Case report

Metabolic and Cardiac Complications in a Case of Adrenal Carcinoma

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Introduction

Adrenocortical carcinoma (ACC) is a very rare and aggressive cancer originating from the adrenal cortex. Most adrenal gland masses are benign, often discovered incidentally during medical imaging, affecting approximately 5–9% of adults. In contrast, malignant adrenal tumors such as ACC are extremely rare, with an estimated incidence of one case per million people per year [1]. These malignant tumors may be hormonally active (functioning), causing significant hormonal imbalance, or inactive (non-functioning), which typically remain symptom-free until the disease advances [2]. Current guidelines strongly recommend manage ACC by a multidisciplinary team, to effectively address its clinical challenges and enhance patient outcomes [3].

Functioning ACC tumors frequently produces excess cortisol, resulting in severe Cushing's syndrome. This hypercortisolism leads to special physical features including central obesity, facial rounding, easy bruising, muscle weakness, high blood pressure, and abnormal glucose metabolism [4]. Diagnosis involves clinical assessment, hormonal testing, and imaging studies to confirm adrenal gland pathology. Effective treatment typically requires surgical removal of the tumor (adrenalectomy), often preceded by medications like metyrapone to reduce cortisol levels preoperatively, improving patient outcomes [5].

The cardiovascular system is particularly vulnerable to the effects of elevated cortisol. Chronic hypercortisolism contributes significantly to metabolic disturbances such as hyperglycemia, high blood pressure, hypernatremia, and hypokalemia, all of which can severely exacerbate pre-existing heart conditions or even precipitate new cardiovascular disease [6]. The interaction between these metabolic abnormalities and cardiovascular health often leads to increased heart workload, fluid overload, reduced cardiac function, and elevated risk of heart failure and myocardial infarction [7]. Thus, effective metabolic and cardiac management remain crucial in improving survival and quality of life for patients.

Our case report emphasizes the complexities involved managing metabolic and cardiovascular complications in a patient with adrenocortical carcinoma and after adrenalectomy, highlighting the essential role of a coordinated multidisciplinary team.

Clinical-Diagnostic Case

A 65-year-old man was initially admitted to the hospital with symptoms including persistent hypertension (176/81 mmHg), facial rounding, easy bruising and was evaluated by our internal medicine and endocrinology teams. As his condition progressed, the patient developed congestive heart failure complicated by myocardial infarction, acute respiratory failure, hypokalemia, anemia, and pneumonia. Meanwhile, the patient had multiple chronic health conditions, including high cholesterol, diabetes, arthritis, osteoporosis, bone compression fractures, and acid reflux. During his hospital stay, the patient was diagnosed with adrenocortical carcinoma by imaging and histopathology. The patient received metyrapone, a medication used to reduce cortisol levels, correct metabolic disturbances, and reduce surgical risks. Subsequent surgical intervention included left adrenalectomy, partial exploration of the adrenal gland with excision of an adjacent retroperitoneal tumor, and complete splenectomy.

In the postoperative period, the patient's pre-existing heart failure remained unimproved, along with recurrent hypertension, atrial fibrillation, pulmonary edema, and infections, accompanied by nausea, weakness, confusion, and irritability. Postoperative vital signs included blood pressure 148/96 mmHg, pulse ranging from 63 to 103 beats per minute, and respiratory rates ranging from 14 to 21 breaths per minute. Physical examination revealed generalized weakness, diminished bilateral lung sounds, and mild abdominal distension with tenderness in the lower right quadrant. Additionally, the patient's extremities showed no signs of cyanosis or clubbing, but grade 2 bilateral upper- and lower-extremity edema was noted.

