Diagnosis and Treatment of Human Hydatid Disease

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Abstract

Echinococcosis or hydatid disease is caused by larvae of Echinococcus. In the life cycle of E. granulosus, humans sometimes become accidental intermediate hosts. Humans can orally take up the E. granulosus eggs from infected carnivore excretions by handling the animals or egg-containing feces, plants, eating vegetables, uncooked fruits, and drinking water with the eggs. The hydatid disease is endemic in some Mediterranean countries, the Middle East, the South America, the South Africa and Oceania. Hydatid disease is seen in subjects of any age and sex. The combination of imaging and serology usually enables diagnosis. Clinical management of hepatic cysts includes albendazole or mebendazole therapy in combination with either surgical resection or the PAIR procedure.

***Key words**: Radiography, CT scan, cystic lung lesions, cavitary lung lesions*

Hidatik Kist Hastalığının Tanı ve Tedavisi

Özet

Ekinokkokozis veya hidatik hastalığına Ekinokok larvası neden olur. Ekinokokus Granulozus'un yaşam döngüsünde, insan bazen tesadüfi olarak konak olur. İnsan E.Granulozus yumurtalarını, ağız yoluyla hayvan sekresyonlarından, enfekte olmuş, yumurta içeren dışkıdan, sebzelerden, pişmemiş meyvelerden, ve içme suyundan alabilir. Hidatik hastalık bazı Ak Deniz ülkelerinde, Orta Doğuda, Güney Amerikada, Güney Afrikada ve Okyanusta endemik olarak görülür. Görüntüleme ve seroloji yöntemlerinin kombinasyonu tanı koymayı sağlar. Hepatik kistleri klinik tedavisi, albendazol veya mebendazol tedavisi ile cerrahi olarak rezeksiyon veya PAIR prosedürünün kombinasyonunu içerir.

***Anahtar kelimeler**: Ekinokkokozis, Hidatik Hastalık, Endemik*

INTRODUCTION

Cystic echinococcosis (CE) is among the most neglected parasitic diseases. Development of new drugs and other treatment modalities receives very little attention, if any, and is slow (1, 2). Human cystic echinococcosis (CE), caused by the larval stage of the cestode Echinococcus granulosus, is a cosmopolitan parasitic zoonosis, affecting mainly the liver (70%) and the lung (20%) of the human intermediate host. Clinical symptoms depend on the location, number, and size of the cysts. Until anthelminthic chemotherapy became available (mebendazole in the 1970s and albendazole in the early 1980s), surgery was the only treatment choice (3). The prevalence of infection varies widely among different countries and in different areas, ranging from 1 to 220 per 100,000 in certain regions (4).

Cystic echinococcosis caused by Echinococcus granulosus (hydatidosis or hydatid disease)

Life cycle

Cystic echinococcosis is a zoonotic illness caused by infection with Echinococcus granulosus. In the life cycle of E. granulosus, humans sometimes become accidental intermediate hosts. Humans can orally take up the E. granulosus eggs from infected carnivore excretions by handling the animals or egg-containing feces, plants, eating vegetables, uncooked fruits, and drinking water with the eggs (5, 6).

Epidemiology

The hydatid disease is endemic in some Mediterranean countries, the Middle East, the South America, the South Africa and Oceania. It is a disease of rural areas where farming is practiced traditionally (7). The hydatid cyst can occur also in non-endemic countries because of the upsurge of emigration and trade (8). Annual incidence rates of diagnosed human cases per 100,000 inhabitants vary widely, from less than 1 case per 100,000 to high levels. For example, rates in the indicated regions are as follows:

•Greece - 13 cases per 100,000 persons

•Rural regions of Uruguay - 75 cases per 100,000 persons

•Rural regions of Argentina - 143 cases per 100,000 persons in Rio Negro province

•Parts of Xinjiang province of China - 197 cases per 100,000 persons

•Parts of the Turkana district of Kenya - 220 cases per 100,000 persons

Cystic echinococcosis causes not only illness but also productivity losses in human and agricultural animal population, and it can have large societal impacts on endemic areas (9). Cystic echinococcosis is rarely fatal. Occasionally, deaths occur because of anaphylactic shock or cardiac tamponade in heart echinococcosis (10).

Parasite biology

Organ involvement

The liver is the most common site of infection followed by the lung in 10 to 30% of cases, and other sites (spleen, kidney, brain, bone) in about 10% cases. In one series of 386 patients with pulmonary hydatid cysts, 59 patients (15%) had extrapulmonary cysts, of which 54 were in the liver, 4 were in the kidney, and 1 was intraperitoneal. Approximately 60% were located in the lower lobes, and a predilection for the right lung was seen in 56% cases (11). Although hydatid cysts may be asymptomatic, but usually produce various symptoms due to compressive effect on surrounding vital structures such as dyspnea, retrosternal chest pain, cough, dysphasia, back pain, and superior vena cava syndrome (12, 13).

