

Amebic Liver Abscess Complicated by Bilateral Adrenal Hemorrhage and Adrenal Insufficiency

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Liver abscess is the most common extraintestinal complication of infection with *Entamoeba histolytica*. Although spontaneous bilateral adrenal hemorrhage may occur in the setting of any severe illness, only rarely has it been associated with amebic liver abscess.¹ This article describes a 70-year-old man who presented with an amebic liver abscess and who developed bilateral adrenal hemorrhage and adrenal insufficiency. The diagnosis and treatment of both amebic liver abscess and spontaneous bilateral adrenal hemorrhage are reviewed.

CASE PRESENTATION

A 70-year-old man was transferred to our institution (a 1200-bed tertiary care center) for further evaluation of a febrile illness of unknown origin. Over a period of 4 months, the patient had noticed progressive fatigue and lightheadedness. Three weeks prior to transfer, he began having intermittent fevers (up to 102.1°F), shaking chills, and soaking night sweats. He had been treated at home with several courses of oral antibiotics (amoxicillin, ciprofloxacin) and for 3 days with intravenous imipenem—all of which failed to relieve his symptoms.

History

His past medical history was remarkable only for retinal detachment in his right eye and an anaphylactic reaction to bee stings. He was allergic to sulfa drugs and was on no medications. He denied any recent travel outside of the United States, although he wintered in Scottsdale, Arizona. He had not experienced nausea, vomiting, or diarrhea.

Physical Examination

On physical examination, the patient was shivering in bed with a body temperature of 99.6°F. His blood pressure was 150/90 mm Hg. His pulse was 80 bpm, and his

respiratory rate was 24 breaths/min. Abdominal examination revealed neither hepatosplenomegaly nor abdominal tenderness. The remainder of the physical examination was unremarkable.

Laboratory and Radiographic Evaluation

Admission laboratory tests showed the following results: hemoglobin mass concentration, 11.2 g/dL; total leukocyte count, $25.8 \times 10^3/\text{mm}^3$ with $23.5 \times 10^3/\text{mm}^3$ neutrophils; platelet count, $555 \times 10^3/\text{mm}^3$; serum sodium, 131 mEq/L; serum potassium, 4.3 mEq/L; serum creatinine, 1.0 mg/dL; blood urea nitrogen, 20 mg/dL; alkaline phosphatase, 662 U/L; aspartate aminotransferase, 95 U/L; alanine aminotransferase, 71 U/L; gamma-glutamyltransferase, 169 U/L; total bilirubin, 0.7 mg/dL; activated partial thromboplastin time (aPTT), 29 seconds; and international normalized ratio (INR), 1.45.

Urinalysis was normal. There were no fecal leukocytes or parasites seen on stool studies. Urine and blood cultures were negative.

Electrocardiogram was normal. Chest radiograph revealed small, bilateral pleural effusions and atelectasis in both lung bases. Computed tomography (CT) of the abdomen and pelvis revealed a 10-cm \times 10-cm, peripherally enhancing, low-attenuation lesion in the right hepatic lobe (Figure 1A), which had increased in size since the scan performed at his local hospital 5 days earlier. On the same CT scan, the adrenal glands were normal, although the left gland was at the upper limit of normal size (Figure 1B).