Laboratory tests performed during the patient's hospital stay showed his sodium levels were consistently high at 150 mmol/L, while potassium levels were decreased at 2.9 mmol/L, aligning with the typical electrolyte disturbances seen in similar cases (Table 1). Additionally, the total CO_2 level at 29 mmol/L and an arterial HCO_3 level of 32 mmol/L, along with a base excess of 6 mmol/L, were indicative of a metabolic alkalosis. Postoperative results showed a significant shift, with sodium levels reducing to 142 mmol/L and potassium levels increasing to 4.2 mmol/L. Notably, the postoperative total CO_2 decreased to 22 mmol/L and arterial HCO_3 decreased to 28 mmol/L, reflecting a correction towards normal acid-base balance. Endocrine function tests were critical considering the patient's adrenal pathology and surgery. Prior to surgery, the patient's cortisol and urine cortisol levels were significantly elevated at 82.7 µg/dL (8 am) and 800 µg/24 hr, respectively, with a corresponding glucose level of 170 mg/dL. Postoperatively, cortisol levels normalized to 14.2 µg/dL (with cortisol supplementation), and glucose levels also returned to the normal range. The adrenocorticotropic hormone (ACTH) levels were suppressed before surgery, at 5 pg/mL, but rebounded postoperatively to 31 pg/mL. Cardiac markers were continuously monitored due to the patient's history of heart failure. Troponin-T levels were elevated pre- and postoperatively, initially measuring 313 ng/L and peaking at 445 ng/L. NT-proBNP levels initially measured 13,432 pg/mL, remaining high at 12,617 pg/mL postoperatively. Postoperative cardiac imaging via X-ray and echocardiography revealed an ejection fraction of 35%, corroborating the diagnosis of congestive heart failure.

Table 1: Principal laboratory results.

Test	Pre-surgery1	Post-surgery2	Reference intervals (RI)
Sodium	150	142	136-145 mmol/L
Potassium	2.9	4.2	3.5-5.1 mmol/L
Chloride	107	112	98-107 mmol/L
Anion gap	9	13	4-14 mmol/L
Total CO_2	29	22	22-29 mmol/L
BUN	20	26	6-23 mg/dL
Creatinine	0.57	0.56	0.67-1.17 mg/dL
eGFRNAA	105	109	≥60 mL/min/1.73 m^2
Calcium	7.7	7.6	8.4-10.2 mg/dL
Magnesium	1.8	2.1	1.6-2.6 mg/dL
Phosphorus	2.7	4.1	2.5-4.5 mg/dL
Troponin-T (Gen 5)	313	445	≤18 ng/L
NT-proBNP	13,432	12,617	≤125 pg/mL

pH, arterial	7.41	7.38	7.35-7.45
pCO_2, arterial	50	35	35-45 mmHg
pO_2, arterial	39	118	83-108 mmHg
HCO_3	32	28	22-26 mmol/L
Base excess, arterial	6	0	-2-3 mmol/L
O_2 saturation, arterial	71	99	92-98%
Glucose	170	95	70-99 mg/dL
Cortisol (0800h)	82.7	14.2	4.8-19.5 µg/dL
Cortisol (U24h)	800	N/A	3.5-45 µg/24hr
ACTH	5	31	7-63 pg/mL

BUN, blood urea nitrogen; eGFRNAA, estimated glomerular filtration rate, non-African American; NT-proBNP, N-terminal pro b-type natriuretic peptide; ACTH, adrenocorticotropic hormone. Pre-surgery1: one week before the surgery; Post-surgery2: one week after the surgery.

The patient's postoperative treatment regimen addressed his adrenal insufficiency, cardiovascular conditions, and electrolyte imbalances. Hydrocortisone (20 mg), furosemide (Lasix; 40 mg), and carvedilol (Coreg; 25 mg) were administered daily to manage adrenal insufficiency, fluid retention, and heart failure, respectively. Losartan (Cozaar; 25 mg daily) was prescribed to manage hypertension, and potassium chloride (10 mmol/L daily) was given to correct hypokalemia. Additionally, low-dose aspirin (81 mg daily) was initiated, along with atorvastatin (Lipitor; 20 mg daily), to reduce the risk of further heart disease and stroke.

