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Case Report

# Conn's Syndrome with an Unusual Presentation of Rhabdomyolysis Secondary to Severe Hypokalemia

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**Abstract**

Conn's syndrome is one of the major causes of secondary hypertension. Premature hypertension, metabolic alkalosis, and hypokalemia usually lead clinicians to suspect the diagnosis. We describe a case of Conn's syndrome in a 28-year-old woman with an unusual presentation of rhabdomyolysis secondary to hypokalemia and complete bilateral lower limb paralysis. An elevated transtubular potassium concentration gradient, asymptomatic severe hypertension, and metabolic alkalosis pointed to possible primary hyperaldosteronism, which was confirmed by a decrease in plasma renin activity (PRA), elevation in plasma aldosterone level and elevation of the plasma aldosterone to PRA ratio. Computed tomography showed an adrenal tumor in the adrenal gland. Her blood pressure, hypokalemia, and plasma aldosterone level returned to normal after left adrenalectomy, further confirming the diagnosis. Histologic examination showed an adrenal gland adenoma. [*Tzu Chi Med J* 2008;20(4):327–331]

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## 1. Introduction

The presentations of hypokalemia vary from mild muscle weakness to cardiac arrhythmias and rhabdomyolysis [1–5]. The combination of hypertension, hypokalemia, and metabolic alkalosis is important for a diagnosis of primary aldosteronism [6]. Primary aldosteronism is the most common curable condition causing secondary hypertension. Idiopathic bilateral adrenal hyperplasia and aldosterone-producing adenoma are the leading causes of this disease. We describe a case of typical Conn's syndrome presenting with rhabdomyolysis, hypokalemia, hypertension, and metabolic alkalosis. These manifestations led to the suspicion of primary aldosteronism, and hormone studies showed a decrease in plasma renin activity (PRA), an elevation in plasma aldosterone level, and an elevation in the ratio of plasma aldosterone to PRA. Moreover, adrenal gland computed tomography (CT) revealed an adrenal gland tumor. Her blood pressure and hypokalemia and plasma aldosterone level returned to normal after left adrenalectomy, and histologic examination showed adrenal cortical adenoma.

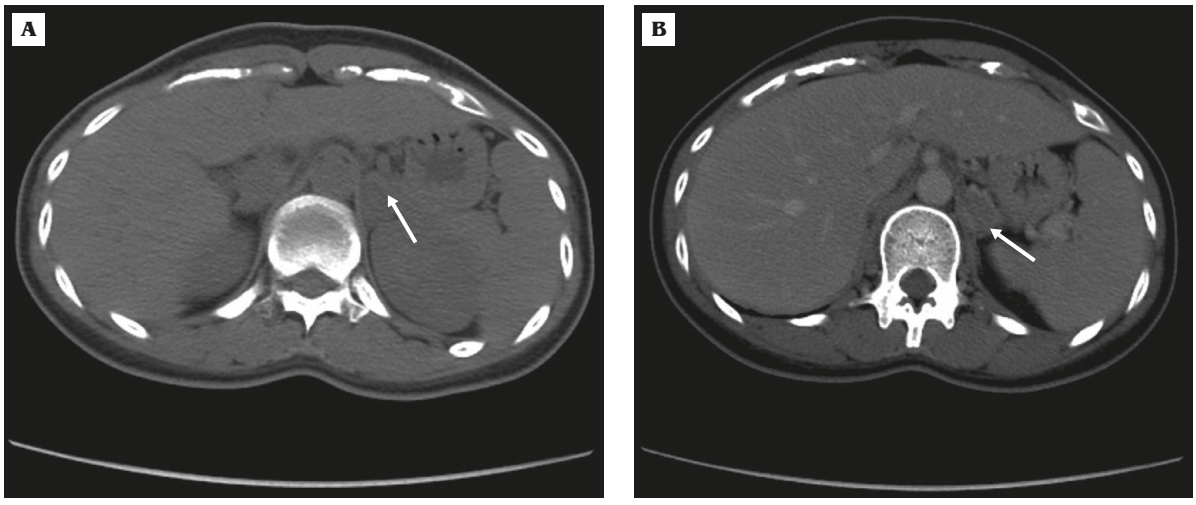


**Fig. 1 — Adrenal computed tomography shows an adrenal gland tumor (arrows) measuring approximately 2.5 × 1.5 × 2.5 cm at the largest diameters: (A) before contrast medium injection; (B) after contrast medium injection.**

