Diagnosis and Management of Hydatid Disease of the Liver

A 15-year North American Experience

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Since 1967, 40 patients with hydatid disease of the liver have been treated at our hospital. Diagnosis was made using clinical criteria, serology, skin tests, and imaging techniques. Thirty-five patients were operated upon. In 18 patients the cyst was uncomplicated (Group I), and in 17 the cyst was infected or communicated with the biliary tract (Group II). Three forms of surgical treatment were used: A) cyst evacuation, scolicidal irrigation, and primary cyst closure, B) evacuation, irrigation, and external drainage, and C) complete or partial cyst resection. Mebendazole was used in six patients, four of whom were also treated surgically. In Group I, one of 11 patients (8%) treated by primary closure had complications, *versus* four of five patients (80%) treated with external drainage ($p < 0.001$). Mean postoperative hospital stay for these two groups was 11.8 *versus* 20.8 days, respectively ($p < 0.001$). Complication rates in Group II were higher, and were evenly distributed among treatments. Patients have been followed yearly, with a median follow-up of 5 years. Active hydatid disease has been found in three patients, who all had known residual disease at initial operation. The best treatment for an uncomplicated hydatid liver cyst is evacuation, scolicidal irrigation, and primary closure. External drainage is used for infected cysts or those communicating with the biliary tract, and excision for extrahepatic and peripheral, easily resectable cysts. Mebendazole is used for intraperitoneal spillage of cyst contents and in patients with inoperable disease.

HYDATID DISEASE is a parasitic infection caused by several species of the cestode *Echinococcus.* The most common form is *E. granulosus,* which gives rise to cysts, primarily in the liver and lungs. Much less common is *E. multilocularis,* which produces an invasive tumor-like replacement of liver tissue.

The adult *E. granulosus* is a worm that resides in the jejunum of dogs and other canines (definitive hosts), and produces eggs that are passed in the stool. Eggs ingested by cows, sheep, moose, caribou, or humans (intermediate hosts), liberate an embryo in the duodenum, which passes through the intestinal mucosa to enter the portal circulation. Over 85% are filtered by the liver and lungs, where they lodge and develop into hydatid cysts. The cycle is completed when the cyst is ingested by a canine carnivore; the larvae within the cyst (scolices) are released into the gut, where they form new adult worms.

The hydatid liver cyst has two layers: the ectocyst, a dense fibrous host reaction to the parasite, and the parasite-derived endocyst, which has an outer laminated and an inner germinal layer. The single-celled germinal membrane gives rise to brood capsules, which contain the scolices, and daughter cysts, which float freely in the clear cyst fluid.

Hydatid disease of the liver is endemic to many parts of the world, including the Mediterranean and Baltic areas, South America, Australia, the Middle East, and Northern Canada. Increasing immigration has led to a rise in the prevalence of this disease in North America, primarily in adults who have harbored the parasite since childhood. For this reason it has become important for us to critically appraise the current approaches being used to diagnose and treat hydatid liver disease.

Patient Material and Diagnosis

Between 1967 and 1982, 40 patients with hydatid liver disease were seen at the Toronto General Hospital; 39 had *E. granulosus,* and one had *E. multilocularis.* The 23 women (57.5%) and 17 men (42.5%) ranged in age from 20 to 69 years with a median age of 42 years. Country or region of origin is shown in Table 1. The majority of patients were Italian or Greek; all patients were originally from a rural area.

Clinical presentation is shown in Table 2. Abdominal pain and tenderness were the most common complaints,

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TABLE 1. *Country or Region of Origin*

Italy	16
Greece (including Cyprus)	11
Turkey/Macedonia	3
Rural Canada	3
India/Tibet	2
Middle East	2
France	1
Germany*	1
Poland	1
Total	40

* Patient with *Echinococcus multilocularis.*

TABLE 2. *Clinical Presentation*

Presenting Sign or Symptom	Number of Patients (%)
Abdominal pain and/or tenderness	34 (87%)
Abdominal mass	23 (59%)
History of fever	9 (23%)
History of jaundice	8 (21%)
Pruritis, rash, or urticaria	6 (15%)
Anaphylaxis	2 (5%)
Asymptomatic	5 (13%)

followed by a palpable mass, usually in the right upper quadrant. Jaundice and fever were usually seen in patients who eventually proved to have biliary communication with their cyst, resulting in extrahepatic biliary obstruction due to daughter cysts, or infection. Seven patients had previous surgery for hydatid disease before being referred to our center.

