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Acute adrenal insufficiency resulting from adrenal hemorrhage as indicated by post-operative hypotension

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Abstract. We examined the incidence, diagnosis and therapy of acute adrenal insufficiency, secondary to adrenal hemorrhage. This insufficiency resulted in temperature irregularities, hemodynamic instability, and a large volume resuscitation requirement post-operatively. The case illustrates that a high level of suspicion should be maintained in a clinical scenario that mimics sepsis or myocardial insufficiency in the intensive care unit.

Key words: Adrenal insufficiency – Post-operative – Hypotension – Hemodynamic instability – Cortrosyn stimulation test – Adrenal hemorrhage – Adrenal neoplasm

Adrenal hemorrhage is a rare cause of adrenal insufficiency in adults. The non-specific clinical manifestations are difficult to distinguish from the fever, tachycardia, hypotension, lethargy, and electrolyte disturbances that occur commonly post-operatively in critically ill patients. Moreover, the definitive diagnosis of adrenal hemorrhage should be made by computed tomography (CT) or ultrasound examination, but has been inadvertently diagnosed by post-mortem examination [1]. However, the clinical diagnosis is empirical and therefore requires a high index of suspicion, because the deterioration in the patient's condition can be acute, and diagnostic data are not available immediately. The prompt institution of appropriate therapy with corticosteroid replacement is lifesaving.

Factors that are known to be associated with adrenal hemorrhage include heparin therapy, sepsis and shock, hypotension, circulating lupus anticoagulant, surgical stress, orthotopic liver transplantation, and adrenocorticotropic hormone administration [1, 2]. Therefore, adrenal insufficiency from peri-operative adrenal hemorrhage should be considered when the clinical condition of a post-surgical patient suddenly deteriorates.

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Case report

A 65-year-old woman was admitted for surgical resection of a tumor in the left kidney. Her remote past medical history included hyperthyroidism that had been treated with radiation; however, no preoperative thyroid function tests had been documented. Her medications included only enalapril-hydrochlorothiazide for long-standing hypertension.

She had undergone a left adrenalectomy 14 months earlier for adrenocortical carcinoma. The neoplasm was initially discovered as an asymptomatic mass evident on an intravenous pyelogram, which was part of a routine medical workup for hypertension. No associated hypokalemia, masculinization, or incresed urinary catecholamine excretion consistent with Cushing's disease was apparent. Contrast-enhanced CT scan showed a 6.8 cm loculated left adrenal mass and a normal right adrenal gland. Intraoperative pathologic studies showed the surgical resection margins to be free of tumor. No vascular invasion was present. Folow-up radiologic studies 6 months later were negative for recurrence or metastasis.

However, 1 year after the initial surgery, a CT scan revealed a tumor in the left kidney extending into the adjacent renal vein with invasion of the inferior vena cava. Again, no associated renal, autonomic, or electrolyte disorder was present.

The patient was taken to the operating room, where a left nephrectomy, distal pancreatectomy, splenectomy, and inferior vena caval exploration were performed to remove the tumor. A standard anesthetic induction sequence was used with fentanyl and midazolam premedication and thiopental anesthesia. Endotracheal intubation was facilitated with d-tubocurarine and succinylcholine, and muscle relaxation was with pancuronium. Anesthesia was maintained with isoflurane and supplemental narcotic.

The resection involved considerable exploration of the inferior vena cava resulting in significant blood loss and hemodynamic instability. The patient's intraoperative course was marked by occasional wide fluctuations in blood pressure (BP), despite volume resuscitation that included 23 units of packed red cells, 12 units of fresh frozen plasma, 20-pack platelets, 3 units of cryoprecipitate, and 4.500 ml of crystalloid, with a peak serum lactate level of 7.5 mmol/l. The hypertension was treated with trimethaphan, and the hypotension was treated with boluses of ephedrine and an infusion of dopamine. However, the response of the heart rate (HR) and temperature appeared to be minimal.