Clinical features

The clinical features of cystic echinococcosis are highly variable (Table 1). The spectrum of symptoms depends on the following; involved organs, size of cysts and their sites within the affected organ or organs, interaction between the expanding cysts and adjacent organ structures, particularly bile ducts and the vascular system of the liver, complications caused by rupture of cysts, bacterial infection of cysts and spread of protoscolices and larval material into bile ducts or blood vessels, immunologic reactions such as asthma, anaphylaxis, or membranous nephropathy secondary to release of antigenic material (9). The initial phase of primary infection is asymptomatic and may remain so for many years. Hydatid disease is seen in subjects of any age and sex, although it is more common in those aged 20–40 yrs (14, 15). The rate of growth of cysts is variable depending on the strain differences and the organ involved. Typical measurements state that the average cyst growth is 1 cm to 1.5 cm/year (9). Patients come to the clinician's attention for different reasons, such as when a large cyst has some mechanical effect on organ function or rupture of a cyst causes acute hypersensitivity reactions. The cyst may also be

discovered accidentally during radiographic examination, body scanning, surgery, or for other clinical reasons (16). Physical findings are hepatomegaly, a palpable mass if on the surface of the liver or other organs, and abdominal distention. If cysts in the lung rupture into the bronchi, intense cough may develop, followed by vomiting of hydatid material and cystic membranes (17).

Diagnosis

The combination of imaging and serology usually enables diagnosis. The standard diagnostic approach for cystic echinococcosis involves imaging techniques, predominantly ultrasonography, computed tomography (CT), X-ray examinations, and confirmation by detection of specific serum antibodies by immunodiagnostic tests. Enzyme-linked immunosorbent assay (ELISA) test using hydatid cyst fluid has a high sensitivity (>95%) but its specificity is often unsatisfactory. Finding a cyst using ultrasound, X-ray, or CT is typically expected in Echinococcus infection (18).

Laboratory and special investigations

Serological tests are commonly employed to supplement the radiological data in the diagnosis of hydatid cyst. The current gold standard serology test for echinococcosis detects IgG antibodies to hydatid cyst fluid-derive native or recombinant antigen B subunits. This is performed using ELISA or immunoblot formats (19). The lipoproteins antigen B (AgB) and antigen 5 (Ag5) are the major components of hydatid cyst fluid and are the most widely used antigens in current assays for immunodiagnosis of cystic echinococcosis (20). General consensus states that the ELISA test with crude hydatid cyst fluid has a high sensitivity of 95%; however, its specificity is low at 61.7% (21).

Imaging

The most valuable diagnostic method in pulmonary hydatid disease is the plain chest radiograph (22).

Radiography

The cysts are most commonly seen as spherical, homogenous masses with smooth borders surrounded by normal lung tissue (11). Occasional appearances are the presence of accompanying pleural effusion (3%), empty cyst cavities appearing as bullae (1%), and calcification (0.7%) (23). An intact cyst is filled with clear fluid. Debris within the fluid may occasionally be seen on ultrasound; this is formed of hooklets and scolices, and is referred to as hydatid sand (24). As the cyst enlarges and erodes into bronchioles, air enters the potential space between pericyst and endocyst, and appears as a thin, lucent crescent (crescent or meniscus sign) (11). When the endocyst completely separates, it collapses internally and can be seen floating freely on the cyst fluid ("water-lily" or "iceberg" sign) (11). Other classically described CT appearances are Cumbo sign (air-fluid level in the endocyst capped with air between the pericyst and endocyst) and "signet ring" sign (bleb of air dissecting into the wall of the cyst) (25). CT scanning can elucidate the cystic nature of the lung mass and provide accurate localisation for planning of surgical treatment of complicated cysts (26).

***Table 1**. Clinical future of hydatid diseases*

Liver
Hepatomegaly
Jaundice
Biliary colic-like symptoms
Cholangitis
Pancreatitis
Liver abscess
Portal hypertension
Ascites
Inferior vena cava compression or thrombosis
Budd-Chiari syndrome
Cyst rupture, peritoneal spread, and peritonitis
Hemobilia
Biliary fistula (skin, bronchial system, gastrointestinal tract)
Lungs
Tumor of chest
Chest pain
Chronic cough, expectoration, and dyspnea
Pneumothorax
Eosinophilic pneumonitis
Pleural effusion
Parasitic lung embolism
Hemoptysis
Biliptysis
Heart
Tumor
Pericardial effusion
Embolism
Breast - Masses that must be differentiated from neoplasms
Spine - Mass with neurologic symptoms
Brain - Mass with neurologic symptoms.

