73-Year-Old Man With Hepatomegaly and Weight Loss

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A 73-year-old man went to his local hospital because of a 13.6-kg weight loss during a 4-month period, early satiety, and increased abdominal distention. He also complained of weakness and fatigue. He denied having fever, chills, nausea, vomiting, or diarrhea. The patient denied tobacco or ethanol abuse. He had been born in the former Czechoslovakia and immigrated to the United States 20 years previously. He had not been outside the United States for the prior 5 years.

On examination, his weight was 57.6 kg, height 1.72 m, temperature 36.7°C, blood pressure 110/58 mm Hg, pulse 80/min, and respirations 20/min. Abdominal examination showed tender hepatomegaly (a liver span of 25 cm), without nodularity. No splenomegaly was present. Neuromuscular examination revealed generalized muscle wasting. Findings on the rest of his examination were normal.

Pertinent laboratory results (and normal ranges) were as follows: hemoglobin 8.2 g/dL (13.5 to 17.5), leukocytes 5.8 X 10⁹/L (3.5 to 10.5 X 10⁹) with eosinophils 11.9% (0.8 to 7.2%), total bilirubin 0.3 mg/dL (0.1 to 1.1), calcium 7.9 mg/dL (8.9 to 10.1), albumin 2.3 g/dL (3.5 to 5.0), and alkaline phosphatase 503 U/L (98 to 251).

1. Which one of the following is the most likely cause of the patient's hepatomegaly?
   a. Inflammatory disorder
   b. Vascular congestion
   c. Extramedullary hematopoiesis
   d. Tumor
   e. Cyst

   The most common inflammatory disorders that cause hepatomegaly are hepatitis (infected and noninfected) and hepatic abscesses. The patient's manifestations make these diagnoses unlikely. Hepatomegaly may be caused by vascular congestion, as seen in congestive heart failure, some valvular diseases, or hepatic vein thrombosis. Findings on physical examination eliminate this diagnosis. The hallmark of extramedullary hematopoiesis is splenomegaly. The absence of splenomegaly and the results of the blood cell counts make this diagnosis improbable. Tumors, benign or malignant, are a main category in the differential diagnosis of hepatomegaly. The patient's age and progressive weight loss suggest the possibility of a hepatic tumor. Liver cysts can be infectious (usually parasitic) or noninfectious. Because they typically enlarge slowly and are asymptomatic, hepatic cysts are less likely to be present.

   An esophagogastroduodenoscopy and a colonoscopy showed a hiatal hernia and sigmoid diverticulosis. Iron studies and a peripheral blood smear suggested anemia of chronic disease. The clinical suspicion for neoplastic disease was high, and another test was considered.

2. Which one of the following diagnostic imaging tests is most appropriate in this patient?
   a. Plain abdominal roentgenography
   b. ⁹⁹mTc sulfur scan of the liver
   c. Abdominal ultrasonography (US)
   d. Abdominal computed tomography (CT)
   e. Arteriography of the hepatic artery

   A plain abdominal roentgenogram has limited value in evaluating hepatic lesions. Occasionally, it may demonstrate air in an abscess or parenchymal calcifications. Radionuclide (⁹⁹mTc sulfur colloid) imaging of the liver is helpful in identifying intrahepatic filling defects and assessing hepatic function and the biliary tract. Because the sensitivity and specificity are low, however, its usefulness today is limited. US is an inexpensive, universally available method of imaging the liver. It can evaluate the size and shape, parenchymal texture, vascular structures, and biliary tree and also distinguish simple cysts from solid masses. US is highly accurate in diagnosing hepatic metastatic lesions and cysts; it can detect lesions as small as 1 cm. CT can detect lesions as small as 5 mm. It identifies fatty infiltration and calcification more readily than US, but it is less sensitive than US for detection of collagen and for defining cystic masses and liver size. Usually, CT is regarded as supplemental to US. When the working diagnosis is tumor, a CT scan of the abdomen is the test of choice.
because it provides more data than US about the abdominal viscera and lymph nodes and may detect possible metastatic involvement. Arteriography of the hepatic artery is an excellent technique for identifying tumors within the liver, but it is an invasive study and has had a lesser role since introduction of US and CT.2

In our patient, CT of the abdomen and pelvis showed a large, bilobular cystic lesion in the anterior portion of the liver (Fig. 1), along with two other similar lesions. Abdominal US was not done.

3. Which one of the following is the most likely diagnosis at this point?
   a. Hepatic amebiasis
   b. Bacterial (pyogenic) abscess
   c. Nonparasitic cyst
   d. Neoplasm with cystic degeneration
   e. Tapeworm (cestode) infestation of the liver

Hepatic amebiasis usually manifests as a single cystic cavity with low-level internal echogenicity. Liver function tests are rarely helpful, and eosinophilia is typically absent. Indirect hemagglutination assays are the confirmatory tests, with a sensitivity of 90%. The absence of epidemiologic risk factors and the polycystic appearance make this diagnosis unlikely in our patient. Clinical features of pyogenic liver abscesses include hepatomegaly, right upper quadrant pain, fever, weight loss, and jaundice. Laboratory abnormalities include leukocytosis with a left shift, anemia, and increased levels of liver enzymes. US is considered the test of choice and will reveal multiple rounded areas that are less echogenic than the surroundings. US- or CT-guided aspiration usually confirms the diagnosis. The "nontoxic" picture in our patient and the size of the cysts decrease the likelihood of this diagnosis.

