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HEPATIC HYDATIDOSIS SURGICAL AND ENDOSCOPIC TREATMENT

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Running Head: Conservative surgical techniques present excellent results in treating hepatic hydatidosis, successfully complemented by endoscopy in facing postoperative complications, mainly related to biliary leaks.

ABSTRACT

Aim: Cystic Hepatic hydatidosis, caused by the tape-worm Echinococcus granulosus, is an ancient disease, endemic in sheep rearing areas. Despite improvement in medical treatment, it remains a surgical disease for the good risk patient and may represent a complicated and challenging problem in liver surgery. However, controversy still exists regarding the appropriate surgical technique.

Methods: We present 200 patients, suffering from cystic hepatic hydatidosis, we operated on consecutively from 1985 to 2001, applying the same operative principles consisting in wide capsectomy and drainage. This surgical technique is described in details.

Results: There was mortality of 0.5 % and postoperative complications of 14 %, most of them related to bile leaks. Endoscopy was selectively performed in bile fistulas, considering the volume and duration of biliary drainage. They all healed and no re-operation was required. There was recurrence in 11 of the 115 patients (10% of the total) who were subjected to follow up, ranging from 4 to 20 years.

Conclusion: Drainage operations, when properly performed, present excellent results regarding total extirpation of the parasite with few postoperative complications and few late recurrences, not requiring more aggressive surgical approaches. Endoscopy may be successfully applied for treating long lasting biliary fistulas.

Keywords: *Hepatic Hydatidosis, Echinococcus granulosus, Drainage Operations, Bile Fistulas, Endoscopy, Recurrence*

INTRODUCTION

Hydatidosis or echinococcosis is a parasitic disease known since the antiquity, when "livers full of water" were mentioned by Hippocrates ["hydor" / ὑδωρ, meaning water in Greek]. The disease is scattered throughout the world, its cystic form been endemic in areas where sheep is raised, including the Mediterranean basin, Australia, South America, Far East, Middle East and Eastern Europe[1]. Despite significant reduction of hepatic hydatidosis in Greece, due to an official campaign against this zoonosis over the last 20 years[2], the disease is still present, either in the form of recurrences or new complicated cases, and may pose challenging surgical problems.

The infection is mainly caused by the tape-worm Echinococcus granulosus and less commonly by Echinococcus multilocularis. The latter confined to the northern hemisphere, represents less than 5 % of total echinococcal disease and practically does not exist in the Mediterranean area. It is characterized by a different infection pattern[3], and presents a more virulent and aggressive form of echinococcosis, resulting in liver invasion by multiple cysts, being much more difficult to cure[4].

Echinococcal disease is cyclozoonotic and the parasite has a biphasic life cycle, first described in 1862 by Leuckhard and Heubner[5], requiring two hosts or carriers to complete its development. The *intermediate carrier*, sheep, camel, goat or man is infected by swallowing ova released by at the feces of the *main carrier* mainly dog. These eggs are dissolved by the pancreatic enzymes and release a small six-hooklet embryo, which enters the portal circulation and carried by the bloodstream reaches the liver where it lodges at the hepatic capillaries. There it matures and creates a small slowly growing cyst, the hydatid cyst, containing a water-like

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fluid, and remaining asymptomatic for long time. The soft, elastic wall of the cyst is called *endocyst* and consists of an outer chitinous
acellular layer (1 to 2 mm), called *laminated membrane* and an inner translucent layer, called *germinal membrane*, 15μm thick, nucleated and able to create the outer laminated membrane for protection. This germinal membrane also proliferates to form scolices and secretes hydatid fluid towards the inner part of the cyst. In addition to scolices and under conditions of stress the germinal membrane produces daughter cysts that later become fertile and also produce scolices. The hydatid fluid may reach high pressure, occasionally approaching 300 mm of water. Through compression of the adjacent liver tissue by the expanding cyst, as well as inflammatory and immunological reaction, a thick, vascular capsule is formed, surrounding the endocyst, called *pericyst*, of particular significance for the surgical treatment. The cysts are mainly located in the liver (70-75%), almost three fourths of them in the right lobe, and the lungs (20-25%), while quite uncommonly, location to almost any solid organ and even bones has been reported[6].