The results of admission liver tests and eosinophil counts are shown in Table 3. Liver tests were abnormal in 40%, the most common abnormality being an elevation of alkaline phosphatase (30%). Eosinophilia, defined as more than 500 eosinophils per mm^3, was noted in 25% of the cases in which differential leukocyte counts were recorded.

Results of hydatid serology and skin tests are summarized in Table 4. The use of these investigations has changed over the 15-year period, skin testing being the only test done in earlier patients, and serology becoming available more recently. Of the serological tests, the indirect hemaglutination test (IHA) was found to be the more sensitive, since 11 of 13 tests (84.6%) were positive, compared to 12 of 18 (66.7%) for the complement fixation test (CFT). The Casoni skin test was positive in 19 of 22 (86.4%) of the patients tested.

The five imaging techniques used were: plain chest and abdominal x-rays, liver scintiscan, selective angiography, ultrasound, and computerized tomographic (CT) scanning (Table 5). The first three were available to all patients, while the latter two became available more recently. The most common abnormal findings on plain x-rays were calcification of the cyst wall (56%), displacement of the stomach to the left, or in the case of concomitant pulmonary disease, cystic shadows in the lung fields. Angiography usually showed an avascular space-occupying mass, which produced displacement of surrounding vessels. Liver scintiscan demonstrated "cold" areas due to decreased uptake of radionuclide. Ultrasound and CT demonstrated cystic lesions in both intrahepatic and extrahepatic locations, as well as identifying the presence of daughter cysts in many cases.

Cysts were found in the right lobe in 29 patients (74.4%), the left lobe in six patients (15.4%), and both lobes in four patients (10.2%). Cysts were single in 30 patients and multiple in nine. Cyst size ranged from 1 cm to 30 cm in diameter, with a mean size of approximately 11 cm. Communication of the cyst with the biliary tract was demonstrated in 11 cases, either by seeing bile in the cyst at surgery (eight cases), or by postoperative introduction of dye into the cyst through a tube, and its subsequent appearance in the biliary tract (three cases). Five patients had extrahepatic cysts, of which two were pulmonary and three were intraperitoneal; two of the latter resulted from known spillage of cyst contents at a previous operation.

Treatment

Five patients were treated nonoperatively. One woman had multilocularis infection that was not amenable to excision, and was treated with mebendazole. Another patient, a 20-year-old woman, had severe pulmonary and pericardial hydatid disease that required several operations; her intercurrent medical problems precluded a surgical approach to her hepatic disease. She has also been placed on several courses of mebendazole. A third patient refused operation, and two more were medically unfit for surgery. The latter three patients were seen prior to the introduction of mebendazole.

Thirty-five patients were treated surgically. These patients were divided retrospectively into two groups: in 18, (Group I), the cyst was uncomplicated, and in 17, (Group II), the cyst was either clinically infected (six patients), communicated with the biliary tract (six patients), or both (five patients). Clinical infection was defined as the presence of pus in the cyst cavity at operation. Operative treatment was of three general types: A) cyst evacuation,

TABLE 3. *Presenting Liver Tests and Eosinophil Count*

	Normal	Elevated	Not Done	Sensitivity (%)
Liver tests				
Bilirubin	32	8	—	20.0
SGOT	34	6	—	15.0
Alkaline phosphatase	28	12	—	30.0
Eosinophil count	28	9	3	24.3

TABLE 4. *Presenting Serology and Skin Tests*

	Normal	Abnormal	Not Done	Sensitivity (%)
Serology				
CFT*	6	12	21	66.7
IHA*	2	11	26	84.6
Casoni skin test	3	19	17	86.4

* CFT = complement fixation test; IHA = indirect hemaglutination test.

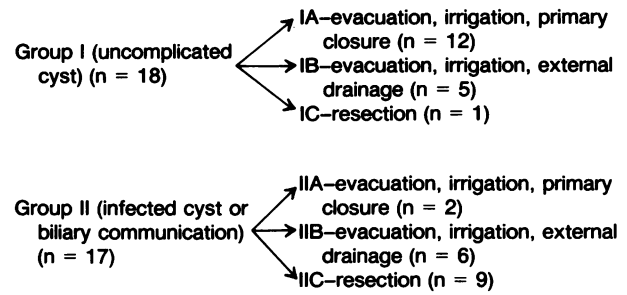

FIG. 1. Grouping of Surgically-treated Patients by Cysts and Treatments.

scolicidal irrigation with hibitane, alcohol, or hypertonic saline, and primary cyst closure; B) evacuation, scolicidal irrigation, and external drainage, either by marsupialization or through a tube; and C) cyst resection, (complete or partial), with or without liver resection or external drainage. These groups are summarized in Figure 1.

