Aldosterone-Secreting Adrenocortical Carcinoma Presenting With Cardiac Arrest

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Adrenocortical carcinoma (ACC) is a rare malignancy that usually is detected as a result of symptoms of hormone excess or mass effect. We describe a rare presentation of ACC with primary aldosterone production leading to profound hypokalemia and cardiac arrest. The patient was previously asymptomatic with low-grade, untreated hypertension and no documented electrolyte abnormalities. She had sudden cardiac arrest, and potassium levels were undetectable. After successful resuscitation, imaging showed a 6-cm left adrenal mass highly suspicious for malignancy. Biochemical workup revealed aldosterone excess as well as cortisol excess, despite the absence of Cushingoid symptoms. Histopathological examination after surgical resection demonstrated high-grade ACC. This case illustrates that the workup of cardiac arrest as a result of electrolyte abnormalities should include evaluation for adrenal pathology.

Freeform/Key Words: adrenocortical carcinoma, hyperaldosteronism, hypokalemia, adrenal mass

Adrenocortical carcinoma (ACC) is a rare primary malignancy of the adrenal gland with a poor prognosis. The majority of ACCs (~60%) includes functional, hormone-secreting tumors leading to tumor detection. Roughly 40% of symptomatic patients with ACC have Cushing syndrome, and 24% have concurrent virilization [1]. Very few of these tumors primarily secrete aldosterone; only ~2.5% of all ACCs produce exclusively aldosterone [2, 3]. Whereas many ACCs are detected by workup for symptoms related to hormonal hyperproduction, the others are found as a result of symptoms from tumor mass effect or are detected on imaging. This case highlights a rare presentation of ACC with electrolyte disturbances diagnosed after cardiac arrest.

1. Case Presentation

We present a 55-year-old woman with past medical history notable only for untreated mild hypertension. She took no regular medications or supplements. Immediately after waking one morning, she felt faint and ultimately became unconscious. Paramedic evaluation revealed pulselessness, and cardiopulmonary resuscitation was initiated within 5 minutes of loss of consciousness. Automated external defibrillator was used to administer one shock, in

Abbreviation: ACC, adrenocortical carcinoma.

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addition to epinephrine administration, with return of spontaneous circulation. Hospital ECG evaluation showed prolonged QT interval, nonsustained ventricular tachycardia, and frequent premature ventricular contractions. Laboratories demonstrated profound hypokalemia (potassium <2.0 mM), in addition to hypomagnesemia and hypophosphatemia. She underwent cooling protocol for cardiac arrest and received centrally administered electrolyte repletion with lidocaine for cardiac stabilization. Echocardiogram showed no anatomic abnormalities. She was noted to have returned to normal sinus rhythm upon electrolyte correction after 24 hours. Subsequent workup with CT imaging revealed a solid left adrenal mass measuring 59 × 45 × 56 mm and Hounsfield units 43 precontrast (Fig. 1). There was a small, indeterminate lung nodule also seen but no definitive evidence of metastatic disease.

Initial endocrine workup (Table 1) was performed following electrolyte correction and prompted by the CT finding of an adrenal mass. Her laboratory work revealed a markedly elevated aldosterone level of 103 ng/dL (normal 0 to 30 ng/dL), renin 0.375 ng/mL/hour (0.167 to 5.35 ng/mL/hour), and aldosterone/renin ratio 275. Plasma and urinary metanephrines were within normal limits. ACTH was low at 3.8 pg/mL (7.2 to 63.3 pg/mL), and random plasma cortisol level was 18.1 μg/dL. Twenty-four- hour urinary cortisol was collected and was found to be elevated both immediately following this acute episode but also several weeks later on an outpatient basis, 249 μg/24 hours and 244 μg/24 hours, respectively (0 to 50 μg/24 hours). Midnight salivary cortisol and dexamethasone suppression testing was not performed. Given absence of any virilization, testosterone levels were also not assessed.

Following the cardiac arrest, she recovered to baseline function and was discharged to home on spironolactone 200 mg, as well as potassium chloride 20 mEq, twice daily. She maintained normal potassium levels on several checks as an outpatient on this regimen. Notably, the patient had no preceding history of muscle weakness or cramping. She was thin at baseline (body mass index 17.6) with no recent weight loss and without any Cushingoid features, virilization, or documented glucose intolerance.

After multidisciplinary evaluation by the University of Washington Endocrine Tumor Program, she underwent surgical resection via open left adrenalectomy with peri-operative stress-dose steroid replacement. The 6-cm mass was found to be well encapsulated without any gross invasion or adherence to surrounding structures. It was quite vascular with multiple surface veins (Fig. 2a). She recovered uneventfully. On postoperative day 1, aldosterone levels were undetectable (<4.0 ng/dL), and potassium was normal. She was placed on steroid taper postoperatively as a result of concern for suppression of the contralateral adrenal gland. Blood pressure during hospitalization was normal.

Pathology revealed high-grade ACC with invasion through the adrenal capsule, although with negative surgical margins, consistent with a pT3 lesion (Fig. 2b). The tumor measured 5.9 cm and weighed 118 g. There was tumor necrosis and lymphovascular invasion. With the use of the American Joint Committee on Cancer Guidelines (AJCC 8th edition, 2017), this was a Stage III malignancy, based on operative pathology [4].