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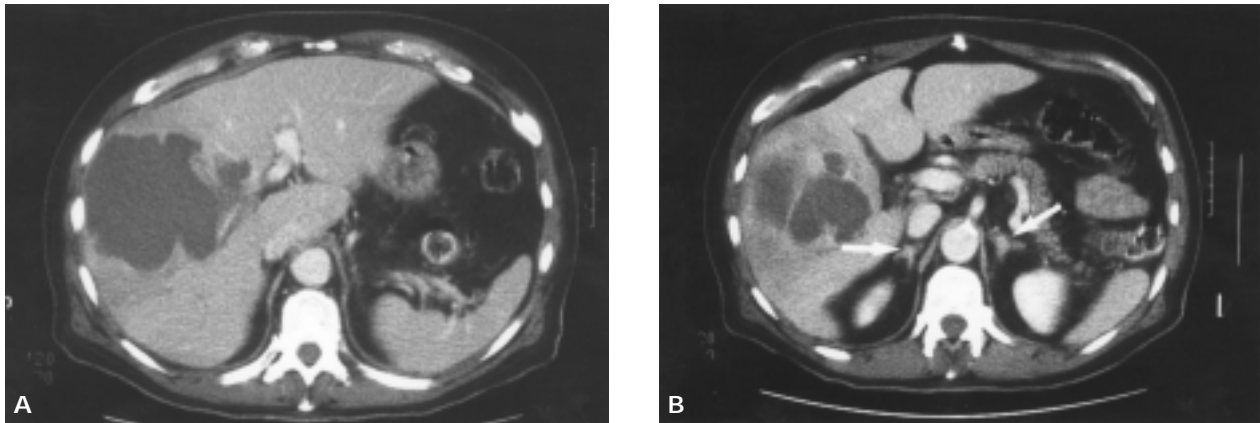


Figure 1. Computed tomography of the patient's abdomen with intravenous contrast at initial presentation shows (A) amebic abscess in the right lobe of the liver and (B) both adrenal glands, which are normal (*arrows*).

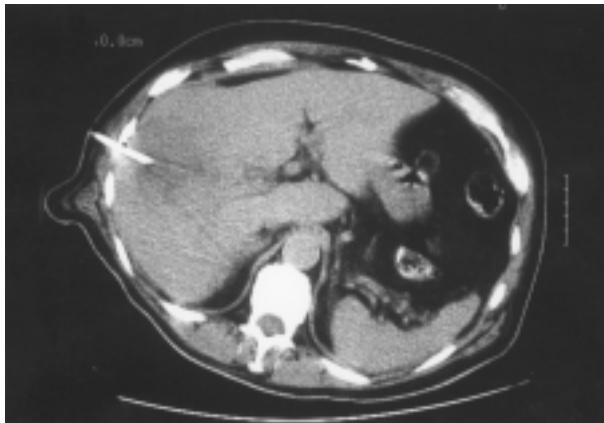


Figure 2. Drainage catheter in the amebic liver abscess with decompression of the cavity.

Hospital Course, Treatment, and Outcome

The patient was empirically started on intravenous (IV) piperacillin/tazobactam and metronidazole. A CT-guided drainage catheter was placed into the abscess cavity (**Figure 2**), and 250 mL of brownish fluid was withdrawn. The fluid contained many leukocytes. However, no organisms were seen on Gram stain, and cultures were negative. Results of serologic testing for *Entamoeba histolytica* were positive, with a titer greater than 1:256. Upon this diagnosis, the patient's antibiotic regimen was changed; his metronidazole was switched to an oral formulation (750 mg, 3 times daily), and paromomycin was initiated (500 mg by mouth 3 times daily). His symptoms resolved. The drainage catheter output diminished, and the catheter was removed. It should be noted that at the time of drainage catheter placement, the adrenal glands were normal by CT scan. After 5 days in the hospital, he was

discharged on a 28-day course of metronidazole and a 1-week course of paromomycin.

Readmission. Three weeks after discharge, the patient was readmitted with fatigue, anorexia, and a low-grade fever. A repeat CT scan of the abdomen showed that the abscess in the right lobe of the liver had nearly resolved (**Figure 3A**). However, there was a new 2-cm, low-attenuation lesion in the right adrenal gland and several smaller low-attenuation lesions in the left adrenal gland; these lesions likely represented bilateral adrenal hemorrhage (**Figures 3B** and **3C**). His platelet count was $479 \times 10^3/\text{mm}^3$, and his aPTT was 27 seconds. INR was 1.30.