The operative approach was abdominal in 25 patients, thoracic in one patient, and combined in nine patients. The decision was based on the location of the hepatic cyst and the presence or absence of extrahepatic disease. Meticulous care was taken in removing fluid and cyst contents, and the peritoneal and pleural spaces were protected from spillage of scolices by packing and suturing a plastic drape to the cyst wall.[1] Extrahepatic intra-abdominal cysts were resected completely whenever possible.

Mebendazole was used perioperatively in three patients, who had known or suspected spillage of cyst contents prior to or during their definitive surgery. One further patient was placed on the drug 6 years after surgery because of recurrent disease.

Results and Complications

Postoperative complications are summarized in Tables 6 and 7. In the 12 Group I patients treated by primary closure (Group IA), only one complication was seen (intra-abdominal abscess requiring surgical drainage), giving a complication rate of 8%. In the five similar patients treated with external drainage (Group IB), one wound infection, two hepatic abscesses requiring reoperation for drainage, and two patients with prolonged drainage from tubes were seen. Only one patient in Group IB was completely free of complications, (complication rate of 80%). The difference in complication rate between Group IA and Group IB is statistically significant. Mean postoperative hospital stay for Groups IA and IB were 11.8 days and 20.8 days, respectively (Student t-test, $p < 0.001$). The single patient in Group IC had two cysts in the left lobe, treated without complication by a left lateral segmentectomy.

Complications were more common in Group II patients (Table 7), and did not differ significantly between those with biliary communication, and those with infected cysts. Of the two patients treated with primary cyst closure, (Group IIA), one developed a hepatic abscess that required drainage. Prolonged tube drainage was a particularly difficult problem in Group IIB patients. Three of the nine patients in Group IIC had no complications; two of these had left lateral segmentectomies for peripheral cysts and one had excision of an extrahepatic cyst along with primary closure of his uncomplicated hepatic cyst. Complications in the other six patients included wound infection, prolonged tube drainage, and hepatic abscess. The one postoperative death in our series occurred after a partial cyst resection in a man who initially presented with septic shock from an infected hydatid cyst.

Follow-up has ranged from 6 months to 14 years (median 5 years). Patients have been followed at yearly intervals, at which time history, physical examination, liver tests, hydatid serology (IHA and CFT) and routine x-rays of the chest and abdomen are performed. Abdominal CT scan or ultrasound is obtained approximately every second visit. Results of follow-up serology are summarized in Table 8. Complement fixation test levels were persistently elevated in six of 18 patients (33%), and IHA levels remained elevated in 14 of 22 (64%).

During the follow-up period, active hydatid disease has been found in only three patients, all of whom had persistently elevated serology and abnormal CT scans. All were known to have residual disease at the time of surgery. Three patients have died. One, the patient with *E. multilocularis,* died of hepatic failure. A second died of an incidental oat cell carcinoma of the lung. The third patient died of an aggressive poorly differentiated adenocarcinoma of the liver.

TABLE 5. *Imaging Techniques*

	Number of Patients Tested	Number Positive	Sensitivity (%)
Plain abdominal or chest x-ray	31	23	74.2
Liver scintiscan	30	29	96.7
Angiography	19	19	100.0
Ultrasound	16	15	93.8
CT* scan	12	12	100.0

* CT = computerized tomographic.

TABLE 6. *Complications in 18 Group I Patients (Uncomplicated Cysts)*

Treatment	Complication	Number of Patients	Total Number of Patients (%) in Group with Complications
A (simple closure) (n = 12)	Intra-abdominal abscess	1	1 (8%)*
B (external drainage) (n = 5)	Wound infection	1	4 (80%)*
	Hepatic abscess	2	
	Prolonged tube drainage†	2	
C (resection) (n = 1)	None	0	0

* Group IA *versus* Group IB, $p < 0.001$ using Z-test for population proportions.
† >3 months duration after surgery.