Upon arrival in the ICU, the patient's BP was 130/70 mmHg, HR 79/min, temperature 35.1 °C, CI 1.7 l/min/m^2, systemic vascular resistance index (SVRI) 3500 dynes $cm^5 \cdot m^2$, and serum lactate 6.5 mmol/l, and she was responsive and awakening from anesthesia. A lumbar epidural catheter delivered preservative-free morphine for pain management. Her initial postoperative course was notable for the requirement of extensive fluid resuscitation. Fluid balance for the day of surgery was

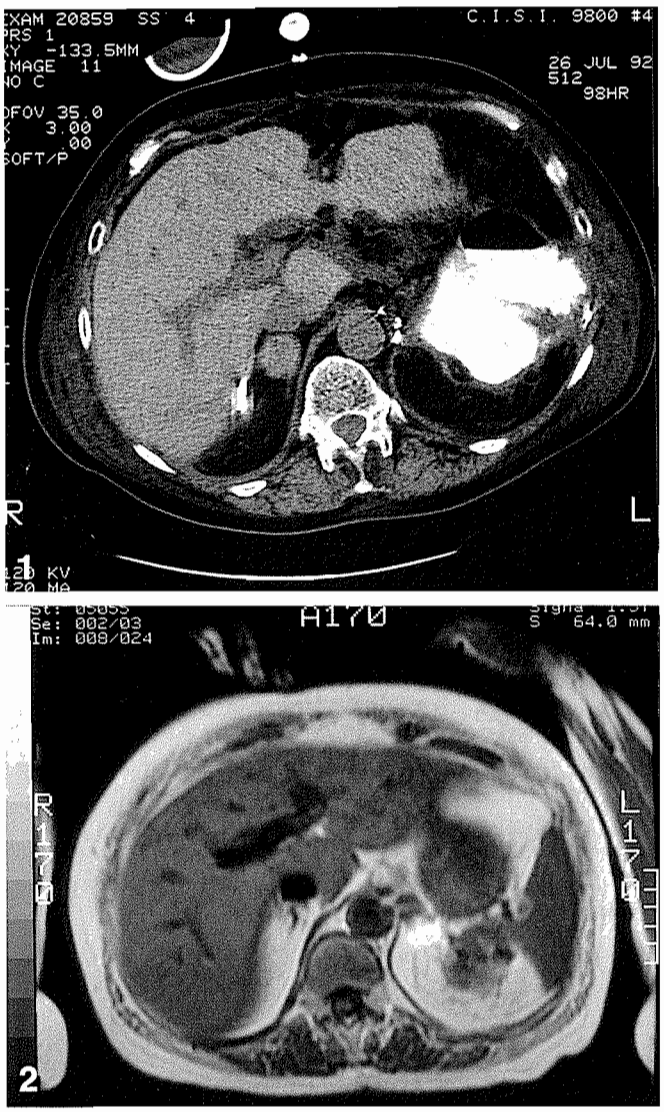

Fig. 1. Abdominal computed tomographic scan (noncontrasted showing right adrenal mass due to hemorrhage

Fig. 2. Abdominal magnetic resonance image showing normal right adrenal gland during preoperative evaluation

positive by approximately 13 l. Electrolyte levels were within normal limits, with a sodium concentration of 145 mmol/l, potassium of 4.4 mmol/l, and chloride of 104 mmol/l. The patient's continued lethargy and need for volume resuscitation precluded early extubation. However, her respiratory status appeared normal and her arterial blood gas values were within acceptable limits, with a pH of 7.46, PCO_2 of 38 mmHg, PO_2 of 146 mmHg, HCO_3 of 27 maintained on an FiO_2 of 0.40, and minute ventilation of 7.0 l/min. Her vital signs and hemodynamic variables remained stable. Cardiopulmonary variables were acceptable, with a pulmonary capillary wedge pressure of 8–11 cmH_2O. Thyroid function tests taken immediately postoperatively in the recovery room suggested thyroid depression as is typically found in ICU patients: thyroxine 3.7 μg/dl, triiodothyronine uptake 1.59, free thyroxine index 5.9 mg/dl, and thyroid stimulating hormone 7.11 μU/ml.