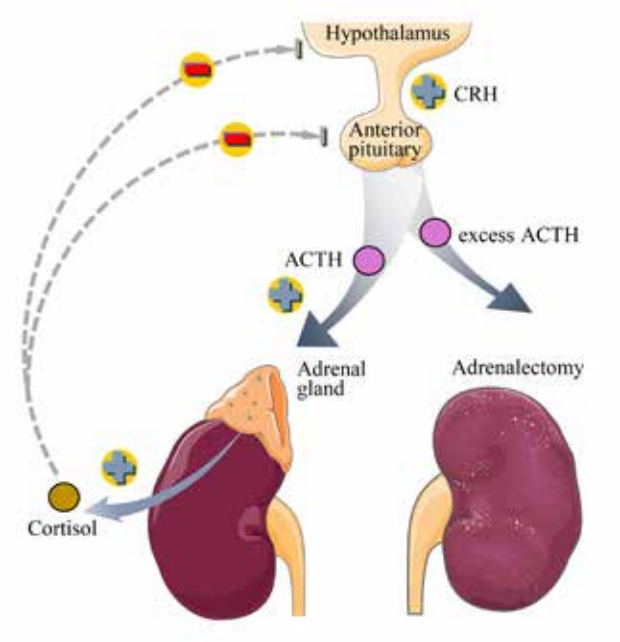
Discussion

Regulation of the hypothalamic-pituitary-adrenal axis

In this case study, a patient with endocrine disease progressed through three distinct clinical stages, each marked by significant changes in hormone levels and clinical symptoms. Initially, the patient's cortisol and urine cortisol levels were both markedly high, which are characteristic of Cushing syndrome. This condition, known as hypercortisolism, was consistent with the patient's clinical presentations, including hyperglycemia and suppressed levels of ACTH. Furthermore, the patient exhibited typical physical features of Cushing syndrome such as pronounced central obesity, facial rounding, and skin changes. The diagnosis of Cushing syndrome was further supported by the presence of hypertension, hypernatremia, hypokalemia, and metabolic alkalosis (Table 1).

Following surgical intervention, including adrenalectomy, the patient experienced a sharp decline in cortisol production due to the loss of adrenal gland function, disrupting the hypothalamic-pituitary-adrenal (HPA) axis (Figure 1). The HPA axis is a central regulatory system that manages the body's response to stress, regulates immune function, and maintains energy storage through the secretion of hormones, predominantly cortisol. This hormonal insufficiency led to a range of symptoms including general weakness, hypotension, and metabolic acidosis. Cortisol deficiency has been observed following adrenalectomy, even in patients with adequate preoperative adrenal function [8].

Figure 1: The hypothalamic-pituitary-adrenal axis under normal conditions and post-adrenalectomy.



Under normal conditions (left), the hypothalamus releases corticotropin-releasing hormone (CRH), which stimulates the pituitary to secrete ACTH. ACTH further stimulates cortisol production from the adrenal glands, maintaining homeostasis through negative feedback. Adrenalectomy (right) eliminates cortisol, disrupting feedback, increasing ACTH and CRH as the body tries to stimulate the absent adrenal gland.

Postoperatively, the patient was immediately treated with steroid hormone therapy to mitigate the effects of adrenal insufficiency. Treatment with hydrocortisone (20 mg daily) effectively normalized his cortisol levels to 14.2 µg/dL and glucose levels to 95 mg/dL. Additionally, his ACTH levels returned to normal (31 pg/mL) within a week, indicating the partial restoration of HPA axis function. During the six-month follow-up, the patient improved in glucose control and cortisol levels, while he was still physical weakness and fatigue persisted. Concurrently, the patient continued to experience hypertension and episodes of atrial fibrillation, which were managed with adjustments to his cardiovascular medications. These conditions highlight the complex and long-lasting complications after adrenal surgery.

Metabolic disorder and cardiac complications

During his hospital stay, the patient's Troponin T levels remained elevated around 400 ng/L. Concurrently, NT-proBNP levels remained around 13,000 pg/mL, indicated significant cardiac distress exacerbated by fluid overload and metabolic disorders. The interplay between metabolic disturbances and cardiac dysfunction created a complex clinical situation.

The patient's Cushing syndrome, characterized by excessive cortisol secretion, contributes to multiple metabolic disturbances, including hyperglycemia, hypertension, and hypernatremia, all of them can exacerbate heart failure [9]. Cortisol promotes gluconeogenesis and induces insulin resistance, leading to persistent hyperglycemia, which contributes to endothelial dysfunction, increased oxidative stress, and myocardial energy dysregulation [4]. Additionally, cortisol enhances vascular sensitivity to catecholamines and stimulates sodium and water retention by activating mineralocorticoid receptors in the kidneys, mimicking aldosterone's effects. This leads to increased intravascular volume, elevated blood pressure, and heightened cardiac workload [6]. Hypernatremia can further exacerbate fluid retention by disrupting osmotic balance, drawing water into the intravascular space, and increasing plasma volume. This expansion of extracellular fluid places additional strain on the heart, promoting left ventricular hypertrophy and impairing diastolic relaxation [10]. As a result, the increased afterload and volume overload associated with Cushing's syndrome can accelerate the progression of heart failure by deteriorating myocardial oxygen demand, reducing cardiac efficiency, and predispose the heart to structural and functional deterioration.

