Shocking Liver
Shaye Kivity*, Menachem Ben-Haim, Larisa Guranda and David Olchovsky
Departments of Medicine A (S.K., D.O.) and Diagnostic Imaging (L.G.), Sheba Medical Center, Tel-Hashomer and the Liver Surgery Unit (M.B.-H.), Tel Aviv Sourasky Medical Center, both affiliated to The Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel

Abstract

Introduction: In rare cases, anaphylaxis may be the explanation for recurrent loss of consciousness. Common causes of anaphylaxis are drugs, food or food additives, chemicals such as latex, systemic mastocytosis, parasites and idiopathic anaphylaxis.

Case: A 63 year old man of Iraqi descendant was hospitalized due to unexplained recurrent loss of consciousness, which responded well to rapid fluid administration. Eosinophils and triptase levels-90 minutes after an episode, were both elevated. An abdomen computed tomographic scan revealed a multilocular hepatic cyst (12 X12cm) with filling defects in the portal vein and two large liver infarcts, caused by embolized daughter cysts. Treatment with hydrocortisone and albendazole was initiated, and the patient underwent surgical intervention.

Summary: Our patient presented with a fluid-responsive shock that was subsequently diagnosed as anaphylaxis due to embolized echinococcal cysts.

Conclusions: Anaphylactic shock can be caused due to an immunological reaction to parasites such echinococcal cysts, even when a latency period of up to 50 years from infection exists.

Keywords: Anaphylaxis; Echinococcal Cyst; Shock

A 63-year-old man was admitted in shock to the emergency room. On examination he was lethargic, dyspneic and pale. His blood pressure was 80/30 mmHg, pulse 159 beats per minute, and body temperature normal. Oxygen saturation was not measurable by pulse oximeter. On physical examination, there was no visible bleeding source, the lungs were clear to auscultation, the heart sounds had normal rhythm and no murrums were audible, and no gross neurologic deficits were observed. The abdomen was soft and non-tender, but there was a palpable mass in the right upper quadrant. He responded well to aggressive fluid therapy and his vital signs and general condition improved dramatically within two hours.

The patient presented with shock to the emergency room. At this stage, the most urgent consideration is to differentiate between life-threatening medical conditions such as cardiogenic shock, arrhythmia, right myocardial infarction, tamponade, massive pulmonary emboli and hypovolemic shock due to bleeding, sepsis or severe dehydration. Physicians are less aware of other less common causes of shock, such as endocrine disorders (Addison’s disease, pheochromocytoma), neurogenic shock and anaphylaxis. His prompt response to fluid resuscitation supported the likelihood of hypovolemic or anaphylactic shock. Lack of such a response would require urgent cardiac evaluation, including echocardiography.

He was able to recall that while resting at home that evening he felt a sudden itching of both hands followed by chest pain, dyspnea and lethargy. His wife called an ambulance without delay and he was brought to the emergency room. The patient was born in Iraq, where his family owned cattle and worked as butchers. He immigrated to Israel at the age of 6 years, and was employed as a building constructor. The patient’s medical history included two episodes of atrial fibrillation which occurred fifteen years earlier and for which he had been treated by warfarin and amiodarone for five years. He had been suffering from recurrent episodes of unexplained syncope during the past 5 years. One year ago, he experienced a suspected mild transient ischemic attack, manifested by hypoesthesia of both left limbs, and he underwent cardiovascular investigations that included cardiac stress thallium nuclear scan, echocardiography and carotid Doppler. All test results were unremarkable. He has since been treated daily with aspirin.

Considering his previous history of cardiovascular events, arrhythmia must be excluded. Rapid atrial fibrillation in a 60-year-old man with normal systolic function is less likely to cause shock. A lethal ventricular arrhythmia (fibrillation or tachycardia) with no structural heart disease is unlikely, unless caused by myocardial ischemia or metabolic disorders. The results of cardiac enzyme tests 3-6 hours after the event, electrocardiogram and 24-hour cardiac Holter monitoring are important. Based on a recent normal cardiac evaluation and the fact that his transient hypotension was preceded by itching, anaphylactic shock should be considered.

Blood tests done at the emergency room were unremarkable except for mild lacticemia. The electrocardiogram exhibited sinus tachycardia and incomplete right bundle branch block. A chest computed tomography with intravenous contrast excluded pulmonary embolism and aortic dissection. He was treated with 4 liters of intravenous normal saline which was followed by rapid normalization of his vital signs. The patient was admitted to our internal medicine department for further investigation that included cardiac enzyme assessment, transthoracic echocardiography, cardiac Holter, and an electroencephalogram. The results of all these tests were normal. Forty-eight hours later, the absolute eosinophil count increased tenfold from baseline (to 650 /UL, 11% of total white blood cell count). A similar episode of hypotension and lethargy recurred on the third hospitalization day. The patient again responded to fluid resuscitation and the addition of hydrocortisone 300mg, intravenously. A blood test for triptase (a marker of mast cell degranulation) was taken 90 minutes after the second episode.