After discharge, she was seen in follow-up after 2 weeks. She had recurrent hypertension with blood pressure 152/92. Laboratories revealed recurrent hypokalemia of 2.9 mEq/L and aldosterone level 5.3 ng/dL. She was restarted on spironolactone and potassium

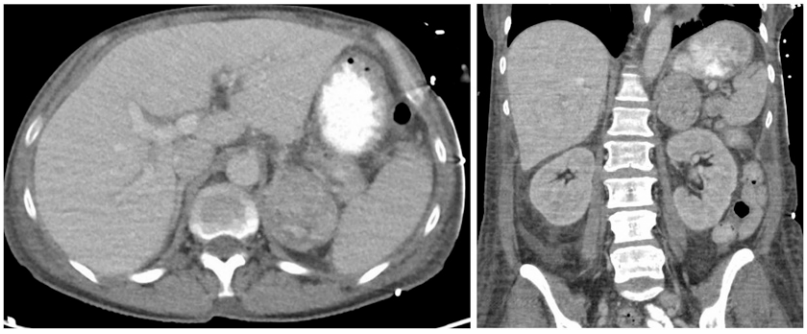

Figure 1. CT scan images: axial and coronal views of the left adrenal tumor.

Table 1. Initial Laboratory Evaluation of Patient Presenting With Cardiac Arrest and Adrenal Mass

Laboratory Test, Units	Result (Normal Range)
Serum potassium, mM	<2.0 (3.5–4.9)
Serum glucose, mg/dL	179 (70–105)
Serum magnesium, mg/dL	1.53 (1.60–2.30)
Serum cortisol, μg/dL	18.1 (2.3–11.9)
Serum ACTH, pg/mL	3.8 (7.2–63.3)
Serum aldosterone, ng/dL	103.1 (0–30)
Serum renin, ng/mL/hr	0.375 (0.167–5.380)
Urine normetanephrine, μg/24 hr	213 (82–500)
Urine metanephrine, μg/24 hr	55 (45–290)
Urine cortisol, μg/24 hr	249 (0–50)

supplementation, which led to normalization of the blood pressure and hypokalemia. Cross-sectional imaging showed an increase in the size of the previously indeterminate lung nodule from 4 to 6 mm and development of three additional 6-mm nodules, suspicious for metastatic disease.

Multidisciplinary evaluation of this patient with a high-grade ACC secreting both aldosterone and cortisol included endocrinology and endocrine surgery preoperatively, as well as medical oncology and radiation oncology postoperatively. Additional treatment options discussed with the patient included external beam radiation to the adrenal bed, mitotane therapy, and systemic chemotherapy. At the current time, she is considering her options for further treatment and has declined immediate initiation of systemic therapy. This case highlights the importance of a high index of suspicion for adrenal etiology of profound electrolyte disturbances presenting with cardiac manifestations.

2. Discussion

The first case report of an ACC with primarily aldosterone production was in 1955 by Dr. Foye and Feichtmeir [5], who described a hypertensive man with increasing weakness as a result of hypokalemia. Hypertension or muscle dysfunction is the most common presenting symptom of aldosterone excess described in the literature, with only rare reports of cardiac dysfunction. Abdo *et al.* in 1998 [6] reported a young woman who presented with ventricular tachycardia from marked hypokalemia. In this case, workup revealed an adrenal tumor; however, pathologic evaluation showed a benign adenoma rather than ACC.

The presence of excess aldosterone and an adrenal tumor can indicate either a benign or malignant process. Given the rarity of ACC, it is much more likely that an adrenal etiology of

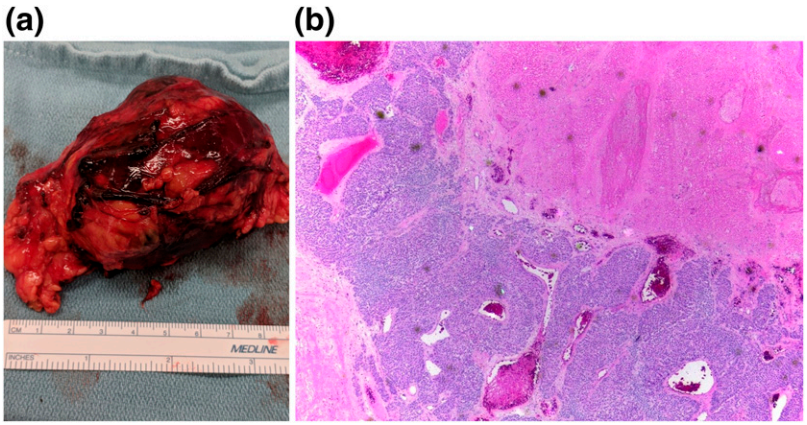

Figure 2. (a) Gross appearance of operative specimen of left adrenal gland and tumor. (b) Histologic section from tumor showing extra-adrenal extension.

excess aldosterone is either an adenoma or bilateral hyperplasia. However, the documented excess of multiple cortical hormones (aldosterone and cortisol) raises suspicion for malignancy. The production of multiple hormones with clinical predominance of the mineralocorticoid effects is illustrated by our case of a woman with ACC presenting with cardiac arrest as a result of hypokalemia.

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References and Notes

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