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Hydatid cyst disease of the thorax

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Abstract

Hydatid disease is a frequently encountered entity in endemic areas and constitutes a serious health problem. The lung is the second most commonly affected organ after the liver. In three of four cases of pulmonary hydatid cyst, the cyst is solitary. The early phase after primary infection is always asymptomatic. Primary symptoms in patients with pulmonary cystic echinococcosis include cough, fever, and chest pain. The clinical and radiological manifestations for the hydatid cyst in the lung depend on the integrity of the cyst. Bronchial fistulization is an important event in the evolution of the cyst. In cases of dubious orientation after the initial study, ultrasonography, conventional tomography, and magnetic resonance imaging prove helpful in delineating the disease accurately. For a specific serologic diagnosis, the immunoglobulin G enzyme-linked immunosorbent assay and immunoelectrophoresis are preferred. Despite the efficacy of new chemotherapeutic regiments, the mainstay of treatment for thoracic hydatidosis remains essentially surgical. In general chemotherapy is used as a complement to surgical treatment to avoid recurrence of the disease. Regardless of the surgical methods adopted, the removal of the parasite intoto, prevention of its dissemination, maximum preservation of pulmonary function, and the immediate obliteration of the remaining cavity are the imperative basis for effective therapy. The most frequent post-surgical complications are pleural infection and prolonged air leakage. The operative morbidity and recurrence rates have been reported with variation. Education of the population in endemic areas regarding the disease transmission cycle and institution of appropriate prophylaxis are essential steps to eradicate the disease completely.

Keywords: Thoracic hydatidosis; Lungs; Treatment; Diagnosis; Radiology

Introduction

Hydatid disease of the thorax is caused by the cestode *Echinococcus granulosus*. The disease has been known since the times of Galen, being described by Thebesius in the 17th century [1, 2]. Over the years, thoracic echinococcosis has been increasingly recognized as an important cause of mortality and morbidity in susceptible populations. Its wide geographic distribution and amenability to primarily surgical treatment are important considerations. In this review, we discuss the epidemiology, life cycle, clinical and radiographic features, laboratory investigations and treatment modalities for thoracic hydatidosis.

Epidemiology

Hydatid disease is found worldwide; being frequently encountered in endemic areas such as Mediterranean countries, New Zealand, Australia, North America, South America, Central America, and Asia [2]. The distribution of *Echinococcus granulosus* is influenced by agricultural, economic, and educational levels, and cultural habits [3]. For the developing world, this has important implications because rural inhabitants in these areas live under poor sanitary conditions [2]. The annual incidence of the disease ranges from less than 1 to 220 per 100,000 inhabitants of various endemic areas [3].

Life Cycle of *Echinococcus granulosus*

The life cycle of the tapeworm includes synanthropic and sylvatic cycles. Humans act as accidental intermediate hosts for the *Echinococcus granulosus*. The adult tapeworm stage is harbored in the small intestine

of a carnivore, (e.g. dogs, coyotes and wol- ves) called the definitive host. The tapeworm eggs are passed in the feces of infected carnivore and are ingested by herbivores (e.g. sheep, cattle and goats) called the intermediate host. The eggs hatch in the intestine of the herbivore, penetrate the mucosal wall and reach the liver via the portal circulation, where they develop into hydatid cysts. Sometimes, they pass through the liver barrier and reach the lungs and virtually any other organ of the body. Humans are affected if they ingest food or water contaminated with feces of definitive host containing the eggs of *Echinococcus granulosus* [2, 4]. Figure 1 shows the life cycle of *Echinococcus granulosus*.

Thoracic Hydatid Cyst Disease

The lung is the second most commonly affected organ after the liver [5]; being infected in 10-40% of the cases [6]. The hydatid cyst can develop anywhere in the lung, but it settles more often on the right side and has a predilection for the lower lobe [6-8]. Its size can range from a few centimeters to giant hydatid cysts that can occupy the whole hemithorax [9]. There is no universally accepted size to define a pulmonary hydatid cyst as "giant"; however, 10 centimeters seems an appropriate length in that it equals nearly half of the hemithorax of most patients [10, 11].

