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An Analysis of Possible Mechanisms of Unexpected Death Occurring in Hydatid Disease (Echinococcosis)

ABSTRACT: Most cases of hydatid disease in human populations are due to *Echinococcus granulosus.* The hydatid life cycle involves passage between definitive hosts such as dogs and intermediate hosts such as sheep. Humans become accidental intermediate hosts following ingestion of food or water contaminated with eggs or by contact with infected dogs. Although hydatid disease may remain asymptomatic, occasional cases of sudden and unexpected death present to autopsy. Causes of rapid clinical decline involve a wide range of mechanisms including anaphylaxis (with or without cyst rupture), cardiac outflow obstruction or conduction tract disturbance, pulmonary and cerebral embolism, pericarditis, cardiac tamponade, myocardial ischemia, pulmonary hypertension, peritonitis, hollow organ perforation, intracerebral mass effect, obstructive hydrocephalus, seizures, cerebral ischemia/infarction, and pregnancy complications. The autopsy assessment of cases therefore requires careful examination of all organ systems for characteristic cystic lesions, as multiorgan involvement is common, with integration of findings so that possible mechanisms of death can be determined. Measurement of serum tryptase and specific IgE levels should be undertaken for possible anaphylaxis.

KEYWORDS: forensic science, hydatid disease, echinococcosis, anaphylaxis, sudden death, embolism

Hydatid disease refers to parasitic infestation by the tapeworm *Echinococcus*, most often occurring in sheep-raising communities (1). The most common species involved in human disease is *Echinococcus granulosus*, responsible for cystic echinococcosis, followed by *Echinococcus multilocularis* that causes alveolar echinococcosis. Rarely humans are infected by *Echinococcus vogeli* and *Echinococcus oligarthrus*. Cystic echinococcosis is responsible for more than 95% of the 2–3 million cases that occur worldwide (2). Although hydatid disease is relatively rare, the incidence rises in certain areas, with between 1 and 220 cases of cystic hydatid disease per 100,000 of the population reported in parts of southern Africa, southern Australia, New Zealand, Iceland, southern South America, and certain Mediterranean countries such as Turkey. These tend to be areas where there is close contact with dogs that are used to herd grazing animals (3). It has been noted, however, that hydatid disease is now no longer restricted to endemic areas given increasing international travel (4).

Many cysts within human carriers remain asymptomatic throughout life and may be completely incidental findings at autopsy. In certain individuals, however, hydatid disease may be responsible for rapid and unexpected death. As such events are rare and the literature has not tended to focus on forensic issues in fatal cases, the following study was undertaken to delineate the range of lethal mechanisms that may be associated with hydatid disease in humans, and to provide an overview of possible autopsy findings. Selected cases from the University of Adelaide Discipline of Pathology museum have been included to illustrate specific pathological features.

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Discussion

The life cycle of the hydatid tapeworm is complex involving three developmental stages within definitive and intermediate hosts, i.e., (i) adult tapeworms are found within the definitive host, (ii) free eggs in the environment, and (iii) metacestodes within the intermediate host. Intermediate hosts for *E. granulosus* are usually herbivores such as sheep and cattle that ingest parasite eggs deposited on grass in carnivore feces. The eggs hatch within the intermediate host lodging in viscera where hydatid cysts develop that contain a multitude of larvae. The larvae are ingested when a carnivore such as a dog or fox either kills an infected animal or scavenges the remains. Feeding of offal to farm dogs has also been responsible for perpetuating the hydatid cycle. Once inside a definitive host, maturation occurs with the formation of adult larvae, which then begin to produce eggs that are shed in feces. Intermediate hosts for *E. multilocularis* include certain types of rodents (2).

Humans become accidental intermediate hosts following ingestion of food or water contaminated with eggs or by contact with infected dogs (5). After ingestion, larvae hatch within the duodenum and enter the portal system, most often lodging in the liver (in 60–75% of cases). In approximately 15–20% of cases larvae bypass the liver and travel to the pulmonary circulation in the lungs. If larvae traverse the lungs they may lodge in any organ including the brain and heart. Cysts have relatively slow growth of 1–5 cm per year and are usually asymptomatic (1,5).

At autopsy hydatid cysts are readily identifiable having a wall composed of three layers: the pericyst derived from host fibroblastic response, the intermediate laminated membrane, and the inner germinal layer (Fig. 1). It is the inner layer that produces daughter cysts. Scolices can be identified within the cyst fluid as oval structures with a circle of hooklets (1) (Fig. 2).