Ultrasonography

Various classifications exist of the ultrasonographic picture in cystic echinococcosis, the most widely used still being the one proposed by Gharbi in the early 1980s (7). In 2003, the World Health Organization Informal Working Group on Echinococcosis (WHO-IWGE) proposed a standardized ultrasound classification based on the active-transitional-inactive status of the cyst as suggested by its sonographic appearance (27). CE1 and CE2 are active

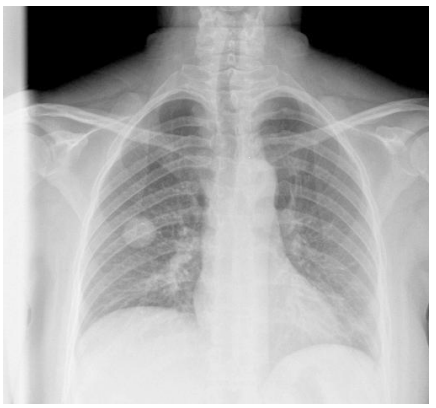

***Figure 1**. Cystic lesion with visible in right middle zone*

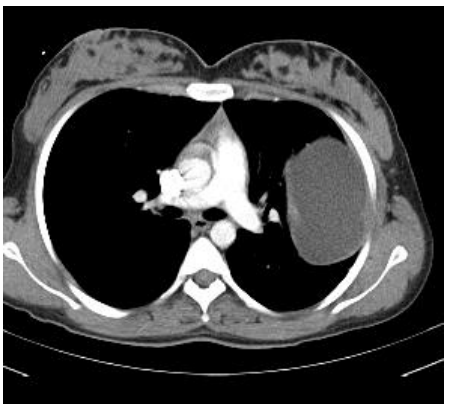

***Figure 2**. Cystic lesion in left lower lobe*

cysts containing viable protoscolices. CE3 has been subdivided into CE3a (detached endocyst) and CE3b (predominantly solid with daughter cysts). This subdivision is supported by a recent work that used high-field 1 H magnetic resonance spectroscopy to evaluate ex vivo the metabolic profiles of cyst contents (28). The magnetic resonance signal characteristics of a hydatid cyst may differ depending on the developmental phase, i.e. whether it is uni- or multilocular and whether the cyst is viable, infected or dead. Information regarding reactive changes in the host tissue, capsule and signal intensity of parent and daughter cysts is also obtained. On magnetic resonance imaging (MRI), cysts show low signal intensity on T1-weighted images and high signal intensity on T2-weighted images (29).

Management

CE is difficult to treat and, even more so, to cure for a number of reasons. The disease is complex and dynamic with an evolving phase and quietly growing cysts (30). Clinical management of hepatic cysts includes albendazole or mebendazole therapy in combination with either surgical resection or the PAIR procedure. Larger cysts (diameter >10 cm) preferably undergo surgical resection(31, 32).

Surgery

Surgical procedures range from simple puncture and aspiration of cyst content to partial resection of the affected organ. The most commonly used procedures can be divided in conservative and radical. Radical procedures aim at complete removal of the cyst with or without hepatic or lung resection. Peripherally located lung cysts of any size and small- to medium-sized centrally located cysts can be excised without sacrificing lung parenchyma. Standard radical procedures are wedge resection of lung parenchyma of less than one segment, and for liver and lung cysts, segmentectomy and lobectomy. Conservative procedures aim at sterilization and evacuation of cyst content, including the hydatid membrane (hydatidectomy), and partial removal of the cyst. The evacuation and the hydatidectomy consists of puncture of the cyst and aspiration of part of the content, to permit introduction of the scolicidal agent, and total aspiration thereafter (30).

Percutaneous treatment

Historically, the first percutaneous treatment used was to puncture the cyst, aspirate cyst fluid, inject a scolicidal agent, and re-aspirate the cyst content (PAIR). The classic PAIR technique is widely known (33, 34). Khuroo and others found PAIR combined with peri-interventional benzimidazole derivatives to be as effective as open surgical drainage with fewer complications and less cost (35). A single-center report from Turkey, experience comparing surgery, laparoscopic surgery, and percutaneous treatments in 355 patients over a period of 10 years and concluded that PAIR is an effective and safe option (36). Safety and efficacy of percutaneous treatments is also related to the anatomical site of the cyst. Percutaneous treatment is mostly used in liver and extrahepatic abdominal cysts, including peritoneal (30).

Other Percuteanous Treatment

Two types of approaches are currently in use: the catherization technique and the modified catherization techniques, in particular PEVAC (percutaneous evacuation)

MoCaT (modified catheterization technique), and DMFT (dilatable multi-function trocar) (37).

Medical treatment

During 1984–1986, the World Health Organization took an early initiative and established two multicenter studies in Europe to directly compare albendazole and mebendazole, using a single standard protocol (38). Mebendazole and albendazole are the two most commonly used drugs to treat. Multiple studies have shown albendazole to be superior to mebendazole in efficacy (39, 40). A small prospective study has shown that combining albendazole with percutaneous drainage results in better outcomes (41).

Conclusion

Surgery is the first choice of treatment in cystic pulmonary echinococcosis. In inoperable alveolar echinococcosis, long-term chemotherapy can be treatment option.

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