In three of four cases, the cyst is solitary. Multiple cysts (either primary or secondary) can be unilateral or bilateral. Ayetac et al. reported that 72% of their cases had single cysts, 15% had multiple unilateral cysts, and 13% had multiple bilateral cysts [12].

Factors Affecting Growth of Hydatid Cyst

The growth rate of the parasite changes with the degree of host sensitization and tissue influences [10]. In the liver, the compact tissue and the hepatobiliary capsules limit the cysts growth but the low resistance of the lung provides an excellent medium for rapid growth of hydatid cysts. The patient's immune response to the parasite and early symptoms during the illness prevent the cyst from growing in an unlimited fashion [10].

Clinical Features of Thoracic Hydatid Cyst Disease

The early phase after primary infection is almost always asymptomatic. Depending on the size and site of the developing hydatid cyst, the infection can remain asymptomatic for months, years, or even longer. In the general population, the overall prevalence of asymptomatic cysts in the liver (2.5%) was found to be much higher than that of cysts in the lung (0.3%), giving a ratio of liver infection: lung infection of 8.3:1. In the symptomatic cases, however, the ratio was only 2.5:1 (based on hospital records) or 4.1:1(based on autopsy records) [13].

After a highly variable incubation period, the infestation may become symptomatic because of a range of different events. For example, pressure effects of the growing cyst cause cough, hemoptysis, pneumothorax and pleuritis. Rupture with spillage of the contents of the cyst leads to hypersensitivity reactions such as anaphylaxis. Superinfection of the cyst causes signs and symptoms of infection and is an urgent indication for surgical intervention [14, 15].

Irrespective of the organ affected, most patients with cystic ecchinococcosis, have single organ involvement with solitary cysts. Simultaneous involvement of two or more organs is observed in 10% to 15% of patients, depending on the geographic origin of the patient and the strain of the parasite, respectively. Approximately, 10% of hepatic cystic ecchinococcosis cases occur in children, whereas the rate of lung infection is significantly increased among this group of young patients and may reach 50% [16].

Imaging the Hydatid Cyst

Before bronchial rupture, the typical image of a simple cyst (intact, close, hyaline) is that of a homogenous opacity, round with definite edges, situated in the pulmonary field itself, or apparently implanted on the liver, heart, or rachis [17]. The entrance of air between hydatid cyst and adventitia through bronchiopericystic fistula allows a perivesicular pneumocyst, air meniscus, or crescent sign.

At the time of bronchial rupture, the radiological examination often shows an important parenchymatous reaction, not only homolaterally but also contralaterally. There is a diffuse dense opacity on the cyst's side; on the opposite sides the opacities are less dense, less homogenous, and less limited, which is related to pulmonary hydatid anaphylaxis. It disappears in 4 to 5 days, revealing the original cystic image with its modifications. After the bronchial rupture, the images are highly varied. The parasitic membrane, partially detached from adventitia, creates a bridge over the fluid: Ivanissevich's double arch's sign or Jaubertand Brun's double outline (two superposed gaseous areas, one intracystic and other intraadventitial, separated by parasitic membrane) [17]. The cystic membrane drops, floating on the surface of the residual fluid and giving the Belot's sign of floating membrane or Lagos Garcia and Segars' sign of the water lily or camalote. A cyst that perforates into the pleural cavity can appear with radiological signs of a hydrothorax or a hydropneumothorax. With multiple primary ecchinococcosis, radiology reveals cysts of different sizes and configurations in one or both lungs. With bronchogenic secondary ecchinococcosis, the cysts are normally bilateral. Secondary metastatic ecchinococcosis manifests as numerous small round opacities that are bilateral and generally symmetric.