Diagnosis of hepatic hydatidosis is today almost exclusively based on the findings of modern imaging techniques such as Ultrasonography and Computed Tomography. When these are interpreted by experienced radiologists significant information can be obtained regarding the nature of a cystic hepatic lesion, its exact location, relation to other organs and structures and morphological characteristics[7]. In doubtful cases where differential diagnosis from simple liver cysts, polycystic disease or cystic neoplasms remains difficult, immunodiagnostic tests, such as the Casoni's intradermal, indirect hemagglutination, ELISA or complement fixation tests might be of assistance, despite their high percentage of false negative and false positive results, ranging overall from 10 to 40%[8,9].

At the time, surgery remains the treatment of choice in hepatic hydatidosis for the good risk patient, aiming at removing totally the parasite and treating the remaining cavity, avoiding bile leaks, responsible for most immediate postoperative complications.

Prevention of the dire consequences of disease recurrences, either locally in the liver or the peritoneum, by applying meticulous surgical technique as well as administering complementary medical treatment, are among the prerequisites of surgery for hepatic hydatidosis. The aim of this paper is to present and describe a type of "aggressive" drainage operation for the surgical treatment of the disease, which has been successfully applied at our institution over the last 20 years.

MATERIALS AND METHODS

Between January 1985 and December 2001, 200 consecutive patients suffering from hepatic hydatidosis were treated surgically at the Department of Surgery of Rion University Hospital, in Patras. Details about the patients and the characteristics of the cysts are presented in Table 1. Twenty-four of these patients (12%) had previously undergone one or more operations for hepatic disease. In all we applied the same type of "aggressive" drainage operation, further described in details.

Table 1. Characteristics of patients and cysts

Patients Characteristics

Men / Women	83 / 117
Age (Years)	16 - 85 (median 61)
Former Surgery	24 (12%)

Cyst Characteristics

Cyst Diametre (cm)	5 - 25 (median 10)
Monolocular/multilocular	22 / 178
Right/left/bilateral lobe	147 / 30 / 23
Infected cysts	72 (36%)

The commonest presenting symptom was upper abdominal pain (82%), followed by fever. Twenty-four patients (12%) gave a history of jaundice, 9 (4.5%) of allergic reactions, while in 23 (11.5%) the disease being asymptomatic was discovered incidentally. The diagnosis in all patients was based almost exclusively on Computed Tomography and Ultrasonography, while Casoni skin test and antiechinoccal antibodies, measured by an enzyme-linked immunosorbent assay, were applied in doubtful cases (25 and 30 cases respectively).

Surgical technique:

An extended right subcostal incision is employed, including upper vertical and left subcostal extension when technical difficulties are encountered. The liver is fully mobilized by dividing hepatic ligaments and the cyst is totally exposed. The incision and the peritoneal cavity are carefully isolated with compresses soaked in scolicocidal hypertonic saline solution (15% NaCl) in order to avoid peritoneal contamination (Figure 1). During the whole procedure special care is also taken to avoid peritoneal spillage of hydatid fluid, which may result in immediate anaphylactic reaction and later peritoneal recurrence. The cyst is initially punctured with a special Y-shaped tru-cut and hydatid fluid is removed in order to reduce intracystic pressure (Figure 2). An opening on the surface of the cyst is made; daughter cysts and hydatid fluid are further removed. The cyst is finally completely deroofed by performing the widest possible capsectomy and the cavity edges are oversewn

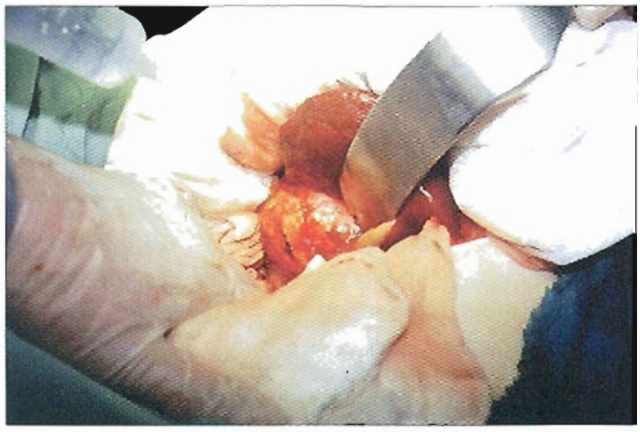

Figure 1: Isolation of the surgical field with compresses soaked in hypertonic saline