During his 4-day hospitalization, the patient remained afebrile, and there was no evidence of active infection. However, his anorexia and fatigue persisted. His blood pressure was 120/75 mm Hg, without an orthostatic drop, and his pulse was 100 bpm (average measurements). Mild hyponatremia was present (128 and 133 mEq/L), and his serum potassium was at the upper limit of normal (ranging from 4.5 to 4.6 mEq/L). On the second hospital day, a corticotropin (ACTH) stimulation test was performed. The baseline cortisol level was 16 $\mu\text{g}/\text{dL}$. At both 30 and 60 minutes, the cortisol level was only 14 $\mu\text{g}/\text{dL}$. On the following day, the patient was started on prednisone (5 mg in the morning and 2.5 mg in the evening) and fludrocortisone (0.1 mg by mouth every other day). He noticed improved energy and increased appetite over the next 48 hours and was subsequently discharged on the fourth hospital day.

DISCUSSION

This case illustrates the most common extraintestinal complication of amebic infection—ie, the formation of

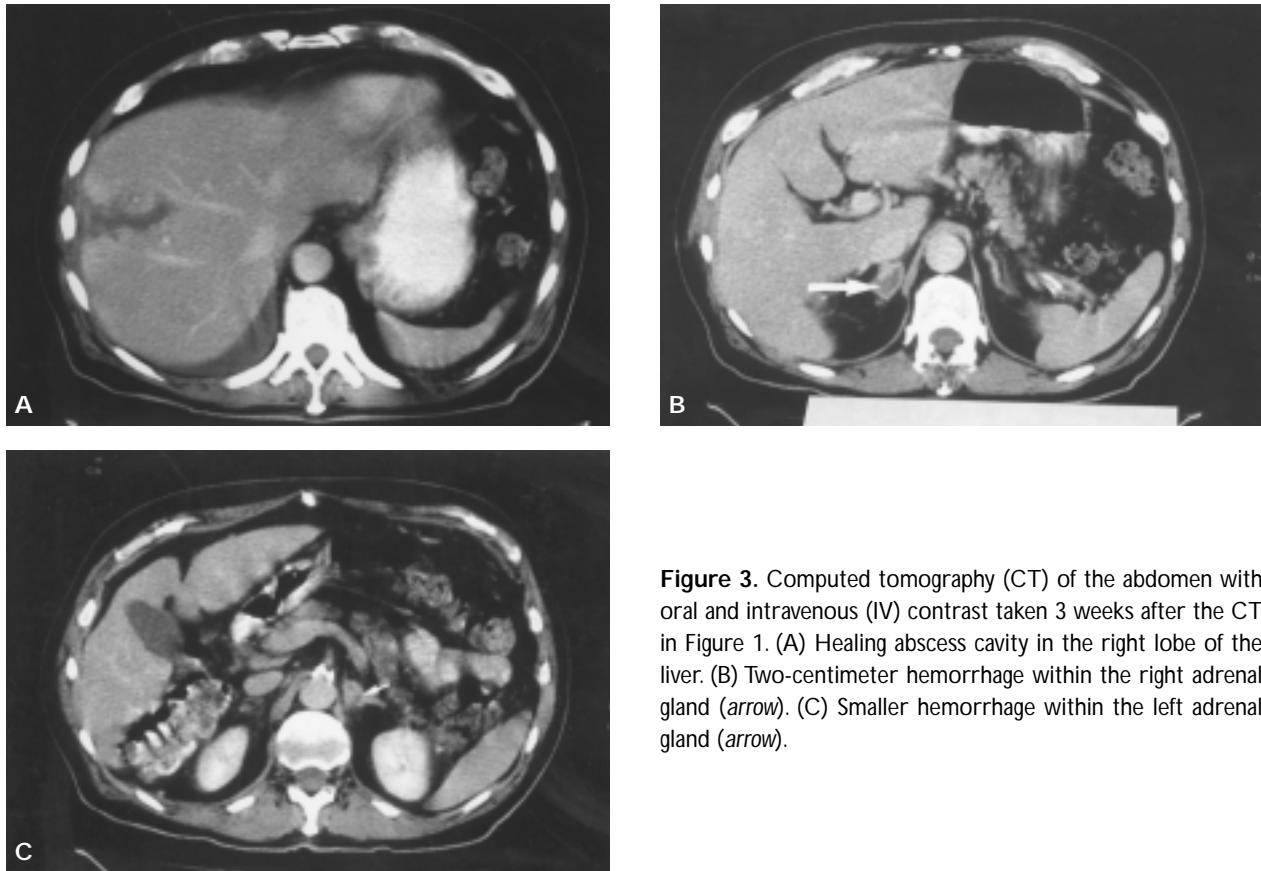


Figure 3. Computed tomography (CT) of the abdomen with oral and intravenous (IV) contrast taken 3 weeks after the CT in Figure 1. (A) Healing abscess cavity in the right lobe of the liver. (B) Two-centimeter hemorrhage within the right adrenal gland (arrow). (C) Smaller hemorrhage within the left adrenal gland (arrow).

a liver abscess.² This case also highlights an extremely rare complication of amebiasis, namely bilateral adrenal hemorrhage and secondary adrenal insufficiency. Only 1 other case with this complication has been described in the literature.¹

Etiology

Entamoeba histolytica cysts usually enter the intestinal tract via the ingestion of contaminated food or water. The authors suspected that the case patient became infected while in Arizona, which is close to Mexico, where amebiasis is endemic. Only 4% of patients with intestinal amebiasis go on to develop a liver abscess.² Concurrent diarrhea occurs in only 33% of these patients and was not present in this case.³ Most patients have a single abscess, usually in the right lobe of the liver.³

Diagnosis

The physical examination of a patient with an amebic liver abscess is generally characterized by right upper quadrant tenderness, which our patient distinctly lacked. Laboratory studies in these patients usually reveal anemia of chronic disease, profound leukocytosis, and an alkaline phosphatase level that is dispropor-