Other Imaging Modalities

In cases of dubious orientation after the initial study, the data facilitated by ultrasonography, conventional tomography, and magnetic resonance imaging are most interesting [18]. These methods can reveal certain details of the lesions and discover others that are not visible by conventional radiography. CT scan

can also visualize signs of onset of complications, such as incipient membrane detachment of small bubbles located in the cyst wall [18]. MRI allows reliable differentiation because the cyst has low signal intensity on T-1 weighted images and high signal intensity on T-2 weighted images [14]. For pulmonary sites, ultrasound examination is unhelpful in most cases, but sometimes it can confirm the cystic nature of the parenchymatous mass that is juxtaparietal [19]. Hepatic ultrasound should be used routinely for diagnosis of associated hepatic involvement as the two entities can coexist.

Laboratory Diagnosis of Hydatid Cyst Disease

If aspiration cytology is performed, trichromic staining of the filtrated aspirate reveals acid fast hooklets [20]. Cytology seems particularly helpful in detecting pulmonary involvement [21]. Viability of aspirated protoscolices can be determined by microscopic demonstration of flame cell activity and Trypan Blue dye exclusion. Laboratory diagnosis of cystic hydatid disease is complementary to the clinical data [22]. For closed cysts whose membrane begins to exfoliate or open ones where the cuticular layer has been fragmented, the true diagnosis is occasionally provided by the microscopic discovery of cuticular remnants or hooklets in expectorated material. The eosinophilia and precocious positivity of Casoni's intradermal reaction were at one time helpful elements, despite their variable sensitivity and limited specificity [23-25].

In the most recent experience, the most sensitive technique was the specific immunoglobulin G (IgG) ELISA test [26]. However, for pulmonary cyst localization, the diagnostic sensitivity is lower than that of hepatic cases. These tests are generally used for primary serological screening. Specificity of such tests increases considerably when using , for example, the antigen 5- precipitation test (arc 5 test) or immunoblotting for a relatively specific 8kD/12kD hydatid fluid polypeptide antigen [27, 28]. The demonstration of parasite specific IgE has attracted particular attention because of its well known relevance in helminthic diseases [29, 30] but has exhibited no significant immunodiagnostic advantage in cystic ecchinococcosis. There are also problems of diagnostic sensitivity and specificity because of cross reactions related not only to infections with heterologous helminthic species but also to malignancies [31, 32] and the presence of anti P1-antibodies [33].

Monoclonal antibodies (MAbs) generated against different parasite antigens have been used for the diagnosis of cystic echinococccosis by detection of circulating antigens in patients' sera or of native proteins in biopsies. Such MAbs have been directed mainly against 2 major E. granulosus antigens: antigen 5 and antigen B [34]. The serological tests are also useful for the postoperative follow up. The antibody production rate shows an elevation during the first 4 to 6 weeks after the operation followed by a drop, more or less abrupt, during the 12 to 18 subsequent months. In patients with recurrence before 2 years, antibody production remains at a level similar to that seen preoperatively [26].

Treatment of Thoracic Hydatidosis

Every pulmonary hydatid cyst that is identified must be treated.

1. Medical Treatment

The treatment is essentially surgical, despite the efficacy of new chemotherapeutic regimens advocated by some quarters [35]. Dogan et al. noted that after applying mebendazole 4 of 28 patients had to undergo urgent operation owing to massive hemoptysis [36]. In general chemotherapy is used as a complement to surgical treatment to avoid recurrence. It is applied preoperatively to prevent the consequences of possible rupture of the cysts during surgery and postoperatively as adjuvant therapy of the cysts that ruptured during the operation. It is also suitable for patients with multiple cysts, where in vitro studies of the parasite show high fertility and viability and patients who cannot undergo surgery [37]. Two benzimidazole compounds (mebendazole and albendazole) and praziquantel have activity against *Echinococcus granulosus* in vitro and in animal models [38, 39]. No controlled studies have ever been performed in humans so far. Albendazole seems preferable to mebendazole because of its better bioavailability. [40, 41] Both drugs penetrate into the cysts [42, 43], but sometimes heroic doses are needed to achieve a therapeutic plasma concentration of mebendazole [44]. The generally accepted therapeutic levels are approximately 250 nmol/L. The former use of albendazole in cycles of 4 weeks, followed by a drug-free interval of 2 weeks, has been replaced more frequently with a continuous treatment [45, 46]. In a small comparative study, all six patients on continuous therapy showed cyst involution, whereas relapse occurred in the cycling group [47].

