CLINICAL VIGNETTE

A Woman with Nausea, Vomiting and Intermittent Urticaria

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History of Present Illness

A previously healthy twenty-year-old female presented to the emergency department with one day of nausea, vomiting, and abdominal pain. She had seven episodes of bilious emesis that became blood tinged an hour prior to presentation. Computed tomography (CT) of the abdomen and pelvis revealed a solitary 8.3 x 6.4 x 8.8 cm uniloculated, hypoattenuating, cystic mass in the right hepatic lobe with an undulating, enhancing capsule. There was also moderate ascites with diffuse mesenteric inflammatory stranding (Figure 1). She was admitted to the hospital for further diagnostic workup and treatment.

The patient was born in Mexico and moved to the United States at the age ten. She made annual trips to Mexico with her family. The most recent was four months prior to admission. She had exposure to feral dogs in Mexico but sustained no bites or known exposures to other animals or insects.

On exam the patient was in no acute distress. She was obese with anicteric sclera. Cardiac exam revealed tachycardia with a regular rhythm. Pulmonary examination was normal. Her abdomen was obese and tender to palpation in the bilateral upper quadrants, right greater than left. There was no rebound, guarding, nor fluid wave.

The white blood cell count was 18,710 per cubic millimeter (reference range 3200-10,600) with 77% neutrophils, 14% bands, and 0% eosinophils. Hemoglobin, platelet count, and comprehensive metabolic panel were within normal limits. *Entamoeba histolytica* IgG antibody was 0.49, index value (IV)(reference range <0.79). Blood cultures on admission were negative for growth at five days. *Echinococcus* IgG antibody was 1.02 IV (reference range 0-0.89, equivocal range 0.90-1.09). Cancer-associated antigen (CA) 19-9 was 5 U/mL (reference range 0-37 U/mL) and carcinoembryonic antigen was 0.8 ng/ml (reference range 0-3.0 ng/mL).

The patient was transferred to the general medicine floor where she was started on piperacillin-tazobactam for broad antimicrobial coverage in the setting of presumed sepsis. On the evening of admission she underwent drainage of the cyst by interventional radiology (IR). The following morning she developed diffuse hives, fever, tachycardia, and wheezing. She had similar episodes over the following days. The episodes of urticaria and wheezing persisted despite changing antibiotic classes. She also developed a peripheral eosinophilia (9.6%, reference range 0-6.0%) during this time.

IR placed a percutaneous Jackson-Pratt drain under fluoroscopy on admission and ten ml of serosanguinous fluid was aspirated. Fungal, aerobic and anaerobic bacterial cultures, and acid-fast bacilli smear and cultures from the fluid demonstrated no growth. Pathology from cyst aspiration demonstrated parasitic organisms with refractile hooklets in the backdrop of abundant neutrophils and eosinophils (Figures 2 and 3). These findings were consistent with an Echinococcal hydatid liver cyst. She was started on albendazole 400 mg twice daily. *Echinococcus* antibody three weeks after admission was elevated at 11.88 IV (reference range 0-0.89).

The patient was subsequently taken to the operating room where she underwent aspiration and instillation of hypertonic saline into the cyst followed by enucleation. Segments five and six of the liver were then resected. Pathology of liver sections revealed a 9.5 x 8.0 x 6.5 cm cyst with abundant eosinophilic infiltrate and rare protoscoleces and cestode hooks. Post-operative CT of the abdomen and pelvis showed complete resection of the cyst. Albendazole was continued for six months. Serial ultrasounds every three months showed no evidence of cyst recurrence.

Discussion

Pathology confirmed the cause of the patient's symptoms was an *Echinococcus* hydatid liver cyst. Hydatid liver cysts are caused by the cestode parasite *Echinococcus spp.*. Four species of *Echinococcus* infect humans, including *E. granulosus, E. multilocularis, E. vogeli, and E. oligarthus;* the former two account for the majority of human infections. Solitary hepatic lesions are classically caused by *E. granulosus,* whereas multi-cystic and pulmonary *Echinococcus* are more likely due to *E. multilocularis.* Dogs are the definitive host for *E. granulosus*, which is distributed worldwide but principally in the former Soviet Union, South America, the Middle East, sub-Saharan Africa, and China. Most cases in the United States occur in

immigrants from endemic countries. Intermediate hosts include sheep, goats, camels, horses, cattle, and swine. Humans are incidental hosts.[1]