Nonparasitic cysts are most frequently congenital but can also be produced by trauma or by infarction after a focal arterial insufficiency. Most of these cysts are asymptomatic. Laboratory findings are typically normal unless the cysts are secondarily infected. Usually, such cysts are incidental findings on US or CT. Large multiple hepatic cysts are rarely seen in polycystic hepatic disease. Virtually any hepatic neoplasm, whether primary or metastatic, can be cystic because of the occurrence of central necrosis. US reveals a filling defect, but the most valuable diagnostic test is CT with late readings after intravenous administration of a contrast agent. The patient's age and weight loss make an intra-abdominal malignant lesion the most likely diagnosis until proved otherwise by pathologic analysis.

Tapeworm infestation of the liver may be first seen incidentally on imaging studies or may manifest as an abdominal mass, abdominal pain, pruritus, recurrent urticaria, jaundice, or symptoms of secondary infection. Imaging studies may disclose a mass that occasionally is calcified around its rim and therefore suggests the diagnosis. US identifies the cysts in the liver but cannot distinguish a cestode cyst from other cysts of the liver unless daughter cysts are within it or calcification of the cyst wall is noted. Serologic tests are useful in confirming the diagnosis. Multiple cysts can form if the primary cyst ruptures and secondary seeding of daughter cysts occurs. Less than 30% of patients have this complication, which is usually associated with severe allergic reactions and anaphylaxis (symptoms not found in our patient).

Carcinoembryonic antigen, α-fetoprotein, and CA 19-9 levels were normal. Aspiration of one of the cysts under US guidance showed an exudate with leukocytosis, but cytologic studies and cultures were negative. The patient was transferred to our hospital for further work-up.

On admission of the patient to our hospital, physical examination revealed findings similar to those previously described. At this point, the patient's eosinophilia raised suspicion of a parasitic infestation. Serologic studies for amebiasis were negative, and serologic tests for a tapeworm were obtained.

4. Which one of the following is the most likely cause of this patient's hepatomegaly?
   a. Taenia saginata (beef tapeworm)
   b. Diphyllobothrium latum (fish tapeworm)
   c. Taenia solium (pork tapeworm)
   d. Hymenolepis nana (dwarf tapeworm)
   e. Echinococcus granulosus

Humans are the sole definitive hosts for T. saginata and D. latum. They become infected with these organisms when inadequately cooked beef and fish, respectively, are ingested. In humans, these two parasites are restricted to the intestines and thus are unlikely to be the infectious
agent in our patient. Infection with *T. solium* occurs after ingestion of inadequately cooked pork that contains infecting cysts. In this instance, humans serve as definitive hosts, and the involvement is limited to the intestinal tract. If humans ingest *T. solium* ova, excystation occurs in the intestine, and the larvae invade the circulation and disseminate to the brain, subcutaneous tissue, skeletal muscles, and other organs. Large liver *T. solium* cysts are usually accompanied by symptomatic neurocysticercosis or deep tissue involvement. Humans serve as both intermediate and definitive hosts for *H. nana*. Infection occurs through ingestion of ova in fecally contaminated food or water or by hand-to-mouth transmission. No extraintestinal forms of *H. nana* infection exist; hence, this organism is not the etiologic agent in our patient. Infection with *E. granulosus* when they ingest ova after hand-to-mouth transmission from the fur of infected dogs or by way of fecally contaminated food or water. Ova excyst in the intestine, and the larvae invade the intestinal mucosa and disseminate to various organs (such as the liver or lungs), where they can produce large cysts. The typical cyst is unilocular and contains brood capsules and protoscolices, which are known as "hydatid sand" and daughter cysts.

In our patient, serologic studies for *Echinococcus* showed normal IgM but elevated IgG. The presumptive diagnosis of echinococcosis was made.