Anaphylaxis, beginning at the 5th-6th decade is more likely to be due

*Corresponding author: Dr. Shaye Kivity, Rheumatology Unit, Medicine Department C, Sheba Medical Center, Tel Hashomer, 52621 Israel, Tel: + 972 3 5302456; Fax: + 972 3 5352472; E-mail: shay.kivity@sheba.health.gov.il

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to drugs, such as non-steroidal anti-inflammatory drugs, antibiotics, as well as any other drugs, even over-the-counter ones. This patient denied taking any medications other than the long-standing aspirin regimen. Food or food additives (such as sulfite which can be present in red wine) can cause anaphylaxis, but the first presentation of an IgE-mediated food allergy is unlikely to occur at this age. Other causes could be exposure to chemicals, such as latex (gloves and other rubber products), systemic mastocytosis (which can present with skin lesions and can be diagnosed either by skin or bone marrow biopsy), as well as idiopathic anaphylaxis. Eosinophilia, although mild, raises the possibility of a reaction to parasites such Echinococcal cysts or Anisakias. Elevated blood levels of tryptase can assist in the diagnosis of mast cell-related events such as systemic anaphylaxis or mastocytosis. Phaeochromocytoma and carcinoid syndrome should be ruled out by measuring urine levels of catecholamines and 5-hydroxytryptamine (5-HT).

An abdomen computed tomographic scan with oral and intravenous contrast was performed and revealed a multilocular hepatic cyst (12 X12cm) with filling defects in the portal vein, two large liver infarcts and suspected inferior vena cava (IVC) invasion (Figure 1). A blood test for echinococcal antibody was sent for enzyme-linked immunosorbent assay (ELISA). The results of an earlier blood tryptase assessment were 26 microgram/ml (normal range 0-13). The abdominal examination remained non-tender and the liver enzymes remained within normal limits throughout the patient’s hospital stay.

Based on these findings, it is reasonable to assume that this patient suffered from recurrent episodes of anaphylactic shock due to invasive hepatic echinococcosis. Daughter cysts apparently entered the adjacent portal veins, causing liver infarcts through local embolization. The facts that this patient was raised in the Middle East (an endemic area for echinococcos granulosis) and that his family owned cattle and sheep can explain his exposure to this hydatid disease. Echinococcal hydatid cysts are usually indolent and asymptomatic, but 10% may cause symptoms related to size and location. Simple uncomplicated echinococcal cysts are generally treated with a PAIR (Puncture, Aspiration, Injection, and Re-aspiration) procedure, but this patient has a cyst complicated with vascular invasion and organ infarction. For him, the treatment of choice is surgical for cyst resection with vascular reconstruction and biliary exploration. Treatment with albendazole, an anti-helminthic drug, given for a few months has been showed to reduce the size of daughter cysts and lower their intraoperative dissemination.

Treatment with albendazole (Abz) was initiated and the patient was referred for surgical intervention. Surgery included supra- and infrahepatic IVC preparation for total hepatic vascular exclusion, controlled cyst aspiration followed by complete peri-cystectomy, caudate and left hepatic lobectomy, IVC and portal vein repairs (Figure 2a and Figure 2b). Biliary fistula mandated cholecystectomy, bile duct exploration and drainage via a T-tube. There were no major complications and the patient fully recovered. The ELISA for echinococcus antibody (IgE) was positive and a histological examination of the extracted specimen revealed echinococcal cyst adherent to liver tissue. He was discharged and continued treatment with Abz for 3 months.

Discussion

Our patient presented with a fluid-responsive shock that was subsequently diagnosed as anaphylaxis. Given the initial uncertainty, various diagnostic procedures were carried out to rule out major cardiovascular and other pathologies. The eventual diagnosis of anaphylaxis in this case was based on clinical presentation and exclusion of other conditions. It is not entirely clear whether his past syncope could be attributed to the same cause. Anaphylaxis usually affects more than one system: the skin is commonly involved (urticaria, angioedema and itching) as is respiration (bronchospasm, adult

Figure 1: Coronal multiplanar reconstruction from contrast-enhanced abdominal computerized tomographic scan at the level of the portal bifurcation. A large multilocular mass within the liver is shown. The mass contains multiple small hypo-attenuating cysts. Eggshell calcifications can be seen within the cyst walls. A small hypo-attenuating cyst is seen within a branch of right portal vein (arrow) with concomitant hepatic infarction.

Figure 2: Coronal multiplanar reconstruction from pre- and postoperative contrast-enhanced abdominal computerized tomographic scans at the level of the inferior vena cava (IVC). The mass compressed and invaded the retro-hepatic IVC (Panel a). The IVC was preserved following cyst and liver resection (Panel b).
respiratory distress syndrome or laryngeal edema) and cardiovascular compromise. In our case, a drop in blood pressure and itching were the only manifestations of anaphylaxis. Our patient also had elevated tryptase levels. Tryptase is a mediator released by mast cells and can be of help in the diagnosis of anaphylaxis and systemic mastocytosis [1]. It is superior to blood histamine measurement since it remains intact for several hours after it is released, while histamine is rapidly degraded. Other causes of an elevated total tryptase must be considered, and they include acute myelocytic leukemia, various myelodysplastic syndromes, hyperesoinophilic syndrome and end-stage renal failure.