## 2. Case report

A 28-year-old-woman was admitted with severe weakness and soreness in bilateral lower limbs. Four days before admission, she had malaise and weakness, which gradually progressed to limb paralysis (lower limbs more severe than upper). On the day of admission, she could not get out of bed or a chair by herself. She denied a recent history of trauma to her back or lifting heavy objects. She denied fever, cough, or changes in urinary habits or bowel movements. She did not have a history of abnormal blood pressure. She did not use laxatives, diuretics or Chinese herbs. None of her family members had experienced these symptoms. Her weight and height were average for her sex and age. She looked well with no distress except for the inability to move her legs.

Her blood pressure was 174/111 mmHg, body temperature was 36.7°C, pulse rate was 60 beats/min, and respiratory rate was 18/min. She was not anemic, and the thyroid gland was not palpable. A decrease in bowel movements was noted. She had a regular heartbeat with no audible murmur, clear vesicular breath sounds, no radiofemoral delay, and no renal bruit. She had lack of muscle tone and poor muscle power (0/5) in both the proximal and distal lower limbs and mildly decreased muscle power in the upper limbs (4/5). Chest radiography showed no abnormalities and electrocardiography revealed sinus rhythm with a flattened ST segment.

Initial biochemistry results disclosed severe hypokalemia (potassium, 1.8 mmol/L). Serum sodium level was 143 mmol/L, serum calcium was 2.34 mmol/L, aspartate aminotransferase was 155 IU/L, alanine aminotransferase was 57 IU/L, lactate dehydrogenase was 517 IU/L, creatine kinase (CK) was 9837 IU/L (rechecked: 12,147 IU/L), and CK-MB was 100 IU/L. Urine myoglobulin was elevated (2744.6 ng/mL). Blood gas analysis revealed pH of 7.588, $PaO_2$ of 124.8 mmHg, $PCO_2$ of 31.5 mmHg, and $HCO_3^-$ of 30.3 mmol/L. Severe hypokalemia with rhabdomyolysis was tentatively diagnosed. The urine transtubular potassium gradient (TTKG) was measured and the level was 5, indicating renal potassium wasting.

Rhabdomyolysis was treated with hydration and forced alkaline diuresis. Potassium was replaced intravenously. Her hypertension was also treated with bisoprolol 5 mg qd per oral and spironolactone 25 mg bid per oral.

PRA was 0.14 $ng \cdot mL^{-1} \cdot hr^{-1}$, and plasma aldosterone was 198 pg/mL (19.8 ng/dL); the aldosterone to PRA ratio was approximately 141 $(ng/dL)/(ng/mL^{-1} \cdot hr^{-1})$. Primary hyperaldosteronism was highly suspected. CT revealed a left adrenal gland tumor measuring about 2.5 × 1.5 × 2.5 cm at the largest diameters (Fig. 1). Left adrenalectomy was performed and specimens from the adrenal gland showed adrenal cortical adenoma (Fig. 2).

The hypokalemia, hypertension and plasma aldosterone level (97.9 pg/mL) dramatically returned to normal following removal of the adrenal adenoma.

## 3. Discussion

Although hypokalemia is a common finding in primary aldosteronism, there are rare reports of cases of hyperaldosteronism complicated by hypokalemia and rhabdomyolysis (7–9). Here, we reported a patient who presented with severe lower limb weakness and biochemistry data showing hypokalemia, elevated muscle enzymes, metabolic alkalosis, and a rise in urine

