A 63-Year-Old Man With Suspected Lung Cancer and Acute Renal Failure*

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A 63-year-old man, a 100–pack-year smoker, presented with a 2-month history of cough, hoarse voice, anorexia, and weight loss. Radiologic studies showed a large, solid, left parahilar mass with mediastinal adenopathy (Fig 1). Bronchoscopy revealed paralysis of the left vocal cord, but was otherwise nondiagnostic on two occasions; “random” bronchial biopsies and cytology specimens were unremarkable. The patient rejected the suggestion of mediastinal exploration. Staging investigations were negative for metastatic disease.

The patient started chemotherapy for suspected lung carcinoma. After three cycles of therapy, there was no radiologic response, and the patient went on to receive thoracic radiotherapy. During the course of this treatment, dizziness and mild ataxia developed; a brain CT scan showed multiple metastatic lesions not present 1 month earlier. The patient was given cerebral irradiation under corticosteroid cover. After radiotherapy, he continued to feel vaguely dizzy, especially when getting out of bed. Three weeks after completion of chemotheraphy, he received a further course of chemotherapy with docetaxel and topotecan. Three days later, diffuse abdominal pain, weakness, and malaise developed, which progressed over 4 days and led to his hospital admission, 7 months after the original presentation.

**Physical Examination**

The patient was pale, cold, and diaphoretic. Pulse rate was 90 beats/min, BP was 100/60 mm Hg, and temperature was 36°C. Oxygen saturation was 94% on room air by pulse oximetry. The neck showed enlarged firm cervical lymph nodes. Chest examination was normal. Cardiac examination revealed distant heart sounds. The abdomen was mildly tender and distended, with a moderate amount of ascites and no organomegaly or masses. Neurologic examination showed a patient who was fully conscious, restless, and apprehensive, with no focal abnormal signs.

**Laboratory Findings**

Laboratory results revealed the following: hematocrit, 49%; hemoglobin, 15.5 g/dL; WBC count, 12,100/μL (88.6% neutrophils, 7.4% lymphocytes, 4% monocytes); erythrocyte sedimentation rate, 43 mm/h; serum sodium, 130 mmol/L; serum potas-
sium, 7.2 mmol/L; glucose, 97 mg/dL; BUN, 94 mg/dL; serum creatinine, 2.9 mg/dL; serum urate, 11.2 mg/dL; liver enzymes, normal. ECG showed sinus tachycardia, and chest radiography showed left hilar enlargement with elevation of the left hemidiaphragm, and clear lungs (Fig 2). The urinary bladder was empty on catheterization; urine was not available for analysis.

What was the cause of this man's acute deterioration?

Figure 2. Chest radiograph showing enlarged left hilum and elevated hemidiaphragm.
Answer: Acute adrenal insufficiency due to bilateral adrenal metastases.

There have been reports of adrenal metastases with most kinds of solid tumors, the most common being carcinomas of lung and breast, followed by gastric and colorectal cancer. Autopsy studies have shown that up to 42% of lung cancers involve the adrenals. Almost half of all adrenal metastases involve both glands. CT is a reliable and sensitive technique that has facilitated the antemortem identification of such metastases.

It is not known how many of these metastases have clinical significance for the patient. Over 90% of adrenal tissue has to be destroyed before symptoms of insufficiency develop. Such symptoms (tiredness, nausea, vomiting, weight loss) are entirely nonspecific; in any case, they are quite common in cancer patients, and it is only incidentally that endocrine dysfunction is detected. There have even been rare reports of Addison disease being the first manifestation of malignancy, which was diagnosed several months later.

Few studies have examined the adequacy of adrenal function in cancer patients. When cosynotropin tests were performed prospectively in patients who had bilateral adrenal metastases on CT scan, it was found that one third (5 of 15 patients) had abnormal cortisol responses to adrenocorticotrophic hormone; no patient had hyperkalemia. On detailed evaluation, all patients with abnormal cortisol responses had evidence of adrenal insufficiency (persistent or recurrent nausea, anorexia, orthostatic hypotension); only one of the patients with normal responses to adrenocorticotrophic hormone had orthostatic hypotension without any other symptoms. No patient ever had an adrenal crisis. Patients with abnormal adrenal function received replacement hydrocortisone, with resolution of nausea and anorexia. On the basis of these findings, it has been recommended that patients with bilateral adrenal metastases and symptoms suggestive of insufficiency should undergo endocrinologic evaluation and given treatment if found to be deficient. Regular replacement therapy with hydrocortisone can ameliorate symptoms and enhance quality of life. With improved survival of cancer patients, symptomatic relief becomes even more important.