**5. Which one of the following is the least indicated therapy for our patient?**

a. Conservative surgical drainage of the cyst followed by excision
b. Radical surgical procedure with pericystectomy or hepatic resection
c. Albendazole, 10 to 15 mg/kg daily, for several 4-week cycles
d. Percutaneous drainage and albendazole, 10 mg/kg daily, before and after the procedure
e. Intracystic instillation of a scolicidal agent followed by cyst removal

Surgical treatment, if possible, remains the preferred management for active hydatid disease (echinococcosis) because of the fewest complications and best associated prognosis. Some reports suggest that the radical surgical approach (pericystectomy or hepatic resection) yields better results than the conservative approach (drainage, excision, and omentoplasty). Medical treatment should be selected for patients who have inoperable hydatid disease or for whom surgical intervention is contraindicated. The drug of choice is albendazole, 10 to 15 mg/kg daily for several 4-week cycles. US-guided percutaneous transhepatic drainage of liver cysts with concomitant albendazole therapy has been shown to be an effective and safe procedure associated with good results. The instillation of scolicidal agents (formalin, 95% ethanol, silver nitrate, or hypertonic saline) into the cyst was considered part of the classic surgical approach to minimize the possibility of recurrent disease attributable to peritoneal spillage. The injection of scolicidal solutions has led to several secondary problems, ranging from transient hypernatremia to sclerosing cholangitis, systemic toxicity, and even death. Some investigators have suggested that this practice should be abandoned and replaced with careful protection of the area surrounding the cyst with heavy moist pads.

Our patient underwent abdominal exploration in conjunction with drainage and excision of the cysts. Pathologic examination showed refractile birefringent hooklets, consistent with an *Echinococcus* scolex (Fig. 2) and degenerated hydatid sand. The patient recovered eventuantly. Therapy with albendazole, 10 mg/kg daily, was begun. Follow-up at 2, 4, and 6 months postoperatively showed substantial improvement in the patient’s clinical status and no evidence of relapse on follow-up abdominal CT scans. Albendazole therapy was discontinued after a total of four 4-week cycles.

**DISCUSSION**

Echinococcosis is a parasitic zoonotic disease caused by infection with the larval stage of *E. granulosus*, *E. multilocularis*, or *E. vogeli*. *E. multilocularis* and *E. vogeli* are transmitted by wild canines and are much less common than *E. granulosus*, which is transmitted by domestic dogs in livestock-raising areas. Cystic hydatid disease has a high prevalence in Latin America, southern and eastern Europe, the Middle East, and Africa. In the United States, it is rare: fewer than 100 cases are identified annually. Within the United States, certain regions—Alaska, Minnesota, and the Southwest—have a higher frequency of the disease than others.

Fig. 2. Smear of cystic fluid, showing refractile birefringent hooklets. (Hematoxylin-eosin with use of polarized light; original magnification, x400.)
The disease is not transmitted from person to person. The sexual stage of the parasite is harbored by definitive hosts: dogs, dingoes, wolves, and coyotes. The asexual stage is harbored by intermediate hosts—herbivores (especially sheep, goats, cattle, swine, and horses) and humans. Humans acquire the disease by ingesting viable parasite eggs. Typically, a single unilocular cyst is present, but in 20 to 30% of cases, multiple cysts may exist in the same or multiple organs. The most common site of hydatid disease is the liver (50 to 70%), followed by the lung (20 to 30%); however, it can be found in any organ of the body.

Most cases of hydatid disease are asymptomatic and are discovered incidentally on radiologic studies or at autopsy. Usually, the manifestations are related to the mass effect of the slowly growing cysts. Acute signs and symptoms are associated with complications—for example, infection in conjunction with fever, rupture that may cause peritonitis, pneumothorax, empyema, anaphylactic shock, and even death.

Radiologic imaging usually raises the suspicion of the diagnosis. Infection may be confirmed by serologic testing. The best initial screen is a highly sensitive test such as enzyme-linked immunosorbent assay or indirect hemagglutination, which are positive in about 85% of the patients. The specificity of the reactive sera is confirmed with immunoblot assays or counterimmunoelectrophoresis. Eosinophilia that exceeds 7% can be found in 30% of patients. Classically, the suspicion of hydatid disease was a contraindication to needle aspiration. In seronegative patients with unilocular cystic lesions of the liver, more invasive diagnostic procedures (US- or CT-guided percutaneous aspiration of the cyst) may be justified.

From 1 to 4% of the diagnosed cases are fatal. Surgical treatment, if possible, is the preferred management of hydatid disease. In asymptomatic patients with small calcified cysts, clinical observation is advocated. The main complication of surgical treatment is secondary echinococcosis that occurs from spillage of the fluid during the operation (20 to 30% of cases). This complication can be prevented by treatment with albendazole before and after the surgical procedure. Benzimidazole drugs are a viable alternative for patients with disease that is inoperable because of dissemination or inaccessible location of the cysts or for those in whom an operation is contraindicated because of coexistent medical problems. The initial compound, mebendazole, was replaced by albendazole, which is better absorbed and has a better penetration into tissues and cysts. Postoperative chemotherapy is used after iatrogenic rupture of cysts and spillage of the contents. Another therapeutic option is US-guided percutaneous aspiration of the cyst fluid in conjunction with concurrent treatment with albendazole. A recent study showed it is an effective and safe alternative to surgical treatment of uncomplicated hydatid cysts of the liver.

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REFERENCES

Correct answers: 1. d, 2. d, 3. d, 4. e, 5. e