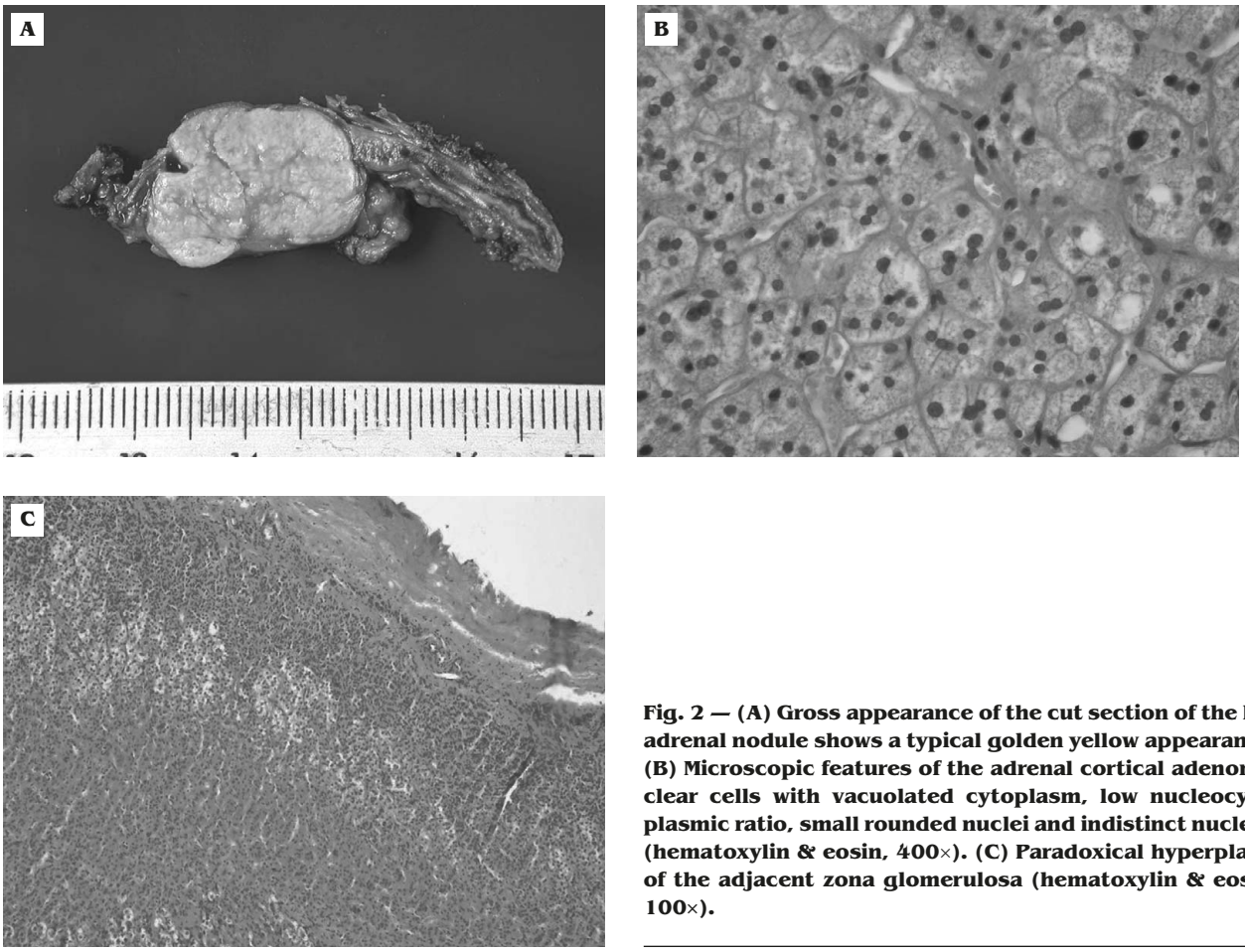


**Fig. 2 — (A) Gross appearance of the cut section of the left adrenal nodule shows a typical golden yellow appearance. (B) Microscopic features of the adrenal cortical adenoma: clear cells with vacuolated cytoplasm, low nucleocytoplasmic ratio, small rounded nuclei and indistinct nucleoli (hematoxylin & eosin, 400×). (C) Paradoxical hyperplasia of the adjacent zona glomerulosa (hematoxylin & eosin, 100×).**

TTKG. In addition, hypertension, elevated plasma aldosterone and PRA levels, and a high plasma aldosterone to PRA ratio were noted, and adrenal CT showed adrenal gland adenoma. Her hypertension and hypokalemia were corrected via left adrenalectomy, and histologic examination showed adrenal cortical adenoma.

Primary aldosteronism complicated by hypokalemia rarely leads to rhabdomyolysis [7–9] because this hypokalemia is chronic and plasma potassium tends to be relatively stable as the potassium-wasting effect of excess aldosterone is counterbalanced by the potassium-retaining effect of the hypokalemia itself [10]. The exact incidence of rhabdomyolysis in primary aldosteronism is unknown. However, in one report, hypokalemia was found in 41% of 148 patients with primary aldosteronism. Very low levels of serum potassium (<3 mmol/L) were found in a minority (6.7%) of these patients. One patient presented with quadriplegia; none presented with rhabdomyolysis [11].