An adrenal crisis (acute adrenal insufficiency) is a medical emergency caused by a sudden and marked absolute or relative deprivation of adrenocortical hormones. It is a rare and dramatic event that may occur in a known addissonian patient, or may be the presenting manifestation of adrenal insufficiency. Its classic association with fulminant meningococcal septicemia (Waterhouse-Friderichsen syndrome) is well known. Destruction of both adrenal glands by metastatic tumor is a rare cause of this phenomenon. When this occurs without previous recognition of the adrenal insufficiency, it may be rapidly fatal.

Most patients with acute adrenal insufficiency demonstrate hypoglycemia, hyponatremia, and hyperkalemia. The diagnosis is confirmed by measuring the plasma cortisol levels, which are decreased as a rule. However, there are several cases with cortisol levels in the normal range. Steroid values should always be interpreted in the context of the patient’s condition: a severely stressed patient may have a relative adrenal deficiency with an inappropriately “normal” plasma cortisol level.

Once the condition is suspected, prompt management is of paramount importance for the patient’s survival. Rapid infusion of normal saline solution and IV steroids may alleviate the acute situation. The use of IV dexamethasone (which does not interfere with the cortisol assay) along with 1M adrenocorticotropic hormone (to stimulate the adrenal cortex) allows the concurrent diagnosis and treatment of the condition. It should be remembered that previous use of corticosteroids (eg, in chemotherapy regimens containing prednisone) may lead to a false-positive adrenocorticotropic hormone test result due to steroid-induced adrenal suppression; interpretation of the test may be problematic.

In our patient, the development of acute renal failure with an empty urinary bladder initially raised the possibility of bilateral ureteral obstruction by lymphatic enlargement. One week before the final hospital admission, his renal function had been normal, with a serum creatinine of 1.16 mg/dL and a BUN of 26 mg/dL. Nephrotoxicity has not been reported with either docetaxel or topotecan, and he had not received any other potentially nephrotoxic medication. Adrenal insufficiency was a belated consideration in the differential diagnosis. A CT scan of the abdomen showed normal kidneys with no evidence of obstruction. The adrenal glands (Fig 3) were completely replaced by large masses of soft tissue density (arrows), measuring 7 cm on the right side and 8 cm on the left side. The liver, spleen, and pancreas were normal. There was a large amount of free peritoneal fluid with soiling of the peritoneal fat, suggestive of metastatic deposits. He was given IV fluids, insulin, corticosteroids, furosemide, and mannitol, but remained completely anuric, and died < 24 h after hospital admission. An autopsy was not performed.

A review of his medical records showed that 2 months earlier his electrolytes had been normal, and an abdominal CT scan had shown normal adrenal glands, indicating that the development of the
metastases leading to the terminal event had been of recent and rapid onset. He had been receiving a tapering regimen of oral steroids for approximately 1 month prior to death, while he was receiving radiotherapy for cerebral metastases. It is likely that this treatment may have masked the symptoms of developing adrenal insufficiency, and its withdrawal may have contributed to the acute clinical picture. The finding of normal cortisol (17 μg/dL; reference range, 6 to 26 μg/dL) and elevated adrenocorticotropic hormone (200 pg/mL; reference range, 10 to 60 pg/mL) values in the hospital admission blood sample, reported postmortem, confirmed the diagnosis of acute adrenal failure leading to severe shock and prerenal azotemia.

**Clinical Pearls**

1. Despite the high (42%) autopsy incidence of adrenal metastases from lung cancer, acute adrenal insufficiency due to metastatic disease is an extremely rare, but possibly lethal occurrence.

2. The symptoms of adrenal insufficiency are nonspecific and are often attributed to the cachexia of malignancy.

3. Adrenal insufficiency may be masked by steroid administration for other indications, and an acute adrenal crisis may develop with corticosteroid withdrawal.

4. Patients with bilateral adrenal metastases may have an abnormal cosyntropin response and may derive symptomatic benefit from corticosteroid replacement therapy.

5. Interpretation of the cosyntropin test may be problematic in patients who have previously received corticosteroids and may have abnormal responses due to adrenal suppression.

**Suggested Readings**


