Adrenal Hemorrhage Complicated by Hypertension

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Introduction

Adrenal hemorrhage is a rare entity leading to adrenal insufficiency in adults.[1,2] Adrenal hemorrhage is described in patients on heparin therapy, with sepsis and shock, and in association with circulating lupus anticoagulant, surgical stress, orthotropic liver transplantation, and adrenocorticotropic hormone administration.[2,3] Its non-specific presenting symptoms (abdominal pain, fever, tachycardia, hypotension, lethargy, and electrolyte disturbances) lead to it being a frequently missed diagnosis.[1,2]

Before computed tomography (CT), diagnosis usually was made by autopsy.[3] Patients frequently are found to have adrenal hemorrhage by CT scan usually performed for other reasons.[4] Our patient with bilateral adrenal hemorrhage presented with abdominal pain and associated acute reversible hypertension.

Case Report

A 66-year-old Caucasian female known to have dyslipidemia, hypertension, primary hypothyroidism, and osteoarthritis of the hip presented to an outside emergency department complaining of persistent, dull, epigastric abdominal pain that started suddenly several hours prior. The pain radiated to the flanks. There was associated nausea. The patient denied alcohol or illicit drug use. Her family history was negative for bleeding, clotting disorders, and endocrinopathies. Her medications were limited to thyroid replacements and antihypertensives.

The patient underwent total right hip arthroplasty eight days prior to presentation, with an unremarkable intra- and post-operative course. Specifically, no hypertension was noted intra-operatively. Warfarin was prescribed for deep venous thrombosis prophylaxis postoperatively, and the patient reported having been compliant with the medication. Her international normalized ratio (INR) on presentation was 2.2.

Vital signs upon transfer revealed a blood pressure of 189/87 mmHg with a heart rate of 85 beats per minute. She was afebrile. She was in moderate to severe distress due to her abdominal pain. Diminished bowel sounds and diffuse abdominal tenderness were noted.

Laboratory analysis is summarized in Table 1. A serum cortisol level the morning following admission was 6 ug/dL (7-18 ug/dL) with a simultaneously drawn adrenocorticotropic hormone (ACTH) level of 660 pg/ml. The serum cortisol was 2 ug/dL, one hour following 250 mcg cosyntropin. The plasma free metanephrine level was within normal limits, but the plasma free normetanephrine level was elevated at 1.15 nmol/l. CT of the abdomen and pelvis revealed bilateral adrenal masses

Table 1. Serum lab values (reference range).

Lab	Value
Sodium	135 meq/l (136-144 meq/l)
Potassium	3.2 meq/l (3.6-5.1 meq/l)
White Blood Cell Count	12.2 cells/cm^3 (4.8-10.8 cells/cm$^{3)}$
Hemoglobin	11.4 g/dl (12.0-16.0 g/dl)
INR	2.2 (0.9-1.2)
Thyroid-Stimulating Hormone Level	6.94 uIU/mL (0.35-5.50 uIU/mL)
Free Thyroxine (Free T4)	0.8 ng/dL (0.6-1.1 ng/dL)
AM Cortisol Level	6 ug/dL (7-18 ug/dL)
Adrenocorticotropic Hormone Level	660 pg/ml (10-60 pg/mL)
Plasma Free Normetanephrine Level	1.15 nmol/l (<0.90 nmol/l)
Free Metanephrine Level	<0.20 nmol/L (<0.50 nmol/L)
Antiphospholipid Antibodies	Nondetected

consistent with hemorrhage measuring 3.5 x 2.6 cm on the right and 2.8 x 2.7 cm on the left (Figure 1). The remaining adrenal tissue was poorly visualized, but no other anatomic abnormalities were noted. No prior CT scans were available for comparison.

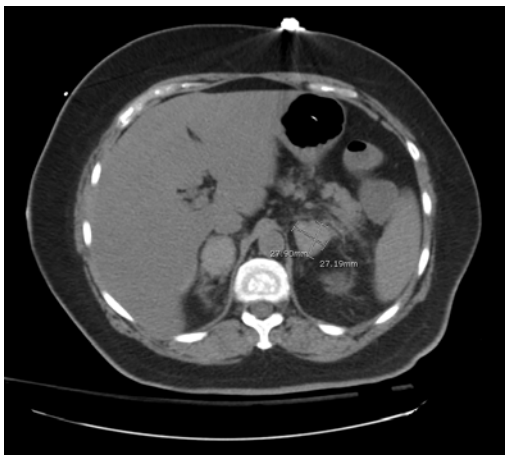

Figure 1. A CT of the abdomen and pelvis with and without contrast revealed a right and left adrenal hemorrhage (see arrows).