At 60 h after a stable post-operative course, the patient had an acute episode of profound hypotension in the surgical ICU while still intubated and mechanically ventilated. She developed a BP of 72/40 mmHg, HR of 86/min, temperature of 39.5 °C, CI of 2.36 l/min/m^2, and SVRI of 1.421 dynes $cm^5 \cdot m^2$. The electrocardiogram (ECG) showed a trigeminy pattern. Hemodynamic instability responded to the administration of dopamine, 10 μg/kg/min, dobutamine, 6 μg/kg/min, plasma protein fraction, 1000 ml by rapid i.v. bolus, and magnesium sulfate, 4 mg i.v. A dose of dexamethasone, 5 mg i.v., was administered empirically to prevent the remote possibility of adrenal insufficiency. Gentamicin was also added empirically to the prophylactic antibiotic regimen. A 12-lead ECG showed no ischemic change, and arterial blood gas analysis was unremarkable. Cardiac isoenzymes were assessed to rule out an acute myocardial infarction and were determined to be negative.

Furthermore, a cosyntropin stimulation test was done, although the results were unavailable until two days later. The baseline cortisol level was extremely low (7 μg/dl) in the context of severe post-operative stress, and a cosyntropin challenge elicited no adrenal corticosteroid response at either 30 min (8 μg/dl) or 60 min (6 μg/dl) after cosyntropin administration. The 11-deoxycortisol level was normal, decreasing the likelihood of a defect in ketosteroid enzymes or growth of an ectopic tumor. Vital signs returned to baseline approximately 6–8 h after the institution of therapy.

An abdominal CT taken the next day showed a high attenuation mass in the right adrenal gland that we believed to represent an acute adrenal hemorrhage (Fig. 1). This lesion was absent on a magnetic resonance imaging (MRI) scan taken preoperatively and was believed to be the likely source of the clinical adrenal insufficiency (Fig. 2). Dexamethasone, 5 mg i.v. daily, was initially used for corticosteroid replacement to avoid interference with the subsequent serum cortisol analysis.

The patient was eventually discharged in stable condition from the ICU on a hydrocortisone dosing regimen reduced from 50 mg t.i.d. to a daily maintenance of 25 mg each mariney and 10 mg each oftereons. (The adrenal glands routinely produce approximately 37.5 mg/day of hydrocortisone equivalent.) Subsequent pathologic studies revealed no evidence of tumor in the spleen or left kidney. However, the inferior vena cava had extensive involvement of the adrenocortical tumor that had previously affected the ipsilateral adrenal gland.

Discussion

Despite the ready availability of diagnostic testing, the diagnosis of adrenal insufficiency resulting from adrenal hemorrhage in the perioperative setting is difficult. Because of the nonspecific nature of the clinical presentation, diagnosis of adrenal insufficiency migth be easily overlooked in favor of more common post-operative causes of acute hypotension such as sepsis, myocardial infarction, and intravascular volume depletion. Furthermore, the results of appropriate diagnostic studies are often not immediately available. Therefore, once other more common sources of hemodynamic instability are addressed, the treatment of acute post-operative hypotension should include the empirical administration of a corticosteroid such as dexamethasone.

We present a case in which acute hypotension, apparent on the third post-operative day, may have been due to one of a variety of causes. A history of complex endocrine problems including previous adrenalectomy may increase the risk of adrenal insufficiency. However, when acute hemodynamic instability occurs, the ability to assess multiple possible causes can be lifesaving. After myocardial infarction and sepsis were addressed, the indwelling pulmonary-arterial catheter aided in the differential diagnosis of hypotension and guided empirical therapy.

The Cortrosyn stimulation test (Organon, West Orange, NJ) measures the adrenal endocrine response to a challenge with a synthetic adrenocorticotropic hormone (ACTH) stimulating subunit, cosyntropin (alpha 1–24

corticotropin) [3]. After baseline serum cortisol levels are obtained, 25 μg i.v. of Cortrosyn is administered and blood is again drawn for serum cortisol levels after 30 and 60 min have elapsed. A twofold increase in the serum cortisol level after Cortrosyn administration is a normal response.

Subsequent testing to verify adrenal insufficiency includes the ACTH assay differentiating primary adrenal insufficiency, with increased ACTH levels, from secondary insufficiency, with decreased levels. The prolonged ACTH stimulation test, in which 50 μg is administered daily for five days and urinary 17-ketosteroids are measured, may also be performed. Decreased urine levels of steroids are associated with primary disease, whereas increased levels are associated with secondary adrenal disease. Interpretation of the ambiguous results in a stressed patient with maximal adrenal output may make diagnosis difficult. In our patient, both the low baseline serum cortisol levels and the absence of serum cortisol increase in response to Cortrosyn are suggestive of abnormal adrenal gland function. Dexamethasone is known not to interfere with cortisol levels obtained during the Cortrosyn stimulation test, and therefore is the agent preferred during an acute crisis [4]. This may be followed by replacement with hydrocortisone featuring balanced glucocorticoid and mineralocorticoid activity.