Human infection begins following ingestion of eggs from infected dog feces. Upon ingestion, embryos (oncospheres) hatch from the eggs and penetrate the intestinal mucosa. Oncospheres are then taken up in either the blood or lymphatic system and migrate to the liver or other organs where they form a cyst. The cyst develops into multiple layers and protoscoleces develop within the cyst. Cysts containing protoscoleces are considered active. The lifecycle is completed when a dog ingests intermediate host tissue containing protoscoleces. The protoscoleces then migrate to the dog's small intestine to form adult tapeworms.[2]

Initial infection with *E. granulosus* is universally asymptomatic and a latent period of several years typically occurs before symptoms arise. Cysts expand at a rate of 1-50 millimeters each year. Some cysts spontaneously resolve while others grow and can rupture years later.[3] In this case, the patient was likely infected before the age of ten when she resided in Mexico. She reported recurrent exposures to feral dogs both as a child and on return trips. As her case highlights, the most common symptoms of infection are right upper quadrant pain, nausea, and vomiting as the cysts expands. Ruptured cysts can cause a variety of symptoms depending on the location of rupture. Rupture into the peritoneum can causes peritonitis and anaphylaxis, whereas rupture into the biliary tree can cause biliary colic, cholangitis, pancreatitis, or obstructive jaundice. Mass effect can mimic Budd-Chiari syndrome or cause cholestasis and/or portal hypertension.[2]

Infection with *E. granulosus* is diagnosed by a combination of typical imaging and serology. Laboratory findings include nonspecific aberrations in blood counts and liver function tests. Eosinophilia is typically only observed after leakage of fluid from the cyst. Enzyme-linked immunosorbent assay (ELISA) is the most sensitive and specific serologic test for *E. granulosus*. However, negative serology does not rule out infection. Liver cysts are more likely to produce a serologic response than lung cysts. False positive are common in the setting of infection with other parasitic infections and in patients with collagen vascular disease.[2,4] The patient described herein presented with classic symptoms of an Echinococcal hydatid cyst. However, laboratory evidence was initially more concerning for bacterial infection and sepsis. Eosinophilia developed after the cyst was aspirated. Initial ELISA IgG was equivocal but became positive two weeks following percutaneous aspiration. Given the patient's anaphylactic-like symptoms following aspiration, spillage into the abdomen was thought to account for delayed positivity in serology and development of peripheral eosinophilia, similar to prior reports.[3]

Imaging is crucial to diagnosis and further management of cystic lesions. Ultrasound and CT are highly sensitive for Echinococcal hydatid cysts. Ultrasound typically reveals a smooth, anechoic, round cyst, similar in character to a simple cyst.[5] Ultrasound can also aid in classifying the cyst as active, transitional, or inactive. Actively growing cysts are characteristically either unilocular or multiseptated. Transitional cysts often have detached membranes, described as the water lily sign. Inactive cysts can be heterogenous and are often solid with calcified walls.[3,6] CT can obtain greater anatomic detail and characterize extra-hepatic lesions. Cysts are categorized based on activity and size using the World Health Organization (WHO) classification system that guides treatment. In this patient's case, her cyst was classified as CE1 because the cyst was unilocular, without septations to suggest formation of daughter cysts. Further, the membranes were not detached and the appearance was suggestive of an active cyst.[3,6]

Definitive management of CE1 lesions involves drug therapy alone for lesions measuring fewer than five centimeters. Albendazole is the drug of choice dosed at 15 mg/kg twice daily. For CE1 lesions measuring greater than five centimeters, treatment consists of albendazole plus percutaneous treatment with puncture, aspiration, injection, and reaspiration (PAIR) of the cyst. PAIR is a catheter-based approach that involves instilling scolecidal agents into the lesion. PAIR has the advantage of being less invasive than surgery and can be both diagnostic and therapeutic.[3] In this case, Echinococcal hydatid cyst was not an initial consideration, and percutaneous aspiration alone was performed for diagnostic purposes.

Given the patient's acute presentation, it is difficult to determine if her cyst ruptured prior to presentation or whether this occurred during percutaneous aspiration of the cyst. However, due to leakage of cyst contents into the peritoneum her case was considered complicated and warranted surgical intervention. Cysts that communicate with the biliary tree, compress vital structures, and those that become secondarily infected or hemorrhage also require surgical treatment.[2]

Per guidelines, the patient received more than one week of albendazole treatment prior to surgery with the goal of inactivating protoscoleces.[2] PAIR was performed prior to definitive resection to minimize additional leakage. Protoscolecidal hypertonic saline was instilled into the patient's peritoneum intraoperatively to prevent peritoneal seeding.