tionately increased when compared with other liver function tests.⁴ The diagnosis is made with a positive serological test and imaging the abscess with ultrasound or CT scan of the liver. Amebae are not frequently present in the stool of patients with liver abscesses.⁵ When the amebic liver abscess is large or there is risk of rupture (as there was in this case patient), placement of a drainage catheter can provide immediate symptomatic relief, can facilitate more rapid diagnosis, and results in no increase in complications.² A culture of the abscess fluid frequently has a low diagnostic yield, because most amebae are in the wall of the abscess.⁵ Treatment of amebic liver abscess requires both metronidazole and an agent known to eradicate the intraluminal encysted organism (eg, paromomycin).⁵

Spontaneous Bilateral Adrenal Hemorrhage

Spontaneous bilateral adrenal hemorrhage is a well described complication in many severe medical conditions.

Risk factors. There are a number of identifiable risk factors for spontaneous bilateral adrenal hemorrhage. The most commonly associated risk factor is a severe medical condition, such as systemic infection, major surgery,

trauma, or burns.⁶ Coagulopathy is the second most common risk factor in patients with adrenal hemorrhage.⁶

The case patient had a mildly elevated INR of 1.45 at his first admission to our hospital, which had decreased to 1.30 when he was readmitted and the adrenal hemorrhages were discovered. At both admissions, his aPTT was normal, and his platelet count was slightly elevated. He was not taking any anticoagulants. Furthermore, there was no history of antiphospholipid antibody syndrome nor had he been on ACTH therapy, both of which are thought to play an etiologic role in bilateral adrenal hemorrhage. However, it is likely that during the stress of his severe amebic infection, this patient had elevated levels of ACTH, which can result in degeneration, necrosis, and hemorrhage of the adrenal cortex in experimental animals.⁶

Clinical and laboratory features. The most common clinical features of bilateral adrenal hemorrhage are pain at the presumed time of the hemorrhagic event, fever, anorexia, weakness, fatigue, and hypotension.⁶ The patient denied experiencing any pain; low-grade fevers, anorexia, and fatigue were his main complaints.