2. Surgical Treatment

Because there is great variability in the pathology among pulmonary hydatid cysts, a uniform treatment cannot be recommended. However, there are two objectives:

1. To remove the parasite; and
2. To treat bronchio-pericystic pathology and other associated lesions.

Therefore, modern surgical treatment must be individualized for each case. Regardless of the surgical methods adopted, the removal of the entire parasite, prevention of its dissemination, maximum preservation of pulmonary function, and the immediate obliteration of the remaining cavity are the basis for effective therapy.

In most cases in intact cysts, simple removal fulfills all these requirements and certainly is the ideal approach. The host membrane is widely opened by a

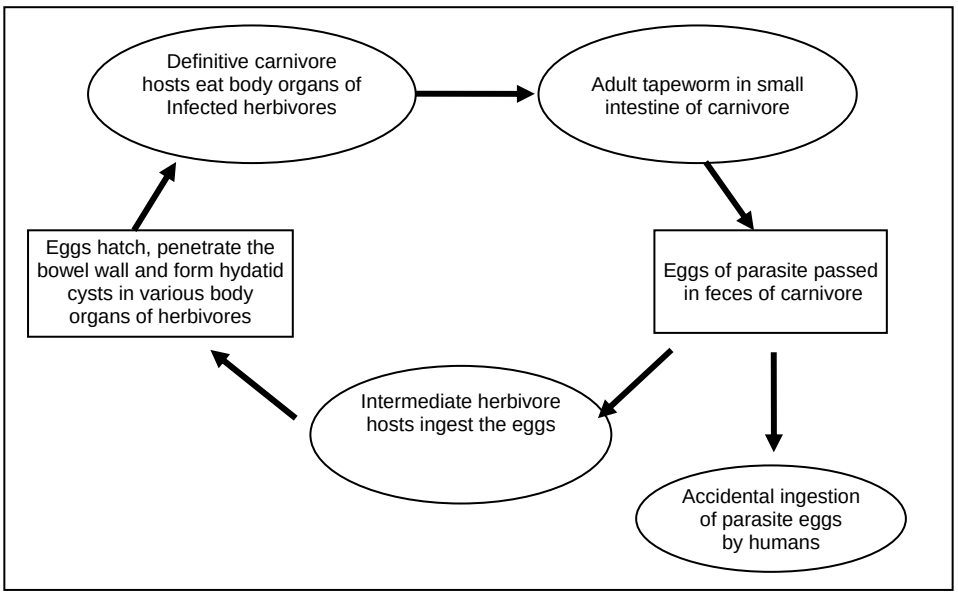

Figure 1. Schematic life cycle of *Echinococcus granulosus* (Redrawn from F.L Andersen, A.G. Barbour, F.J. Schoenfeld, Proceedings of 78th Meeting of United States Animal Health Association 78:370, 1974)

short incision that surrounds the most superficial part of the cyst in the visceral pleura. Until hemostasis is secured, the enucleation method, originally described by Ugon [48] and Barret [49], is the most adequate technique to remove intact small and medium pulmonary cysts. Peschiera [50] suggested that the live contents should initially be evacuated to prevent the risk of contamination by rupture of the cyst during removal. During evacuation of the contents of large cysts, a scolicidal solution is used to avoid contamination of operative field. Formaldehyde solution or pure formaldehyde has been suggested by many authors, but leakage of these substances is harmful to the pericystic tissues and therefore interferes with the healing process and increases the incidence of bronchopleural fistula [51]. The use of hypertonic saline is less harmful to the tissues and is recommended by many surgeons [52].

