A 33-year-old woman was transferred for management of an unresolved pneumonia. She had been hospitalized for a right lower lobe infiltrate and pleural effusion after a nonproductive cough failed to respond to oral erythromycin. A ventilation-perfusion scan demonstrated a right lower lobe matched defect believed to be secondary to the pneumonia. There was a history of easy fatigability during the previous 1 year and hypothyroidism that required hormone replacement.

Physical Examination

Vital signs: temperature, 37.8°C; pulse, 83 beats/min; respirations, 12/min; BP, 110/75 mm Hg. Skin: vitiligo over face and torso. Cardiac: no murmur. Chest: decreased breath sounds over right lower lobe. Abdomen: no organomegaly. Extremities: no clubbing or cyanosis.

Laboratory Findings

Hematocrit, 36.5 percent; WBC, 5,100/μl; normal differential; platelets, 363,000/μl; Na⁺, 133 mEq/L; K⁺, 5.0 mEq/L; HCO₃⁻, 18 mEq/L; creatinine, 0.7 mg/dl; glucose, 78 mg/dl; calcium, 9.0 mg/dl; thyroxine, 8.2 μg/dl (normal, 4.5 to 12.0 μg/dl). HIV antibody: negative. Sputum: negative stains and cultures. Pleural fluid: exudative, neutrophil predominance, normal pH. ECG: normal. Chest radiograph: right lower lobe infiltrate and pleural effusion (Fig 1).

Hospital Course

The patient was treated with intravenous erythromycin and cefuroxime for pneumonia and an uncomplicated parapneumonic effusion. Two days later, she developed acute dyspnea and became pulseless, requiring intubation and cardiopulmonary resuscitation. In the ICU, persistent hypotension necessitated infusion of 13 L of intravenous fluid over 36 h and pressor support with norepinephrine and dopamine. A pulmonary angiogram demonstrated intra-arterial defects in both upper lobes consistent with pulmonary embolism (Fig 2). Abdominal computed tomographic findings were normal.

What complicating condition requiring urgent therapy may have contributed to the intractable hypotension?
Diagnosis: Adrenal insufficiency

Adrenal insufficiency is an uncommon disorder which, if unrecognized, can significantly contribute to patient morbidity and mortality. The signs and symptoms suggesting the diagnosis are nonspecific and include weakness, fatigue, anorexia, abdominal pain, hyperpigmentation, hypotension, salt craving, postural symptoms, and muscle and joint pains. A prior patient or family history of autoimmune disorders, such as hypothyroidism, hypoparathyroidism, diabetes mellitus, hypothalamic amenorrhea, celiac disease, chronic active hepatitis, vitiligo, and alopecia, can be found in up to 70 percent of cases and should increase the index of suspicion for this disorder. Laboratory findings suggesting adrenal insufficiency include hypernatremia, hyperkalemia, hypercalcemia, and eosinophilia. The two most common causes of adrenal insufficiency are autoimmune destruction (80 percent of cases) and Mycobacterium tuberculosis infection (15 percent of cases). Autoimmune or idiopathic adrenal insufficiency is most often seen in young, white females, which contributed to the suspicion of this diagnosis in the present case. Other causes of adrenal insufficiency include adrenal hemorrhage, AIDS, metastatic carcinoma, lymphoma, fungal infection, sarcoidosis, amyloidosis, hemochromatosis, drugs, and surgical removal of both adrenal glands.

Suppression of normal adrenal gland function, resulting in adrenal insufficiency, can also be produced by the administration of exogenous glucocorticoids, which act by suppressing the hypothalamic-pituitary axis. Prednisone at doses of 25 mg twice daily for 2 days, 12.5 mg/d for 6 months, 10 mg/d for 2 years, or 5 mg/d for 5 years has been shown to result in suppression of normal adrenal function. Patients who have received glucocorticoids within the previous year, who have received more than 40 mg of prednisone daily for 2 weeks prior to ICU admission, or who have developed cushingoid features while receiving exogenous glucocorticoid therapy should be considered to have adrenal insufficiency.

Two other important causes of adrenal insufficiency to consider in the intensive care setting are adrenal hemorrhage and AIDS. In the setting of an acute medical or surgical illness, the postoperative state, or the presence of a coagulopathy, bilateral adrenal hemorrhage should be suspected as a cause of adrenal insufficiency. Abdominal, flank, back, or chest pain may suggest the diagnosis, which can usually be established by abdominal computed tomography. In patients with AIDS, a high index of suspicion of adrenal insufficiency is necessary because many of the nonspecific signs and symptoms suggesting hypothalamic-pituitary axis insufficiency are commonly observed as general clinical manifestations of the underlying AIDS. Cytomegalovirus, Mycobacterium avium-intracellulare, fungal infection and Kaposi's sarcoma have all been associated with adrenal destruction in patients with AIDS.

