中文題目：以高血壓與嚴重低血鉀症為表現的腎上腺皮質癌：個案報告

英文題目：A 60-year-old Woman with Hypertension and Profound Hypokalemia

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Introduction

Hypokalemia is a common clinical problem. Increase in urinary potassium wasting by enhanced mineralocorticoid activity is one of the main causes. The most common causes of primary aldosteronism are aldosterone-producing adenomas and bilateral adrenal hyperplasia. Adrenocortical carcinoma (ACC) is a rare and neglected cause. ACC is also a rare adrenal malignancy of prevalence about 1.8-3.0 % among adrenal tumors. ACC in adults develops mostly in the fourth to fifth decade of life, with female predominance (Female-to-male ratio 1.5 to 2.5). The most common symptoms of ACC were excessive adrenal hormone production including hyperaldosteronism.

Case presentation

A 60-year-old woman with history of hypertension came to our emergent department due to malaise and sudden onset of paralysis over bilateral lower limbs.

She was with clear consciousness. The blood pressure was 200/127 mmHg. The serum blood potassium level was 1.6 mEq/L. Vein blood gas analysis showed metabolic alkalosis (pH 7.473, pCO_2 54.3 mmHg, HCO_3 35.2 mmol/L). The blood creatinine kinase level was 4188 U/L. An electrocardiography showed prolonged PR interval and flattened T wave. She stated no high carbohydrate meals, no nausea, no vomiting, and no diarrhea recently. Severe hypokalemia complicated with rhabdomyolysis was diagnosed, and mineralocorticoid excess was suspected on the basis of hypokalemia, hypertension, and metabolic alkalosis.

Her current medications included amlodipine, valsartan and propranolol, but no diuretics or licorice. She had no family history of thyroid disease.

Urine biochemistry panel on admission (Table 1) suggested hypokalemia with renal loss. Normal renin level and high aldosterone level were found even under angiotensin receptor blockers, and spironolactone, indicating primary aldosteronism. Computed tomography (CT) of abdomen disclosed inhomogeneous adrenal tumor and para-aortic lymphadenopathy (Figure 1). Preoperative endocrine panel also revealed borderline primary hypercortisolism and significant hyperandrogenism (Table 2).

Table 1. Urine electrolyte panel

Variables	Creatinine mg/dl	Sodium mEq/L	Potassium mEq/L	Chloride mEq/L	Osmolarity mosm/L	UPCR mg/mEq	TTKG
On Admission	9.9	62	9.5	58	192	9.59	8.86

Table 2. Pre-operative endocrine panel

Variable	VMA(24Hr) mg/day	Epinephrine ug/day	Norepinephrine ug/day	Dopamine ug/day	DHEA-S ug/dl
Before Operation	1.25	<3.0	8.2	73	1000
Normal value	1.00 - 7.50	<27.0	<97.0	<500.0	18.9 - 205

She received hand-assisted laparoscopic right adrenalectomy after the diagnosis. Pathology report revealed adrenocortical carcinoma, Ki67 40%, mitotic counts > 50/50 HPF, and ruptured capsule. Final AJCC staging is cT3N1M0, stage III. The further adjuvant mitotane therapy was suggested but the patient hesitated.

Her serum aldosterone level decreased transiently, but then doubled 3 months after the operation (Table 3). CT of chest and abdomen revealed local recurrence with S6 liver and IVC involvement, with multiple bilateral lung metastases.

She was admitted again due to short of breath, bilateral legs edema, and abdominal distention. Chest radiography revealed multiple nodules of lung metastases. Abdominal sonography showed local recurrence, multiple liver metastases, and ascites. She received mitotane and salvage chemotherapy immediately, but she died from sepsis.

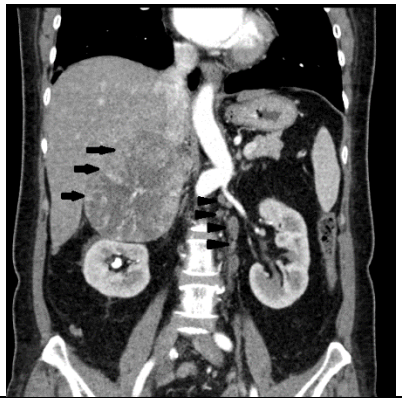

Figure 1. Right adrenal gland tumor (Arrow) with left paraaortic lymphadenopathy (Arrowhead). Hetero-enhanced tumor, 11.5 X 8.3 X 9.7cm.

Table 3. Adrenal gland function markers as ACC markers

Variable	Initial	D1	D43	D100	Normal values
Potassium (mEq/L)	1.6	3.8	3.4	4.6	3.5 - 5.1
Cortisol 8 AM (ug/dL)	15.0	18.5	10.6	21.3	6.0 - 18.4
ACTH 8 AM (pg/mL)	NA	<1.0	1.1	NA	7.2 - 63.3
Renin (ng/mL/hr)	0.4	NA	0.7	3.6	0.3 - 1.8
Aldosterone (pg/mL)	1451.8	NA	331.5	563	68 – 173

D1: operation day, D43, post-operative day 43, D100: post-operative day 100

Discussion

The patient presented typical hypokalemia resulting from mineralocorticoid excess. Most causes of mineralocorticoid excess are benign adrenal tumor or adrenal hyperplasia. Adrenocortical carcinoma is rare. This patient had a tumor greater than 4cm in diameter, with higher attenuation values, inhomogeneity, lymph node enlargement, and possible invasion of surrounding structures, which resembled ACC. This case reminds us that not all adrenal tumors with hypokalemia are benign. When malignancy is suspected, staging workup including CT of the chest and liver and bone scan are required to survey liver, lungs, lymph nodes, or bone metastasis. This case was a stage III tumor, with 30-50% 5-year-survival. Pathological report disclosed mitotic rate > 50/50 HPF and Ki67 more than 10%, indicating high recurrence risk. Therefore, adjuvant mitotane therapy is necessary. For advanced or recurrent ACC, etoposide, doxorubicin, and cisplatin (EDP)-mitotane regimen is considered the standard chemotherapy.

Conclusion

We report a rare case of adrenocortical carcinoma with initial presentation of profound hypokalemia with paralysis, which remind us not all primary hyperaldosteronism are benign. Early surgical intervention and a well-timed systemic therapy are crucial to prolong survival of patient of adrenocortical carcinoma.