Hydatid cysts often remain asymptomatic for many years as in Fig. 1, however they may become infected or cause organ dysfunction from local mass effects. A variety of clinical manifestations

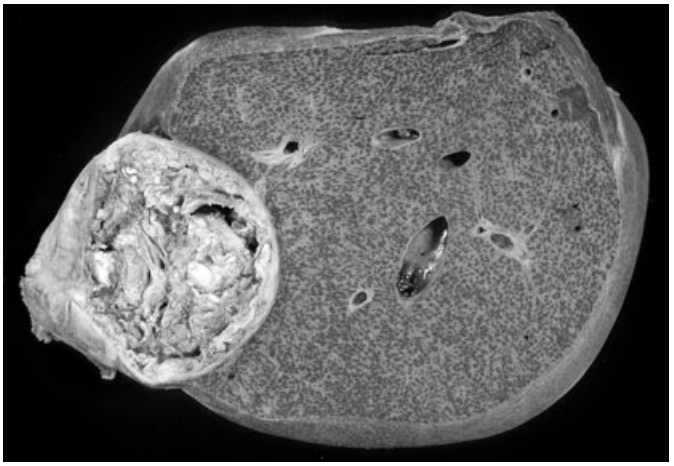

FIG. 1—*An incidental hydatid cyst of the liver found at autopsy in a 72-year-old man who died of pneumonia and congestive cardiac failure. Venous congestion of the liver can also be seen.*

may occur associated with obstruction of the biliary tract, bronchi, renal outflow tract, and cerebrospinal fluid pathways. Antemortem symptoms and signs may therefore include jaundice, urticaria, abdominal pain, biliary colic, cough, dyspnea, hemoptysis, and generalized seizures (6–8). Scolices may be vomited (hydatid emesis) or passed in the feces (hydatid enterica).

Sudden death is usually due to anaphylaxis (in 20% of cases) following rupture of a cyst and release of highly antigenic hydatid scolices (9). Rupture tends to involve cysts within the liver and less often the heart, and may be precipitated by relatively minor chest or abdominal trauma or by increased pressure within the cyst (3,8,10). Between 1 and 8% of infected individuals may suffer cyst rupture into the peritoneal cavity. This may result in rapid death from anaphylaxis or delayed death from sepsis and multiorgan failure (10). At autopsy the site of cyst rupture should be ascertained and measurement of serum tryptase and specific IgE levels should be undertaken, as with all cases of suspected fatal anaphylaxis (11). On occasion anaphylaxis has been reported without apparent macroscopic evidence of cyst rupture (12).

Cardiac hydatidosis is uncommon and occurs in only 0.5–3% of cases. Although the left ventricle is most often involved (60%), cysts may be found in all parts of the heart including the right ventricle (17%), interventricular septum (9%), right atrium (8%), left atrium (4%), interatrial septum (2%), and very rarely within the pericardial sac (5,9). Unexpected death may follow cyst rupture with anaphylaxis, or fatal embolization of hydatid material to the lungs (from the right side of the heart) or the cerebral circulation (from the left) (13,14). An example of the latter was a 12-year-old boy who collapsed in a school ground and died from hydatid embolization to the brain following rupture of a left ventricular cyst (15). Systemic embolization may also occur with obstruction of the distal aorta, iliac, or femoral iliac arteries resulting in lower limb ischemia (9,16). Cyst rupture with embolization is often precipitated by chest trauma and may occur at all ages (7,9). Other potentially lethal complications may occur from cardiac echinococcosis with a range of conduction disturbances and arrhythmias including complete atrioventricular block, anterior hemiblock, and paroxysmal ventricular tachycardia associated with compression of conduction tracts and surrounding myocardium (17–20). Cardiac tamponade, pericarditis, and fatal anaphylaxis have also been caused by rupture of cysts into the pericardial sac (5,21). Large intraventricular cysts have also been associated with outflow obstruction and valvular distortion (1,20,22) (Fig. 3). Coronary artery compression may also compromise myocardial perfusion with presentations of chest pain associated with typical ECG findings of ischemia (9,23,24). Pulmonary hypertension with right heart failure has been reported as a chronic response to previous embolization of hydatic cyst contents from the liver to the pulmonary circulation (25).