Patients undergoing surgery for cystic echinococcosis without evidence of cyst leakage can be treated with albendazole for one month post-operatively. Spillage into the peritoneum warrants six months of treatment, although the ideal duration of treatment remains uncertain.[2,7] For this patient, surveillance for relapse was conducted with serial abdominal ultrasounds every three months while on albendazole therapy. She has had no evidence of recurrent disease and will be followed with serial ultrasounds every 3-6 months.

Figures

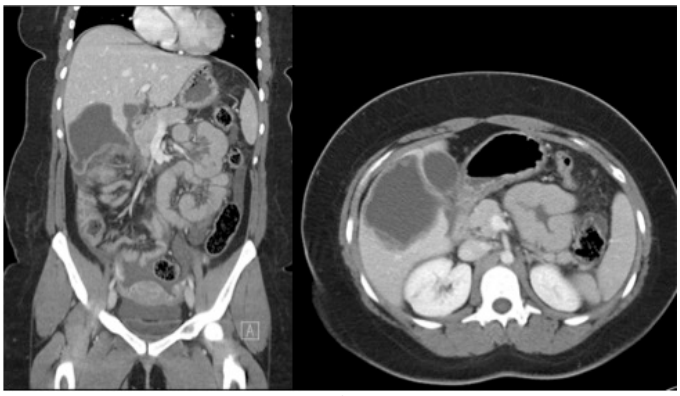

Figure 1: Coronal and axial sections of CT abdomen and pelvis demonstrates a solitary 8.3 x 6.4 x 8.8 cm uniloculated, hypo-attenuating, cystic mass in the right hepatic lobe with an undulating, enhancing capsule.

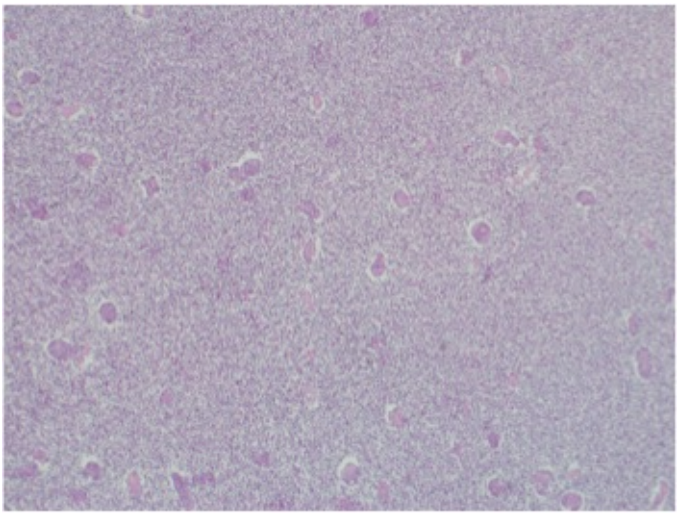

Figure 2: Low power magnification of hepatic cyst aspirate reveals multiple protoscoleces with abundant background inflammation (HE stain)

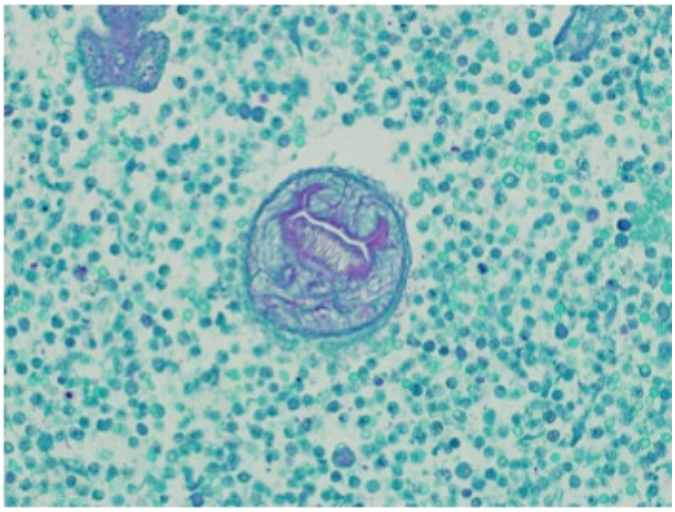

Figure 3: High power magnification of PAS-stained hepatic cyst aspirate demonstrates a solitary protoscolex, highlighting the organism's hooks and two suckers in the backdrop of abundant inflammation with a neutrophilic and eosinophilic predominance (PAS stain).

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Submitted March 11, 2019