Due to its rarity and the fact that it can occur de novo (adrenal hemorrhage) or be present as an unrecognized chronic condition (autoimmune adrenal insufficiency in the unstressed patient), a high index of suspicion is necessary for the diagnosis of adrenal insufficiency. Once suspected, the diagnosis and treatment of adrenal insufficiency are tempered by the condition of the patient. In the hemodynamically stable patient, adrenal function can be evaluated before the administration of “stress doses” of glucocorticoids. A baseline serum cortisol level should be obtained followed by the administration of adrenocorticotropic hormone (ACTH), 250 μg of Cortrosyn (Organon, West Orange, NJ), as an intravenous bolus; cortisol samples should then be obtained 30 and 60 min later. Baseline cortisol concentrations less than 10 μg/dl during an acute illness associated with a lack of doubling following ACTH administration indicate adrenal insufficiency. Some authors suggest that a peak cortisol level greater than 20 μg/dl following the rapid ACTH stimulation test is a sufficient single criterion to exclude the diagnosis of adrenal insufficiency. If adrenal insufficiency is diagnosed, additional studies should include measurement of serum ACTH (to evaluate for a thalamic-pituitary disorder) and aldosterone (to evaluate mineralocorticoid function).

In up to one third of patients receiving exogenous glucocorticoids, the rapid ACTH stimulation test may produce false-negative results because it does not directly test the response of the hypothalamic-pituitary axis to stress. The insulin tolerance test (by producing a stress from hypoglycemia) and the metyrapone test (by blocking the synthesis of cortisol) are more direct methods of assessing the degree of glucocorticoid-induced suppression of adrenal function.

For the hemodynamically unstable patient, prompt aggressive therapy is urgently required due to the life-threatening nature of this disorder. Fluid resuscitation with normal saline or lactated Ringer's solution should be begun immediately. Dexamethasone sodium phosphate (4 mg intravenously) should be administered because it does not interfere with cortisol measurements, and, if necessary, vasoressor agents should be added to treat the hypotension. Animal studies have shown that blood vessels may lose their ability to contract and to respond to catecholamines in the absence of adrenal steroids. The lack of mineralocorticoid activity of dexamethasone is compensated for by the vigorous administration of intravenous fluids during the 1 hour required for performance of the rapid ACTH stimulation test. Once this test has been performed (as described above), hydrocortisone sodium succinate should be started at a dose of 100 mg.
intravenously every 6 to 8 h. During this phase of treatment the patient’s electrolyte and glucose levels and fluid status need to be carefully monitored. As soon as the acute illness is controlled, the hydrocortisone dosage should be tapered to a maintenance level.

In the present patient, the stress of the thromboembolic event appeared to precipitate acute adrenal insufficiency. A high index of suspicion for underlying chronic adrenal insufficiency based on the patient’s gender, past history, physical findings, and electrolyte abnormalities allowed for appropriate treatment to be initiated with stress doses of glucocorticoids, resulting in stabilization of the patient’s hemodynamic values. The diagnosis of adrenal insufficiency was confirmed by the rapid ACTH stimulation test, which revealed a baseline serum cortisol level of 6.6 μg/dl followed by 30- and 60-min values of 8.2 and 9.4 μg/dl, respectively, after a bolus injection of 250 μg of synthetic ACTH. The patient went on to make an uneventful recovery.

**Clinical Pearls**

1. Adrenal insufficiency is a potentially reversible cause of hemodynamic compromise in the hospitalized patient. A high index of suspicion is required to establish the diagnosis in the appropriate setting.

2. Prednisone at doses of 25 mg twice daily for 2 days, 12.5 mg/d for 6 months, 10 mg/d for 2 years, or 5 mg/d for 5 years has been shown to cause suppression of normal adrenal function.

3. When adrenal insufficiency is suspected in an acutely ill patient, fluid resuscitation and intravenous dexamethasone (4 mg) should be started at once. Although dexamethasone does not interfere with serum cortisol measurements, its lack of mineralocorticoid activity necessitates vigorous administration of intravenous fluids during the 1 hour required for performance of the rapid ACTH stimulation test.

4. A baseline cortisol level and a rapid ACTH stimulation test should be performed to establish the diagnosis of adrenal insufficiency, followed by the administration of intravenous hydrocortisone (100 mg every 6 to 8 h). In patients treated with exogenous corticosteroids, direct suppression of the hypothalamic-pituitary axis can occur. In these individuals, the rapid ACTH stimulation test may be normal despite the presence of a compromised hypothalamic response to stress.

**Suggested Reading**