Anaphylaxis to a parasite is rare in the western world. The most common parasite known to cause an allergic reaction is the *Anisakis simplex* (and related species such as the sealworm, *Pseudoterranova* sp., and the codworm *Hysterothylacium aduncum*) found in fish products [2]. Human allergy to *A. simplex* has become more ubiquitous due to the high rate of fish contamination by this parasite. *A. simplex* poses a health risk to humans even when thoroughly cooked [2]. Diagnosis of an allergic reaction to *A. simplex* can be made by a history of fish consumption and skin test to its products.

The cystic echinococcosis of our patient was caused by *Echinococcus granulosus* sp. *E. granulosus*, also called the hydatid worm, is a cyclophyllid cestode that parasitizes the small intestine of canids as an adult, but has important intermediate hosts such as livestock and humans, where it causes hydatid disease. Human infection is acquired by the ingestion of eggs passed into the feces of infected carnivores. Once ingested, the eggs liberate embryos that migrate to the liver, lung, and other organs. *E. granulosus* is known to occur on all continents and in at least 100 countries. High parasite prevalences are found in parts of Eurasia (for example, the Mediterranean region, the Russian Federation, India and China), Africa (northern and eastern regions), north and west Canada, Australia, and South America [3]. Cystic echinococcosis is regarded as one of the major public health problems in China. Prevalence of echinococcal cyst carriers in these above-cited regions was shown to be 2:2000. Once infected, the hydatid cyst may grow up to 3 centimeters annually. Symptoms may appear 5-20 years after exposure and are due to local expansion, secondary infection, and cyst rupture causing allergic reactions (fever, urticaria, eosinophilia, asthma and anaphylaxis). Leakage without cyst rupture can also cause minor allergic symptoms. Most cysts (68%) are hepatic and may grow up to 15 centimeters in diameter. They can cause abdominal tenderness and fullness, jaundice due to biliary obstruction, biliary fistula and hepatic outflow obstruction (including portal vein thrombosis and Budd chiari syndrome). Lung cysts (18%) can cause cough, hemoptysis or chest pain due to leakage or rupture into the bronchial tree. Cysts may occur in the brain, heart, spleen, and musculoskeletal system. The diagnosis can be supported by eosinophilia, elevated liver enzymes and hypergammaglobulinemia. Immunoblot (Western blot) and ELISA for the *E. granulosus* antigen are 80-90% sensitive for hepatic cyst but only 50-55% for lung and other organs. When a cyst ruptures, there is an abrupt production of antibodies, but senescent, calcified, or dead cysts are seronegative.

Most cysts are asymptomatic and incidentally diagnosed by imaging. The gold standard treatment for symptomatic hepatic cysts is surgery, with intraoperative injection of ethanol or hypertonic saline. Recurrence due to daughter cyst dissemination has been observed. The PAIR procedure is preferred in experienced centers [4]. Albendazole is the pharmacological treatment of choice, especially for non-operable patients, patients with multiple cysts or for reducing postoperative recurrence [5]. The drug is given orally for at least four days preoperatively and up to three months thereafter and was shown to reduce cyst seeding by killing protoscolices. The addition of praziquantel to albendazole may improve outcomes [6].

In endemic areas, prevention in dogs is primarily via prophylactic treatment with praziquantel on a monthly basis to remove the adult tapeworms. ELISA can be used to detect *E. granulosus* in dog populations. Ranchers should be educated not to feed their dogs scraps from butchered animals. Prolonged freezing or thorough cooking of meat (>50 degrees Centigrade) kills cysts in tissue. Large controlled studies with sheep have shown that vaccination with a recombinant oncospherical *E. granulosus* antigen (EG95) induces high degrees of protection, reducing the cyst numbers in vaccinated animals by approximately 90-100% [7,8]. A high degree of immunity (about 80%) persists for 6 months (in the absence of reinfection), and pregnant ewes vaccinated before lambing transfer high levels of antibody to their lambs. Regrettably, the vaccine is not yet commercially available.

In addition to the clinical diagnosis of recurrent anaphylaxis, the imaging studies in our case revealed portal cyst invasion with liver infarction probably due to daughter cysts embolization. Our patient did not complain of abdominal pain or tenderness nor did he have elevated liver enzymes or any abnormal laboratory markers of cell destruction (e.g., elevated lactate dehydrogenase or creatine phosphokinase). It should be emphasized that our patient’s clinical presentation did not match either the imaging or the surgical findings.

There are some reports of portal vein invasion by hydatid cysts, [9] but we are unaware of any previously reported cases that resulted in embolism and liver infarction. Reports based mostly on postmortem examinations described IVC or hepatic vein echinococcal embolization, while others described left ventricular echinococcosis with peripheral or pulmonary artery embolism [10].

This case emphasizes the importance of including anaphylaxis in the differential diagnosis of patients presenting with recurrent shock in whom no other causes can be found, and that an echinococcal cyst should be considered in the patients who come from endemic areas.

References