Laboratory features of bilateral adrenal hemorrhage can include hyponatremia, hyperkalemia, and azotemia. However, at least 50% of all patients have little or no clinical evidence of adrenal dysfunction. Confirmatory tests should include a CT scan to visualize the adrenal hemorrhages and a short ACTH stimulation test to evaluate for adrenal failure. The CT scan will reveal enlargement of the adrenal glands, and the hemorrhages may appear as high- or low-attenuation lesions. Acutely, in the first several days, the hemorrhages will appear as high-attenuation lesions, but gradually thereafter, they become low-attenuation. Adrenal function is considered abnormal if the plasma cortisol level is below 20 µg/dL after 250 µg of intravenous ACTH. The ACTH level will exceed 100 pg/mL in cases of primary adrenal insufficiency.⁷

Treatment. For emergency treatment of acute adrenal insufficiency, a high dose of IV hydrocortisone is administered (100-mg bolus, followed by a continuous infusion of 100 to 200 mg over the next 24 hours). Fluid resuscitation with normal saline is also indicated in patients with volume depletion or hypotension.⁷ If the diagnosis of adrenal insufficiency has not been confirmed, 4 to 8 mg of IV dexamethasone may be administered. Dexamethasone will protect the patient from hemodynamic decompensation and does not interfere with the measurement of cortisol or the use of the ACTH stimulation test.⁶

Patients with chronic primary adrenal insufficiency require daily administration of oral corticosteroids in

divided doses. Usually, the initial dose is 15 to 25 mg of hydrocortisone in the early morning and 10 to 12.5 mg in the evening. (This dose corresponds to the 5-mg morning and 2.5-mg evening dosages of prednisone, respectively, used in the case patient.) The total daily steroid dose may eventually be decreased to the equivalent of 15 to 20 mg of hydrocortisone, and is titrated to the patient's sense of well-being, strength, and appetite. In addition, all patients with primary adrenal insufficiency should receive 50 to 200 µg/day of fludrocortisone; this amount should be adjusted until a normal blood pressure and serum potassium levels are achieved. All treated patients should carry some form of identification stating they have adrenal insufficiency. They should be instructed to double or triple their dose of glucocorticoid whenever they are injured or develop fever.⁷

Prognosis. The prognosis for patients with spontaneous bilateral adrenal hemorrhage remains grave if the diagnosis is missed. The advent of CT scanning has allowed more frequent detection of this entity. If patients survive the underlying illness which predisposed them to the adrenal hemorrhage, and if their adrenal insufficiency is appropriately treated, they have an excellent prognosis.⁶

SUMMARY/CONCLUSION

This case illustrates the clinical features and appropriate management of a patient with an amebic liver abscess. In addition, it also describes the complication of spontaneous bilateral adrenal hemorrhage. Adrenal insufficiency secondary to adrenal hemorrhage can be life threatening and should be considered for any patient who deteriorates with a severe medical condition, coagulopathy, or after major surgery. **HP**

REFERENCES

1. Risse M, Adebahr G, Weiler G: A rare cause of 2 unclear fatalities: undiagnosed acute and chronic amebiasis. *Z Rechtsmed* 1986;96:235-243.
2. Fujihara T, Nagai Y, Kubo T, et al: Amebic liver abscess. *J Gastroenterol* 1996;31:659-663.
3. Li E, Stanley SL Jr: Protozoa. Amebiasis. *Gastroenterol Clin North Am* 1996;25:471-492.
4. Vukmir RB: Pyogenic hepatic abscess. *Am Fam Physician* 1993;47:1435-1441.
5. Ravdin JI, Petri WA: *Entamoeba histolytica* (amebiasis). In *Principles and Practice of Infectious Diseases*, 4th ed. Mandell GL, Bennett JE, Dolin R, eds. New York: Churchill Livingstone, 1995:2395-2408.
6. Rao RH: Bilateral massive adrenal hemorrhage. *Med Clin North Am* 1995;79:107-129.
7. Oelkers W: Adrenal insufficiency. *New Engl J Med* 1996;335:1206-1212.