Warfarin was held. The patient's blood pressure normalized over the next 72 hours. Because of suspicion that the rise in normetanephrine was strictly secondary to stress from her hypertension, clonidine suppression testing was performed approximately four days after her presentation, resulting in suppression of the normetanephrine level to less than 0.9 nmol/l.

The patient was discharged without anti-hypertensive medications. She was placed on hydrocortisone 50 mg twice daily and fludrocortisone 50 mcg twice daily as adrenal replacement, with a tapering dose as an outpatient. Follow-up CT of the adrenals revealed resolution of hemorrhage without the presence of adrenal neoplasia. The patient was seen for follow-up after six months and adrenal function had not recovered.

Discussion

The adrenal glands play an important role in maintaining blood pressure and electrolytes during periods of physiologic stress.[5] Adrenal hemorrhage has been explained by several mechanisms. One states that during physiologic stress an increase in cytokines (TNF alfa and IL-6) leads to suppression of the hypothalamic pituitary adrenal axis.[4] Furthermore, those inflammatory mediators lead to activation of the coagulation cascade, inhibition of fibrinolysis, and endothelial damage thus leading to adrenal hemorrhage.

Another potential mechanism observes that during physiologic stress ACTH rises,

thus leading to an increase in blood flow to the adrenal glands.[1,4] The adrenal gland is supplied by the three suprarenal arteries that divide into fifty to sixty branches. The capillaries branching from the arteries form a plexus around the zona reticularis.[4] The shift from the arterial system to the capillaries is an abrupt process.[1] The drainage is by a few venules that join to form the central medullary vein.[1,4] This anatomic vasculature structure, also known as the "vascular dam," puts the adrenal gland at an increased risk for hemorrhage.

A high index of suspicion for adrenal hemorrhage is necessary in unexplained abdominal pain or hypotension, as presenting symptoms are vague and routine laboratory studies frequently are not helpful.[5] The most common presenting symptoms and signs for bilateral adrenal hemorrhage (BAH) are hypotension or shock (more than 90 percent), abdominal, flank, back, or lower chest pain (86 percent), fever (66 percent), anorexia, nausea, or vomiting (47 percent), neuropsychiatric symptoms such as confusion or disorientation (42 percent), and abdominal rigidity or rebound tenderness (22 percent).[6] In contrast, our patient presented with hypertensive urgency. The mechanism of this presentation is unknown.

The etiology of this patient's adrenal hemorrhage remains unknown. The differential diagnosis for bilateral adrenal hemorrhage typically includes sepsis (usually secondary to *N. Meningitides*, *P. aeroginosa*, *E. Coli*, and *B. Fragilis)*, antiphospholipid syndrome, heparin-associated thrombocytopenia, warfarin, and severe physiologic stress.[7,8] With the exception of her hypertension, this patient's workup and clinical scenario were highly suggestive of bilateral adrenal hemorrhage secondary to warfarin. The patient was not septic and her platelet count was within normal limits. The timing of her presentation was consistent with other patients who underwent joint replacement surgery and were anticoagulated, with subsequent adrenal crisis as a result of adrenal hemorrhage.[9]

Hemorrhagic pheochromocytoma was noted in 42 cases between 1944 till 2004.[10] Patients usually presented with symptoms of abdominal pain with associated hypertension or hypotension. Usually there was no precipitating event, and most of the cases were identified perioperatively. Our patient's presentation increased the suspicion of hemorrhagic pheochrome-cytoma. Appropriately suppressed free metanephrine and normetanephrine levels, along with a normal follow-up CT scan, make pheochromocytoma less likely, but do not rule it out. It is possible that she had a pheochromocytoma in one or both adrenal glands that was destroyed by the hemorrhage.

Conclusion

The presentation of bilateral adrenal hemorrhage, while classically associated with hypotension, abdominal pain, hyperkalemia, and hyponatremia, is clinically heterogeneous and may include hypertension.

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