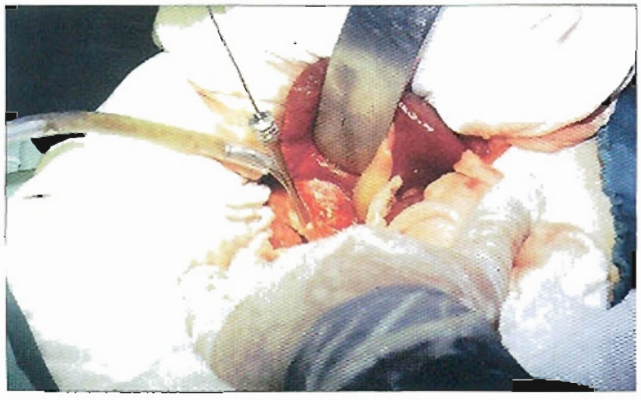

Figure 2: Evacuation of the cyst content results in reduction of intracystic pressure.

with an interlocking braided suture of either polyglycolic acid (Dexon) or polyglactin 910 (Vicryl), in order to avoid bleeding and bile leaks. If cholelithiasis coexists, if the gall bladder is located near the cyst or in the presence of cystobiliary communications, a cholecystectomy is added, and a cholangiogram through the cystic duct will show the presence of duct pathology (small daughter cysts, hydatid debris and uncommonly stones). In such cases bile duct will be explored. Cystobiliary communications are identified by infusing normal saline through the cystic duct after performing Pringle maneuver and obstructing the peripheral common bile duct with an atraumatic clamp. Backflow of the saline will reveal these communications which are then sutured with 3/0 Dexon or Vicryl (Figure 3). The inner surface of the residual cavity is carefully searched by inspection and Ultrasounds for identification of small satellite cysts, which are simply drained through the cavity wall (Figure 4). In cases of complicated, multilocular cysts, the possibility that satellite cysts exist in the liver parenchyma is extremely high, thus intraoperative ultrasonography, either trans-hepatic or through the remaining cavity is used, in order to reveal their presence. Omentoplasty