Hypokalemia is a complication of both Cushing's syndrome and heart failure treatment, and it plays a critical role in cardiac function deterioration. Potassium is essential for maintaining myocardial excitability, and its depletion disrupts normal cardiac electrophysiology by prolonging repolarization and increasing the risk of arrhythmias, including ventricular tachycardia and fibrillation [7]. Hypokalemia also impairs myocardial contractility by reducing the activity of sodium-potassium ATPase, leading to inefficient cardiac muscle function. Furthermore, arterial blood gas analyses revealed metabolic alkalosis, with elevated total CO_2 and base excess.

Metabolic alkalosis in this patient was likely influenced by renal bicarbonate reabsorption and hydrogen ion loss in response to potassium depletion [11]. Metabolic alkalosis further compromises cardiac function by reducing ionized calcium levels, decreasing myocardial contractility, and exacerbating vasoconstriction, which can increase vascular resistance and further burden the failing heart.

Additional diagnostic considerations

To fully investigate the patient's metabolic disorder, it would be necessary to comprehensively evaluate his hormonal levels. According to the current clinical practice guidelines, a thorough assessment of cortisol levels requires repeated measurement of 24-hour urinary-free cortisol for assessing cortisol production postoperatively [12]. However, our patient did not have his postoperative 24-hour urinary-free cortisol levels measured. Obtaining this test would have helped evaluate the effectiveness of the adrenalectomy and monitor for any recurrence of hypercortisolism. Moreover, with persistent metabolic alkalosis, measuring serum aldosterone and plasma renin activity would have helped evaluate his mineralocorticoid status. Elevated aldosterone levels with plasma renin activity could indicate primary hyperaldosteronism, while low aldosterone levels might suggest other causes of mineralocorticoid excess or pseudo-hyperaldosteronism. An ACTH stimulation test could have provided valuable information about the residual function of the patient's remaining adrenal tissue. This test assesses the adrenal gland's ability to produce cortisol in response to exogenous ACTH, which is crucial in patient's post-adrenalectomy to determine the need for long-term glucocorticoid replacement therapy [13]. Regular monitoring of vital signs, electrolyte levels, renal function, and cardiac markers remained integral to managing the patient's complex metabolic state. For example, the patient's blood urea nitrogen levels increased from 20 mg/dL preoperatively to 32 mg/dL two months later, and his creatinine levels remained stable at 0.56 mg/dL, indicating the need for careful renal monitoring. The estimated glomerular filtration rate remained above 100 mL/min/1.73 m², suggesting preserved renal filtration but warranting vigilance due to potential prerenal azotemia from hypovolemia or heart failure [14].

Collaborative management involving endocrinology, cardiology, nephrology, and oncology specialists was essential to address the multifaceted challenges in this patient's care. Developing his treatment plan required an interdisciplinary approach to optimize outcomes and improve his quality of life.

Take home messages/Learning points

This case highlights that disruption of the hypothalamic-pituitary-adrenal (HPA) axis due to adrenocortical carcinoma significantly impacts endocrine and metabolic functions, leading to complex clinical challenges. It emphasizes the necessity of recognizing biochemical disturbances, including elevated cortisol levels, suppressed ACTH, electrolyte abnormalities (hypernatremia, hypokalemia, etc.), and metabolic alkalosis, typical in severe Cushing's syndrome. Clinicians must be aware of the disease process through hormonal assessment to provide appropriate treatment. Furthermore, electrolyte imbalances arising from endocrine dysfunction can severely worsen pre-existing cardiac conditions, highlighting the need for integrated endocrine and cardiac management. Finally, comprehensive postoperative hormonal monitoring is critical for detecting residual tumor activity or recurrence, ensuring effective long-term management, and improving patient outcomes.

Ethical approval and consent to participate

The IRB of The University of Texas MD Anderson Cancer Center determined that the study met the criteria for exemption under Category 4 (secondary research on data or specimens, no consent required), and a waiver of HIPAA authorization was granted for use of PHI.

Author contributions

All authors confirmed they have contributed to the intellectual content of this paper. Lechuang Chen: Writing – original draft, Investigation, Formal analysis, Data curation. Jieli Li: Writing – review & editing, Resources, Investigation, Data curation. Qing H. Meng: Writing – review & editing, Supervision, Resources, Project administration, Methodology, Investigation, Data curation, Conceptualization.

Disclosure statement

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