TABLE 7. *Complications in 17 Group II Patients (Biliary Communication or Infected Cyst)*

Treatment	Complication	Number of Patients	Total Number of Patients (%) in Group with Complications
A (simple closure) (n = 2)	Hepatic abscess	1	1 (50%)
B (external drainage) (n = 6)	Wound infection	1	5 (83%)
	Bowel obstruction	1	
	Prolonged tube drainage*	5	
C (resection) (n = 9)	Wound infection	3	6 (67%)
	Hepatic abscess†	2	
	Prolonged tube drainage*	3	
	Death‡	1	

* >3 months duration after surgery.
† After partial resection.
‡ Due to sepsis.

Discussion

Although uncommon in North America, hydatid liver disease is prevalent enough to be seen by most general surgeons during their careers. Patients may go for many years without symptoms, and usually present with mild nonspecific complaints. The disease must be diagnosed and treated, however, because the complications of cyst infection or rupture, anaphylaxis, biliary obstruction, and eventual liver replacement, may be life threatening.[2]

Diagnosis

The diagnosis of hydatid liver disease has in the past been based on a history and clinical findings that are compatible with the disease, in an individual who has had contact in the past with an appropriate definitive host. Imaging techniques such as x-ray, ultrasound, and nuclear scanning have allowed accurate localization and definition of hepatic lesions. Furthermore, several skin and serological tests based on the host immune response to the echinococcus organism have provided additional diagnostic tools.

In our experience, the most common clinical presentations were abdominal pain and/or right-sided abdominal mass. Jaundice, fever, and abnormal liver tests were uncommon and allergic reactions were rare. In addition, the fact that 13% of patients were asymptomatic indicates that a high index of suspicion for this disease is necessary in patients from endemic areas who present with relatively nonspecific abdominal complaints.

With the exception of plain x-rays, all of the imaging techniques in our series were highly sensitive for hepatic cysts. However, since x-ray combined with one other modality will reveal virtually all hydatid cysts, and because of its low cost and wide availability, chest and abdominal x-rays should be done in any suspected case. Angiography demonstrated a lesion in all cases in which it was done, but because it is an invasive procedure, it should be reserved for situations in which resection is contemplated and knowledge of the hepatic vascular anatomy is important. Ultrasound and nuclear liver scanning are widely available and are very sensitive. We prefer ultrasound to nuclear scanning, because of its ability to identify certain characteristic features of hydatid disease, including a thick cyst wall, daughter cysts, and hydatid "sand."[3]

Currently, the most effective imaging technique available to us is the CT scan. It is noninvasive, highly sensitive, demonstrates the unique characteristics of hydatid cysts, and may also discover additional small intrahepatic or unsuspected extrahepatic lesions. For these reasons, our initial approach is to utilize CT scanning in combination with abdominal and chest radiography.

Until fairly recently, the Casoni skin test was the only

TABLE 8. *Results of Follow-up Hydatid Serology in Surgically Treated Patients*

	Follow-up	
At Diagnosis	Elevated	Normal or Decreasing
Complement fixation test		
Elevated	3	1
Normal	0	2
Not done	3	9
Total	6	12
Indirect hemagglutination test		
Elevated	6	1
Normal	0	1
Not done	8	6
Total	14	8

way of testing for exposure to hydatid disease, and it is still used widely despite the high false-positive and false-negative rates reported in some series.[4] There are several problems with this diagnostic method. Firstly, the Casoni test itself may sensitize the host, thereby leading either to antibody production and a false-positive serological assay, or to anaphylaxis in an already sensitized host. Secondly, there is a high frequency of false-positive reactions due to poor standardization of nitrogen content in the antigen used. For these reasons, many medical parasitologists have now abandoned this test.[4]

There are now many new sensitive and specific serological tests available, such as the IHA, the CFT, the enzyme-linked immuno-sorbent assay (ELISA), ARC 5 precipitation, and specific hydatid IgE tests.[5,6] A recent large trial in Kenya indicated that the IHA had the highest sensitivity (86.7%), whereas the CFT had a 63.3% sensitivity.[7] These results agree closely with our own. With the additional problem of false-positives, which we did not address in this study, most authors would suggest that the optimal approach is to use a combination of several serological techniques, in addition to clinical and radiological assessment.[6]

Occasionally, there is some difficulty in distinguishing a pyogenic liver abscess from a hydatid cyst in a patient with right upper quadrant pain and a filling defect in the liver. Although many of the presenting features are similar, the major points of differentiation are: the incidence of fever (23% in hydatid disease versus 95% in abscess[8]), the chest x-ray findings (right upper quadrant calcification in 56% of hydatid patients *versus* atelectasis and pleural effusion in 63% of abscess patients[8]), the finding of daughter cysts and hydatid sand on ultrasound and CT scan, the presence of positive hydatid serology, and a past history of living in an endemic area. It is very important to make this distinction, however, because the use of needle aspiration, which may be very helpful in the management of pyogenic abscesses,[9] may produce intra-abdominal spillage or anaphylaxis in patients with hydatid disease.