Rhabdomyolysis is an uncommon clinical finding characterized by muscle necrosis and the release of intracellular muscle constituents into the circulation. There are a variety of causes which can lead to rhabdomyolysis, including direct muscle injury such as crush injuries (prolonged compression after coma or extraordinary physical exertion are the most common), although heritable muscle enzyme deficiencies, electrolyte abnormalities, infections, drugs, toxins, and hyperthermia can also be associated with it [1]. This patient's history and initial serum potassium level were compatible with hypokalemia-induced rhabdomyolysis.

The clinical manifestations of hypokalemia are varied and include muscle weakness, fatigue, frank ileus, polyuria, fatal cardiac arrhythmias and respiratory failure [2,3]. Cardiac complications and rhabdomyolysis usually present with serum potassium levels <3 mmol/L [2,4,5]. The differential diagnosis of this patient's severe hypokalemia included: (1) poor intake; (2) acute cellular shift from increased insulin availability [12–14], elevated beta adrenergic activity from catecholamine excess [13,15] and thyrotoxic periodic paralysis [16–21]; (3) increased gastrointestinal loss; and (4) increased renal loss. Hypokalemia with TTKG>4 suggests renal potassium loss due to increased distal potassium secretion. In addition, the triad of unexplained renal hypokalemia, hypertension and metabolic alkalosis should lead to the suspicion of primary hyperaldosteronism, as seen in our patient. A high plasma aldosterone level (>500 pmol/L or 15 ng/dL) and a high plasma aldosterone to PRA

ratio [>30 (ng/dL)/(ng·mL$^{-1}$·hr$^{-1}$)] are the most useful screening tests for suspected primary hyperaldosteronism [6,22–24], and these were positive in our patient.

Primary hyperaldosteronism can be divided into unilateral adrenal aldosterone hypersecretion (adenoma, unilateral hyperplasia or carcinoma), and bilateral aldosterone hypersecretion (idiopathic adrenal hyperplasia or glucocorticoid remediable aldosteronism). Conn's syndrome, or aldosterone-producing adrenal cortical adenoma, is the most common cause of secondary hypertension. It is caused by an aldosterone-producing adrenal cortical adenoma, and is important because it is surgically curable. Older studies suggested a prevalence of primary aldosteronism of less than 1% in hypertensive patients, and it usually occurred between the ages of 30 and 50, with twice as many cases in women than in men [23,25]. However, the wider application of measurements of aldosterone and PRA in recent years has suggested that it is probably a more common cause of secondary hypertension than previously thought [26,27]. The final diagnosis is usually made by surgical intervention followed by histologic confirmation. The treatment of primary hyperaldosteronism due to Conn's syndrome should be with combined medication and surgery. Medical control with mineralocorticoid receptor antagonists such as spironolactone is effective in both the pre- and postoperative periods [28,29]. Other potassium-sparing diuretics such as amiloride and triamterene can be used as alternatives but not as first-line treatment [30,31].

Unilateral adrenalectomy is usually associated with improvement in all patients and a cure in 30–60% of hypertensive patients [32]. Correction of hypokalemia and marked reductions in aldosterone levels have been noted after surgery [33,34]. Although surgery is an effective measure, more severe glomerulosclerosis and renal arteriolosclerosis, and a worse left ventricular mass index prior to surgery are related to persistent elevated blood pressure after adrenalectomy in some patients [35]. Resolution of hypertension after adrenalectomy may be independently associated with younger age, lack of family history of hypertension, a short duration of hypertension, use of no more than two antihypertensive medications during the preoperative period, a higher preoperative ratio of plasma aldosterone concentration to PRA, and a higher urine aldosterone level [34].

## 4. Conclusion

Rhabdomyolysis may be present in a variety of hypokalemic cases, but its association with Conn's syndrome is relatively uncommon and has only been seen in a few case reports [7–9]. Because our patient presented with hypokalemia, rhabdomyolysis, hypertension, and metabolic alkalosis, we strongly suspected primary aldosteronism. Our suspicion was confirmed by a decrease in PRA, elevation in plasma aldosterone level, and a high plasma aldosterone to PRA ratio. An adrenal tumor was seen on adrenal gland CT. Further confirmation was made when her hypertension and hypokalemia returned to normal after left adrenalectomy and histologic examination showed an adrenal gland adenoma. Therefore, we recommend that primary aldosteronism be considered a possible etiology in patients who present with hypokalemia, hypertension and rhabdomyolysis.

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