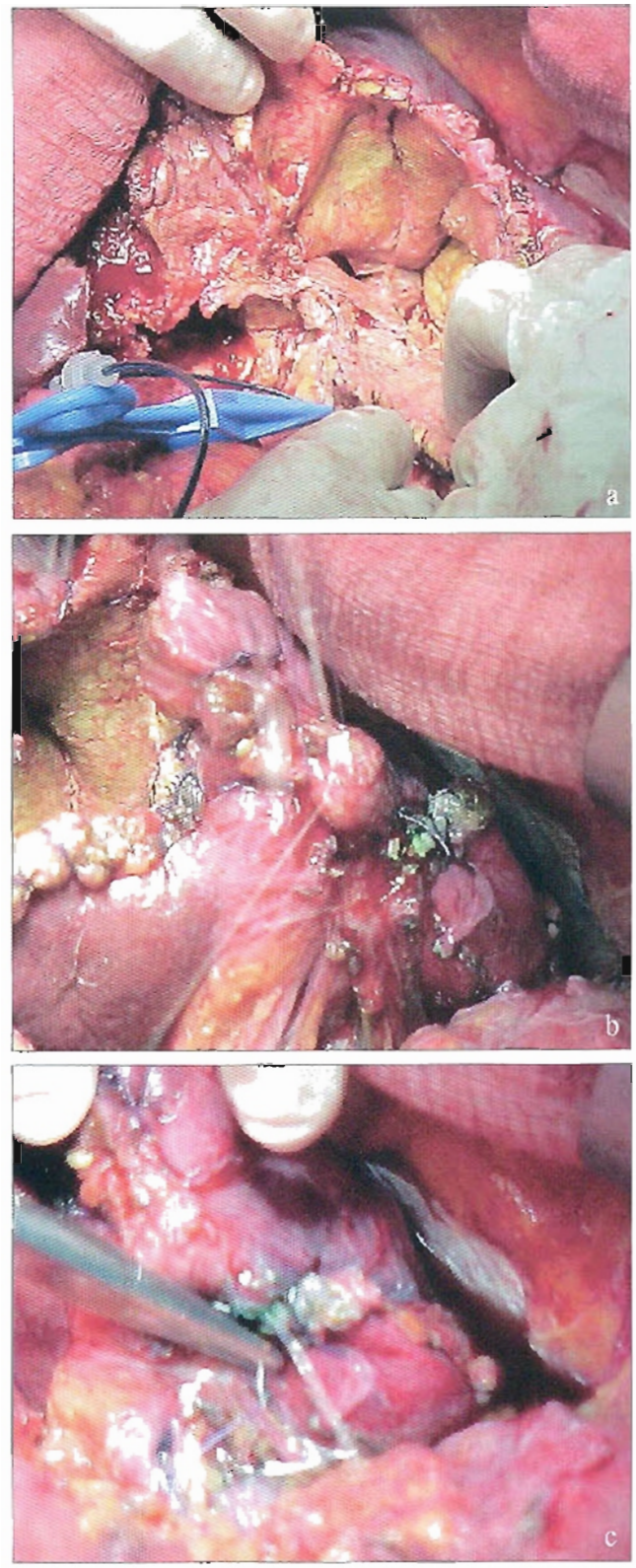

Figure 3: Identification and treatment of cystobiliary communication.
a) A catheter is inserted in the cystic duct and after performing Pringle maneuver, normal saline is injected with pressure
b) The cystobiliary communication is easily identified in the residual cavity by the back flow of the injected saline
c) The communication is obliterated by suturing it with 3/0 absorbable suture

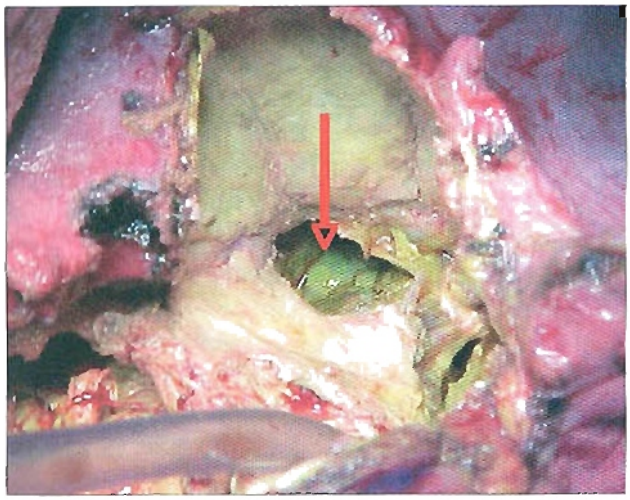

Figure 4: Drained satellite cyst. The cyst (arrow) after been identified by using intraoperative ultrasounds, is drained through the pericyst of the remaining cavity

is not added as routine, but only according to the surgeon's preference.

The cavity is drained with one or two negative-pressure, closed system drainage systems (Jackson - Pratt bulb drain, Cardinal Health Medical Products, Ohio, USA), often temporarily anchored at the desired position of the remaining cavity by 3/0 Vicryl or Dexon suture.

We administered anthelminthic drugs (imidazole compounds) two weeks preoperatively, in an effort to sterilize the cyst fluid and three months postoperatively, even if there has been no obvious intraoperative spillage of hydatid fluid. At the beginning of our series we administered mebendazole (50 mg/kg of body weight) while nowadays exclusively albendazole (10 mg/kg of body weight).

Diagnosis of postoperative bile fistulas was based in clinical examination, laboratory findings and imaging techniques. After the establishment of the fistula and the verification of complete external drainage of bile, based mainly in ultrasonography, all patients were subjected to conservative and supportive treatment, depending largely on the amount of bile excreted and the duration of the fistula. As routine, we treated endoscopically high output fistulas (> 300 ml bile/day) of more than one week duration without signs of reduction, as well as low output fistulas (< 300 ml bile/day) of more than three weeks duration without signs of reduction. An endoscopic retrograde cholangiopancreatography was performed in order to reveal and treat the reason for increased intrabiliary pressure, but even if no such existed, endoscopic sphincterotomy, with or without insertion of a stent or a nasobiliary catheter under low suction (10-15 cm H_2O), immediately reduced the amount of bile excreted and helped the fistula heal in very short time.