Hydatid cysts within the peritoneal cavity or ovaries are rare (<1% of cases) with hydatid disease during pregnancy occurring in only 1/20,000–30,000 of mothers in endemic areas (26). Problems may however arise for both the mother and child related to the manifestations of hydatid disease such as cyst rupture and anaphylaxis. It has also been hypothesized that hydatid cysts may grow faster during pregnancy due to decreased maternal cellular immunity and are therefore more likely to become symptomatic. Specific problems associated with pelvic hydatid cysts include dystocia, premature labor, and uterine rupture (26,27). A rare case of unexpected death in the immediate postpartum period of a 16-year-old adolescent due to pressure necrosis of the duodenum with retroperitoneal necrotizing fasciitis has been reported that was caused by a large upper abdominal hydatid cyst (4).

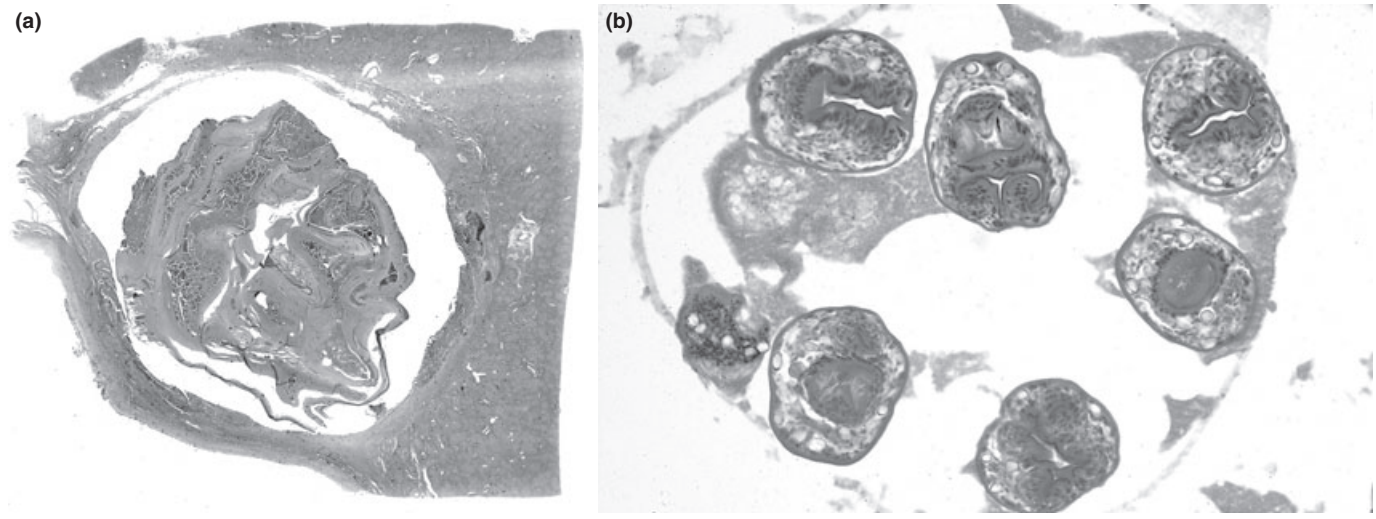

FIG. 2—*A whole mount section of a hepatic hydatid cyst demonstrating daughter cysts (a) and characteristic scolices (b) (Hematoxylin and eosin ×300).*

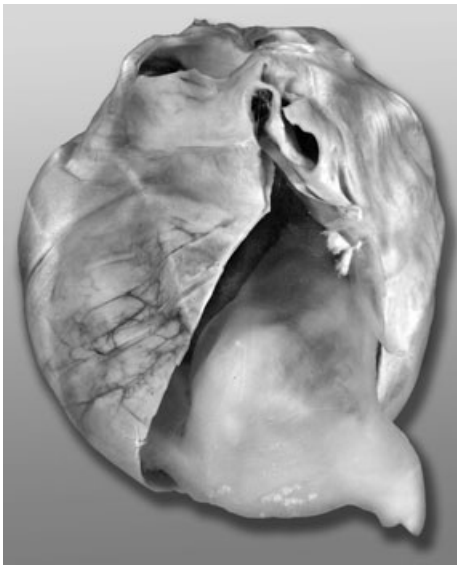

FIG. 3—*Filling of the left ventricular cavity with a large 10 cm diameter hydatid cyst in a second 12-year-old boy. Death was due to outflow obstruction with no evidence of cyst rupture.*

Intracranial hydatid cysts may cause a range of neurological symptoms and signs ranging from seizures to repeated episodes of hemiparesis and aphasia (28). Neurologic signs may result from raised intracranial pressure with or without hydrocephalus (Fig. 4) or may be due to embolization from distant sites such as the heart with cerebral ischemia/infarction and seizures (15). Either of these outcomes may be associated with a fatal outcome. Seizures are not however specific for central nervous system disease and have also been caused by hepatic hydatid cyst rupture with anaphylaxis (8). Intracerebral mass effects may be particularly significant if cysts are located within the brainstem (29).