Surgical Treatment

Surgery is still the primary treatment for hydatid liver disease, the objective being to completely remove all parasitic cysts and fluid. A variety of approaches have been described,[10,11] but there are basically two surgical alternatives: resection, or evacuation combined with scolicidal irrigation.

Resection of small or pedunculated cysts may be simple and safe, but in the majority of cases cystectomy involves a major liver resection, with its attendant increase in operative risk. Although a number of authors have advocated this approach,[12,13] we feel that resection should be reserved for peripherally placed cysts, usually in the left lateral segment, for pedunculated lesions, and for extrahepatic intra-abdominal cysts.

Cyst evacuation allows complete removal of the parasite without the risks of liver resection, and is our preferred treatment in most patients. Attention to detail is important. In order to prevent the disaster of intra-abdominal hydatidosis, the peritoneal cavity must be carefully protected during cyst evacuation. We have previously reported our technique, which involves abdominal packing and suturing a plastic drape to the cyst wall before opening the cyst.[1] Saidi has advocated a cryogenic cone, which seals the cyst wall and allows for evacuation and instillation of a scolicidal agent.[14] The actual method used is probably unimportant, as long as complete protection of the peritoneum is afforded while the cyst fluid, daughter cysts, and germinal membrane are being removed.

There are many types of scolicidal agents available. For many years, formalin was used widely, but it is now recognized that this is a dangerous practice due to the risk of absorption and systemic toxicity.[15] Many agents, such as chlorhexidine, 80% alcohol, 0.5% cetrimide, and hypertonic saline are effective scolicidals, and appear to be safe, even when biliary tract communication exists.[10]

The most controversial aspect of hydatid surgery is the management of the cyst cavity. In essence, there are two alternatives: a) drainage of the cavity (using various tubes,[16] marsupialization, or internal drainage), and b) closure or obliteration of the cavity without drainage (using methods such as saline instillation and primary closure,[17] "capitonnage,"[11] or omentoplasty[18]). Sayek et al. found that drainage was followed by a significantly higher morbidity rate and longer hospital stay, although it is uncertain which of their patients had cysts that were infected or communicated with the biliary tract.[19]

In our study we were able to retrospectively examine a relatively homogeneous group of patients with uncomplicated cysts (Group I), and to compare the results with and without external drainage in this group. There was a greater morbidity rate (80% *versus* 8%) and a longer postoperative hospital stay (20.8 *versus* 11.8 days) in the group of patients with drainage of their cyst, compared to those with primary cyst closure. We therefore feel strongly that external drainage be done only when the cyst is infected or communicates with the biliary tract. In the latter situation, we use closed suction drainage in order to minimize the likelihood of converting a sterile cavity into an infected one.[20]

Medical Treatment

Until the recent advent of mebendazole, no medical therapy was available for hydatid disease. Although high-dose mebendazole has been reported to be effective in some cases,[21] little objective evidence is available to sup-

port these claims. Subjective improvement has been reported in up to 70% of patients.[22] We believe that this drug should be reserved for cases that are not amenable to surgery, and in which there has been known intra-abdominal spillage of scolices. Our experience, however, is not extensive enough at this time to prove the validity of this approach.

Summary

Forty patients with hydatid disease of the liver were reviewed. A high index of suspicion for this infection is needed in patients from areas where the disease is endemic who present with upper abdominal complaints. Plain x-ray plus ultrasound or CT scan and a combination of serological tests are recommended as diagnostic procedures. Uncomplicated cysts should be managed by careful evacuation, scolicidal irrigation, and primary closure. Infected cysts or cysts communicating with the biliary tract should be treated by evacuation, scolicidal irrigation, and external drainage. Resection is used for easily accessible, peripherally placed cysts and for extrahepatic cysts. Mebendazole should be given in cases where surgery is contraindicated or refused and where there is intra-abdominal spillage of cyst contents.

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