Follow-up of the patients was based in Ultrasonography and Computed Tomography, six months after the operation and every two years thereafter in the asymptomatic patient. Recurrence was defined as hydatid disease discovered in the liver by ultrasonography and verified by computed tomography. Computerized tomography was also necessary for the verification of peritoneal recurrence.

RESULTS

A significant reduction in the number of patients with hepatic hydatidosis treated at our Department was noted since 1985. Postoperative hospital stay was also shortened over time, mainly due to increased surgical experience and optimized treatment of complications. Several diagnostic imaging techniques and blood tests were evaluated. It was clearly shown that Computed Tomography and Ultrasonography were very effective in giving the correct diagnosis (sensitivity 96% and 93% respectively). Cholecystectomy was performed in 79 patients (40% of the total) and bile duct disease was found in 24 (12%). In all these 24 cases the common bile duct was explored, it was cleared from small daughter cysts, hydatid debris or uncommonly biliary stones and was drained by a T-tube. Omentoplasty was arbitrarily performed in 41 cases (20% of the total).

Mortality and morbidity rates are shown in Table 2. There was mortality of one patient (0.5%), an 81 year old man who died on the fourth postoperative day due to a cerebrovascular accident. Twenty-seven of the patients (14%) suffered from immediate postoperative complications, twenty of them (10% of the total) related exclusively to bile leaks. Three patients developed subdiaphragmatic abscesses, due to malfunction of the suction drain. Two of them were drained percutaneously and one surgically. Two developed biliary peritonitis and had to be reoperated on the first postoperative day. In one this was due to an accessory bile duct at the gall bladder

Table 2. Postoperative complications

Complications	Number of Patients	Percentage (%)
Bile leak - related	20	10
- Biloma / Abscess	3	1.5
- Bile peritonitis	2	1
- Bronchobiliary fistula	1	0.5
- Biliodermal fistulas	14	7
Intraoperative Aphylactic Shock	2	1
Pneumonia	3	1.5
Postoperative Hemorrhage	1	0.5
Heart Infarct	1	0.5
Death	1	0.5

bed and the other to ineffective drainage of cystobiliary communication. Fifteen patients developed biliary fistulas, one of them bronchobiliary. Of these fistulas nine, (60% of all) healed by expectant management, most of them at an outpatient basis. They required an average of 30 days until the drain was removed. The remaining six (40% of all fistulas) including the bronchobiliary fistula, were subjected to ERCP as previously described. They all healed within two weeks and the drain was removed shortly after (Figure 5).This also meant that 18% of the low and 100% of the high output fistulas required some kind of endoscopic intervention.

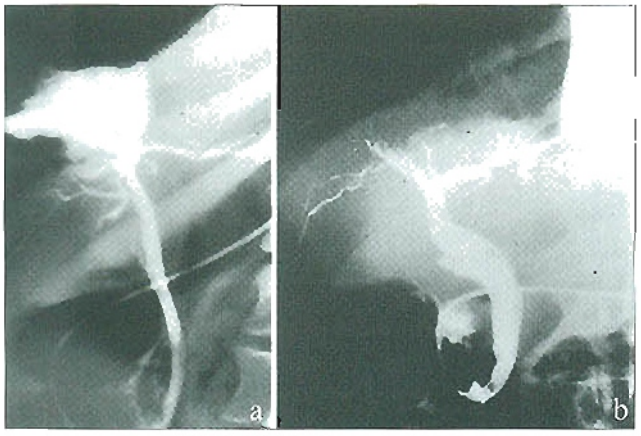

Figure 5: Treatment of a biliary fistula by placing a naso-biliary catheter.
a) Before treatment. Obviously there is massive leak of bile in the remaining cavity
b) Fifteen days after treatment, the leak has been completely stopped

Table 3 shows that there has been no significant benefit regarding hospital stay and postoperative morbidity by the addition of an omentoplasty in the procedure.
We managed to have a complete follow up ranging from four to twenty years in 115 patients (58% of the total). There were recurrences in 11 patients (10% of those subjected to sufficient follow up). Seven of these were in the liver and four peritoneal.