After the removal of the cyst, the remaining cavity can be treated in a variety of ways. In 1948, Perez-Fontana [53] from Uruguay suggested the resection of host membrane, pericyst, with the intact cyst, as routine to prevent infectious complications that result from residual cavities with walls that are too thick to collapse spontaneously. The resection of the host membrane identifies bronchial leaks into the parasitic chamber. They are sutured, and then the cyst is closed with a spiral suture that approximates the walls surrounding the wound left in the pulmonary parenchyma caused by the removal of the cyst and its adventitia. In Perez-Fontana pericystectomy [53], there is more bleeding and air leakage.

Regarding the management of cystic cavity in complicated or intact cysts, Delbet [54] first described the method called capitonnage, which is the folding of the pericystic zones by sutures. Crausaz [55] reported that purse-string sutures from the base of the pericyst cavity upward could be used to obliterate the cavity.

It is generally agreed, however, that the most important point in the management of the residual pericystic cavity is closure of patent bronchial openings. Saidi [51] pointed out that approximating and suturing cavity edges is not necessary because the pulmonary parenchyma obliterates the space, and the surface of the lung at the site of residual cavity is covered by pleura.

If intraoperative pleural contamination occurs, flooding the cavity with scolicidal agents is worthwhile. Hypotonic (distilled water) or hypertonic (10% saline) solutions, or 10% formaldehyde solution may be employed. The potential complications associated with spillage of hydatid cysts include anaphylactic shock, pleural contamination with resulting secondary hydatidosis, and contralateral bronchial dissemination. The routine use of double-lumen endotracheal tubes or bronchial blockers avoid, during manipulation of the effected lung, hydatid material going into the bronchial tree [56].

3. Role of PAIR In Thoracic Hydatidosis

Puncture, aspiration, injection of a helminthicide, and reaspiration (PAIR) have been propagated for hepatic forms of hydatidosis. A meta-analysis comparing clinical outcomes for hepatic cystic echinococcosis found that the rate of clinical and parasitologic cure ($p=<0.0001$) was greater in patients receiving percutaneous aspiration-injection-reaspiration (PAIR) plus chemotherapy (albendazole or mebendazole) as compared to patients receiving surgical intervention. However, this form of therapy was associated with a higher rate of fever and minor allergic reactions as compared to surgical intervention [57]. For pulmonary hydatidosis, this technique is generally not indicated [45].

Results of Treatment

The operative morbidity has been variably reported in different studies. [10, 25, 58] The most common complications are pleural infection and prolonged air leakage; seen in 2.54% and 2.19% cases respectively. [23] Operative mortality, in general, today does not exceed 1% to 2%. The nature of intervention is a less important factor than the general condition of the patient, the characteristics of the cyst(s), the degree of repercussion on the remaining parenchyma, and the associated lesions.

Recurrence of Disease

The recurrence rate is also variable; commonly ranging between 1.5% to 2.5% [59]. Chevret et al. [60] reported a series of 1397 pulmonary hydatid cysts, with 7 early recurrences successfully operated on and 34 late recurrences with a more than 3-year disease-free interval. The early recurrences were attributed to a lack of knowledge of incipient microcysts and the later ones to re-infestations. The authors thought that removal of the whole cyst, an excellent intervention surgically speaking, did not allow specific immunity to develop, so the individual was prone to re-infestation. In 14 patients, the recurrence was literally explosive from a true confluence of bilateral cysts, leading to death from respiratory failure.

It remains unclear how to proceed in case of asymptomatic patients detected at screening or with imaging for unrelated medical problems. In one small series of 28 patients followed for more than 10 years, 75% of patients remained free of symptoms [61].

Conclusions

Despite the low mortality and limited recurrence rate, thoracic hydatid disease imposes an important disease burden in endemic areas. Some of the complications of the disease can be potentially devastating. Prophylaxis is therefore warranted. [6] Measures for preventing hydatidosis, theoretically easy to formulate, are regretfully difficult to apply, especially in countries with a high hydatid prevalence rate. This is most likely due to a lack on awareness of the disease in the populace. The sources of infestation must be suppressed or sterilized, and the chain of transmission of the parasite must be interrupted. The population must therefore be widely informed through carefully tailored campaigns.

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