Until recently, most diagnosis of adrenal hemorrhage were made postmortem. Ultrasound, CT scan, and MRI all can confirm the anatomic diagnosis of adrenal hemorrhage, but can rarely be used in an the acute care setting. Once the clinical diagnosis of adrenal insufficiency is made and the appropriate therapy instituted, the underlying cause can be investigated.

Adrenal insufficiency is common in the intensive care setting, and a variety of causes have been described. Previous glucocorticoid therapy; autoimmune disease; cytomegalovirus, tuberculosis, or meningococcal infections; abdominal surgical, specifically genitourinary, procedures; anticoagulant and other medications; and prolonged hypotension are all known to predispose patients in the ICU to adrenal insufficiency [3–5]. Patients often exhibit autonomic dysfunction with hypotension and temperature instability accompanied by evidence of hyponatremia, hypoglycemia, or hyperkalemia in laboratory studies (Table 1). Although determination of the cause is important, the treatment of acute addisonian crisis with glucocorticoids is urgent, regardless of the underlying etiology.

The cause of adrenal hemorrhage in the patient we describe was never determined. The adrenal glands receive their blood supply via the aorta and inferior phrenic and adrenal arteries, which form a subcapsular plexus. Necrosis and hemorrhage may occur during hypotension and stress as a result of ischemia, or during adrenal stimulation from vascular engorgement and stasis [6–8]. Ligation of the right adrenal vein during orthotopic liver transplantation is a recognized cause of venous engorgement and infarction leading to hemorrhage within the right adrenal gland [9].

Table 1. Post-operative adrenal insufficiency

Predisposition	Presentation
Adrenal	Anorexia
Hemorrhage	Azotemia
Resection	Confusion
Anticoagulation	Fever
Atherosclerosis	Hyperkalemia
Thermal burn	Hypoglycemia
Corticosteroids	Hyponatremia
Liver transplant	Hypotension
Malignancy (abdominal)	Temperature instability
(hyperthermia, hypothermia)	
Sepsis	Weakness
Shock	Surgery (urologic)
Vasculitis	

[1, 7, 8]

We conclude that acute adrenal insufficiency should be considered as a potential cause of unexplained hypotension in the ICU and that empirical therapy including glucocorticoid replacement be instituted pending laboratory or radiologic confirmation of the diagnosis.

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References

1. Clark OH (1975) Postoperative adrenal hemorrhage. Ann Surg 182:124–129
2. Dahlberg PJ, Goellner MH, Pehling GB (1990) Adrenal insufficiency secondary to adrenal hemorrhage: two case reports and a review of cases confirmed by computed tomography. Arch Intern Med 150:905–909
3. Chin R (1991) Adrenal crisis. Crit Care Clin 7:23–42
4. Knowlton AI (1989) Adrenal insufficiency in the intensive care setting. J Intensive Care Med 4:35–45
5. Jurney TH, Cockrell JL, Lindberg JS, Lamiell JM, Wade CE (1987) Spectrum of serum cortisol response to ACTH in ICU patients. Correlation with degree of illness and mortality. Chest 92:292–295
6. Siu SC, Kitzman DW, Sheedy PF II, Northcutt RC (1990) Adrenal insufficiency from bilateral adrenal hemorrhage. Mayo Clin Proc 65:664–670
7. Jacobson SA, Blute RD Jr, Green DF, McPhedran P, Weiss RM, Lytton B (1986) Acute adrenal insufficiency as a complication of urological surgery. J Urol 135:337–340
8. Miller EH, Woldenberg DH, Gittler RD, Zumoff B (1986) Bilateral adrenal hemorrhage following surgery. NY State J Med 86: 651–653
9. Bowen AD, Keslar PJ, Newman B, Hashida Y (1990) Adrenal hemorrhage after liver transplantation. Radiology 176:85–88