities in clinical medicine and an important cause of acute flaccid paralysis in adults. It can result from reduced potassium intake, transcellular potassium uptake, and extrarenal or renal potassium loss [3]. In Asian populations, hypokalemic periodic paralysis accounts for 75% of cases of extreme weakness, of which the most common subgroup is TPP [4]. The reported incidence of TPP in Chinese patients with thyrotoxic is 1.8%; the male to female ratio ranges from 17: 1 to 70: 1, despite the fact that hyperthyroidism is more common in females (female-to-male ratio: 9: 1) [5].

The underlying mechanism of TPP is the disruption of cellular transport channels, particularly overstimulation of the Na^+/K^+-ATPase pump in the cell membranes of skeletal muscles. The intracellular trapping of potassium results in hypokalemia; loss of function mutation, or hormone (adrenalin or insulin)-mediated inhibition may lead to muscle paralysis [6,7]. The adrenergic response to increase Na^+/K^+-ATPase pump activity can explain why males are at a higher risk of TPP despite thyroid disease being more common in females [8]. Increased awareness and early diagnosis and management of the TPP can prevent severe complications, such as cardiac arrhythmias.

Primary aldosteronism is characterized by dysregulated aldosterone production. Approximately 95% of sporadic cases are caused by aldosterone-producing adenoma or bilateral adrenal hyperplasia [9]. It is characterized by hypertension with low plasma renin and elevated aldosterone levels and is often associated with hypokalemia. The distinctive clinical and laboratory features characterize the underlying pathology. Adrenal cortical hyperplasia usually observed in older individuals, predominantly among males, is more often normokalemic, and is associated with less severe hypertension. In contrast, aldosterone-producing adenomas tend to appear at an earlier age, occur more often in females, and are more often associated with hypokalemia and severe hypertension [10]. A recent study found 9–37% overall incidence of hypokalemia in patients with documented PA [11].

Both TPP and PA are causes of hypokalemic paralysis. Concomitant occurrence of both conditions in a hypokalemic patient is rare. Similar cases have been reported earlier [12–14]. However, the lack of attention to the concomitant renal potassium wasting and metabolic alkalosis delayed the diagnosis of the real cause of hypokalemia until the lack of response to potassium supplementation was noticed. Different strategies for potassium supplementation are employed in these two diseases. For TTP, potassium loading should be cautious because of the risk of rebound hyperkalemia on suppression of the catecholaminergic state. However, hypokalemia due to primary aldosteronism requires vigorous potassium replenishment to avoid lethal arrhythmia. Therefore, a comprehensive diagnostic approach is required in a patient with hypokalemia [15–20] (Figure 2). We should note that measurements of blood and urinary electrolyte levels and acid-based should be performed step by step to assess a patient with hypokalemia, regardless of the clinical presentation. Comprehensive workup of the patient is recommended as cases with combined etiology are reported more and more often. In the present case, the presentation of hypokalemic paralysis and hyperthyroidism was noted initially. However, the recognition of the presence of metabolic alkalosis, high renal potassium secretion rate, and low urine calcium/phosphate ratio (usually more than 1.7 in TPP) [19] in the spot urine assessment prompted

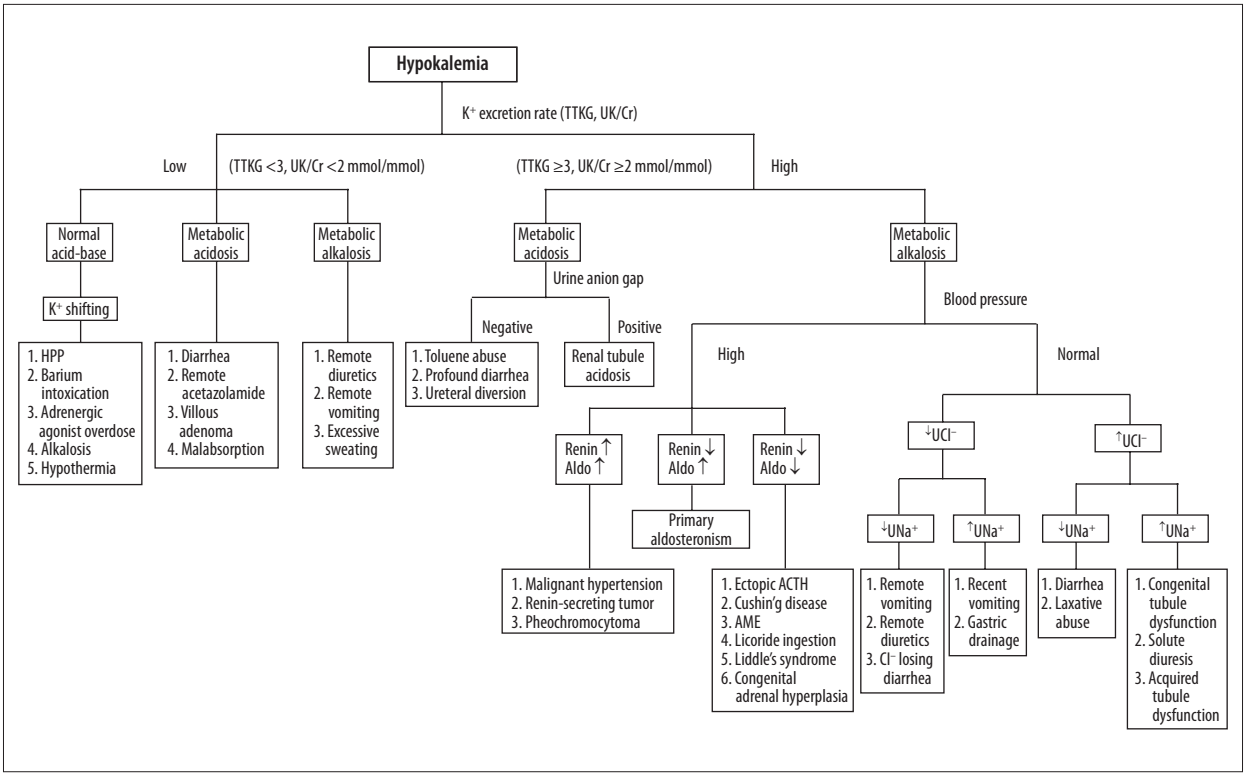

Figure 2. Schematic illustration of the recommended diagnostic approach to hypokalemia.

us to associate the severe potassium deficit with a primary cause. Further, elevated aldosterone and suppressed renin levels pointed towards primary aldosteronism as the real etiology.

Conclusions

In conclusion, it is incorrect to arrive at a diagnosis of TPP quickly in patients who present with hyperthyroidism and hypokalemia. Potassium secretion in spot urine and arterial blood gas could offer vital information to identify the cause of hypokalemia.

Statement

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