Unilateral Adrenal Enlargement Due to *Histoplasma capsulatum*

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Human infection with *Histoplasma capsulatum* runs the gamut from asymptomatic to disseminated disease. CT-directed fine-needle aspiration of bilaterally enlarged adrenal glands has been used in diagnosing serious infections with this ubiquitous organism. Three cases have previously been reported in which *H. capsulatum* infection caused unilateral adrenal enlargement; this enlargement was diagnosed post-mortem. We describe three patients with unilateral adrenal enlargement due to *H. capsulatum* whose conditions were diagnosed antemortem. We encourage clinicians to include infection with *H. capsulatum* as well as other granulomatous diseases and tumors in the differential diagnosis of unilateral adrenal enlargement.

Disseminated histoplasmosis is uncommon, but if it is untreated it is usually fatal [1]. Both acute and chronic disseminated disease present diagnostic challenges to the clinician. The prominent clinical features are nonspecific and include fever, weight loss, and malaise. One useful clue in the diagnosis of disseminated histoplasmosis is bilateral enlargement of the adrenal glands [2, 3]. A microbiologic diagnosis can be made with CT-guided fine-needle aspiration of the adrenal glands [2]. There was bilateral involvement in all the reported cases in which the diagnosis of adrenal histoplasmosis was made while the patient was alive; although in three cases the diagnosis of unilateral adrenal involvement was made post-mortem [4].

We report the cases of three patients whose conditions were diagnosed as widespread histoplasmosis with unilateral adrenal enlargement while they were living. To our knowledge, this is the first report of unilateral adrenal enlargement diagnosed antemortem. Thus histoplasmosis should be considered in the differential diagnosis for patients with a systemic illness and a single enlarged adrenal gland.

Case Reports

Case 1. A 42-year-old man who was a resident of eastern Oklahoma presented to the hospital with a 1-month history of fatigue, malaise, night sweats, anorexia, and a nonproductive cough. Three years earlier he had experienced a flu-like illness of 1 month’s duration following demolition of a chicken coop. His travel and medical history were unremarkable.

The patient was acutely ill, with fever (temperature of 39.4°C) and an enlarged tender liver. The levels of liver enzymes and serum bilirubin were abnormal, as was the prothrombin time. A test for HIV was negative. Findings on a chest roentgenogram were normal. A serum CF titer for antibodies to *Histoplasma capsulatum* was 1:64, but immunodiffusion was negative. Progressive hepatosplenomegaly and pancytopenia were observed. Antibiotic therapy was given without success, and he was transferred to our hospital.

A computed tomogram of the abdomen confirmed the hepatosplenomegaly and showed a normal-sized right adrenal gland and an enlarged left adrenal gland. Smears of theuffy coat of centrifuged venous blood and of bone marrow aspirate showed many *Histoplasma*-laden macrophages. Despite therapy with amphotericin B and aggressive support, the patient died on the fourth hospital day. The autopsy showed disseminated histoplasmosis involving multiple organs including the liver (5,610 g), spleen (1,840 g), bone marrow, lymph nodes, ileum, and left adrenal gland (53 g) (figure 1). The right adrenal gland (9 g) was normal by gross examination, although microscopic examination of specimens from the gland showed occasional intracellular *H. capsulatum*.

Case 2. A 59-year-old man who was a native of Oklahoma and whose lung had been resected because of squamous cell cancer was seen for weight loss and fatigue. The results of routine laboratory tests were normal, and serology for HIV was negative. An abdominal computed tomogram showed left adrenal enlargement and a calcified pulmonary nodule in the right lower lung field. He was referred to us because of continued weight loss, hyponatremia, and pancytopenia.

Examination of a bone marrow aspirate and biopsy specimen showed dyserythropoiesis, one small granuloma, and no acid-fast organisms. The results of routine blood cultures were negative, as were serological tests for fungi. The result of a short corticotropin stimulation test was normal. A repeated abdominal computed tomogram showed further left adrenal enlargement. Fine-needle aspiration of this gland was performed under...
CT guidance, and microscopic examination of the aspirate showed intra- and extracellular *H. capsulatum* (figure 2). Culture of the bone marrow aspirate and two lysis-centrifugation blood cultures yielded *H. capsulatum*. 

**Case 3.** A 65-year-old man who was a resident of Oklahoma City had weakness and weight loss on presentation; laboratory tests revealed slightly elevated levels of liver enzymes. Serology for HIV was negative. Findings on an abdominal computed tomogram were believed to be normal. One month later, vertical diplopia developed. MRI and CT studies of the brain showed multiple densities. Numerous other studies were nondiagnostic. The original computed tomogram of the abdomen was reviewed; a 2 × 3.5-cm lesion in the left adrenal gland was identified, and the right adrenal gland appeared normal in size and configuration.

A corticotropin stimulation test did not indicate adrenal insufficiency. A CT scan of the abdomen that was performed 2 months after the first scan was remarkable for further enlargement of the left adrenal gland and enlargement of the right gland.

Fine-needle aspiration of the left adrenal mass yielded necrotic tissue with some intact cells containing numerous organisms compatible with *H. capsulatum*. Cultures of the aspirate were not performed. The patient received therapy with amphotericin B (total dose, 2.0 g), and a repeated CT scan performed 5 months after the second scan showed normalization of the right adrenal gland and a decrease in size of the left adrenal gland.

**Discussion**

In addition to the adrenal glands, disseminated histoplasmosis frequently involves the liver, spleen, bone marrow, gastrointestinal tract, CNS, and lymph nodes [1]. *H. capsulatum*, more than other pathogenic fungi, has a predilection for the adrenal glands [5, 6]. The reason for this is not understood, although the production and release of glucocorticoids and a relative paucity of reticuloendothelial cells in the glands may contribute to localization of *H. capsulatum* to the adrenal glands.

To our knowledge, we report the first three cases of unilateral adrenal gland enlargement diagnosed antemortem in patients with histoplasmosis. In a previous report, van Zeben et al. [7] referred to a patient with unilateral adrenal enlargement due to histoplasmosis. This patient was one of our own, and this patient's case had been reported in an earlier series [3]; in this case, an ultrasonogram showed only an enlarged left adrenal gland. However, this same patient had bilateral adrenal enlargement on the basis of findings of a computed tomogram performed within a few days of the ultrasonographic examination [2, 3].

Fine-needle aspiration of the adrenal gland should be reserved for patients with suspected disseminated histoplasmosis for whom less-invasive modalities, especially antigen testing [8], have not been helpful. CT scans were performed to assess hepatosplenomegaly in patients for whom no clear diagnosis could be made. When adrenal biopsy is performed for detection of bilateral or unilateral adrenal disease, histoplasmosis should be sought by special histologic staining and by culture.

Unilateral adrenal enlargement was an unexpected finding that led to the diagnosis of histoplasmosis in two of our three cases. Thus, in addition to various tumors, other granulomatous diseases, and adrenal hemorrhage, infection with *H. capsulatum* should be included in the differential diagnosis of unilateral as well as bilateral adrenal enlargement. This is especially true in...
areas where histoplasmosis is endemic, as this illness is an important cause of morbidity and mortality in HIV-infected individuals [9].

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References