Individuals with pulmonary hydatid disease may be asymptomatic or may present with cough, hemoptysis, and chest pain

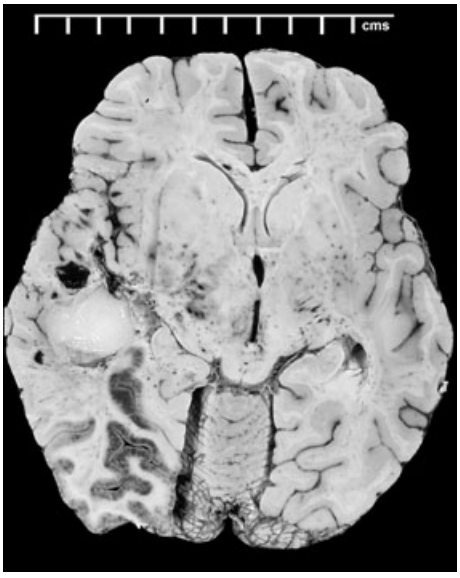

FIG. 4—*A large hydatid cyst present in the left temporal lobe of a 16-year-old girl who died following surgery. She had presented with a short history of headache, vomiting, and drowsiness.*

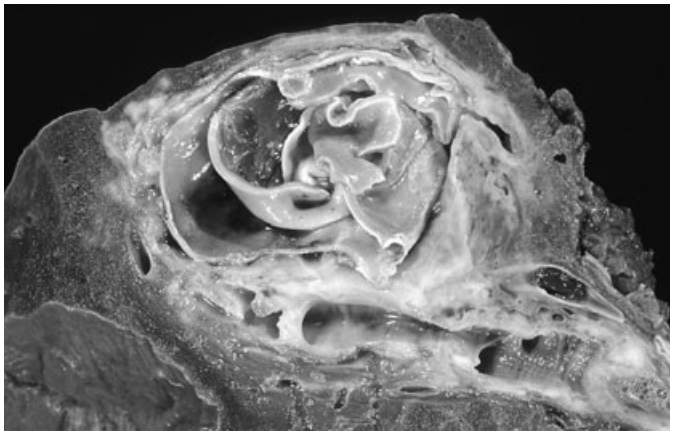

FIG. 5—*A lobectomy specimen from a 23-year-old male who presented with cough and hemoptysis revealing a hydatid cyst abutting a main bronchus.*

(Fig. 5). The mortality rate tends to be low with most cases being amenable to surgical cure (6). Postoperative complications include bronchopleural fistulas and infection of cyst cavities (30). Rupture of mediastinal cysts has also been associated with the development of pneumothoraces (31).

As the clinical diagnosis of hydatid disease in humans relies on imaging techniques including computed tomographic scanning and magnetic resonance imaging (32), these modalities may become extremely useful in future autopsy work. Immunological diagnosis has depended on the identification of IgG antibodies to hydatid cyst fluid utilizing native or recombinant B or five subunits in ELISA or immunoblot formats (32). Other components of hydatid cyst fluid have been tested for, in addition to the development of mitochondrial DNA-based techniques for identifying particular strains of *Echinococcus,* and stool-based PCR (copro-PCR) techniques for identifying infected animals (32,33).

Thus, although rare in many countries, hydatid disease remains a possible cause of sudden and unexpected death that may be encountered in forensic practice. This is particularly so given cases occurring outside endemic areas associated with increasing global travel (4). The autopsy assessment of cases requires careful examination of all organ systems for characteristic cystic lesions as

TABLE 1—*Features associated with unexpected death in cases of fatal echinococcosis.*

Immunological
Anaphylaxis
Cardiovascular
Outflow obstruction
Conduction tract disturbance
Embolization
Tamponade
Pericarditis
Myocardial ischemia
Pulmonary hypertension
Intra-abdominal
Peritonitis
Hollow organ perforation
Intracerebral
Mass effect/obstructive hydrocephalus
Seizures
Cerebral ischemia/infarction
Pregnancy
Dystocia
Uterine rupture

multiorgan involvement is common. Meticulous dissection of cysts should be undertaken to determine whether rupture has occurred. Similarly, dissection of the vasculature should be performed to check for embolization of cyst contents. Laboratory analysis for serum tryptase and specific IgE levels will assist in the evaluation of possible anaphylaxis. Mechanisms of death may be quite complex and involve many organ systems (see Table 1).

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