Table 3. The effect of omentoplasty on postoperative hospitalization time and incidence of biliary complications (*NS = Non Significant)

	No omentoplasty (159 patients)	Omentoplasty (41 patients)
Hospitalization Days		
Mean ± SD	11.6 ± 9.6	12.8 ± 7.8
Median (range)	9 (3-94)	11 (4-40) *NS
Biliary complications	17	3 *NS
Fistula	14	1 *NS
Biloma / abscess	2	1 *NS
Bile peritonitis	1	1 *NS

DISCUSSION

Hepatic hydatidosis presents worldwide distribution, being more common in sheep-rearing rural areas with sub-optimal hygienic conditions, where close proximity of living between intermediate (man, sheep, cattle etc) and definitive carriers (mainly dog) helps the maintenance of the parasite's life cycle. At the moment surgery remains the preferred treatment for the good risk patient, and although reports of experts have been published of successful laparoscopic approaches in selected cases of hepatic hydatidosis[10, 11], open laparotomy is still the approach of choice. Alternative, less invasive techniques like percutaneous drainage of the cysts followed by injection of sclerosing agents or hypertonic saline have also been recently reported with good results[12,13]. However, the dire consequences of peritoneal dissemination, namely aphylaxis and peritoneal recurrence, as well as the often presence of multi-septated cysts containing thick fluid, resulting in insufficient evacuation of the cyst content, render physicians skeptic and unwilling to widely apply this new treatment policy.
Numerous surgical approaches have been applied for the effective extirpation of the parasite, while there is still controversy regarding the best[14]. They are grossly divided into "radical" and "conservative" surgical procedures. Radical called operations attempt to remove the cyst totally, en block with the pericyst, which is the outer adventitial layer, formed by the compressed and fibrotic liver. They include pericystectomies and hepatectomies[15]. Conservative operations attempt to neutralize the parasite and evacuate the contents of the cyst without removal of the pericyst[16].
Despite unnecessary loss of hepatic parenchyma, it has been claimed that radical operations in experienced hands reduce bile leaks, shorten hospital stay and reduce recurrence, mainly by removing the so called "exogenous" or satellite daughter cysts, responsible for local recurrence[17].
It is the authors' opinion that radical surgery for the treatment of hepatic hydatid cysts is over-treatment for a benign liver disease. A significant amount of hepatic parenchyma is unnecessarily removed, particularly in hepatic resections, while pericystectomies for centrally located cysts, adhering to major vessels are far to be considered as safe surgery.
The alternative method of performing partial pericystectomy, has the advantage of avoiding intraperitoneal spillage by removing an intact cyst[15]. Resections are reserved only for penduculated or small peripheral cysts. "Conservative" drainage surgery, when properly performed, is considered as the method of choice for treating large hepatic hydatid cysts[18].

The role of omentoplasty in surgical treatment of hepatic hydatidosis remains controversial[19,20]. In our series, there was no significant advantage regarding hospital stay and postoperative morbidity, by adding omentoplasty in the proposed procedure. Consequently this technique is nowadays considered only optional in surgery for hepatic hydatidosis at our Department.

Major complications of surgery include hemorrhage and the leak of bile from the communications between this cavity and the biliary tree. Cystobiliary communications are quite common while the incidence of intrabiliary rupture of cysts has been reported to reach 25 %[7,21]. After drainage, a pressure gradient facilitates bile flow through these communications towards the cavity rather than to the duodenum[22]. This bile leak represents the main source of immediate postoperative complications. If not properly drained, it may result in formation of abscesses in the residual cavity or passage to the peritoneum and bile peritonitis. If drained effectively outwards, an external biliary fistula will develop and this is the commonest complication.

It seems that by using closed system negative pressure drains, we achieve better results in terms of draining all fluid outwards, avoiding at the same time external contamination of the residual cavity, a common and mostly feared complication in the past[18]. There are hardly any indications for open surgery nowadays for the treatment of external biliary fistulas. Endoscopic intervention with sphincterotomy, biliary stenting, dilatation of strictures or nasobiliary drainage in persistent fistulas has eliminated the need for the complex reoperations of the past[23]. Even when formation of bronchobiliary fistulas takes place, a complication associated with high rate of morbidity and mortality, extremely difficult to manage, the insertion of an endoprothesis and the following reduction of the intrabiliary pressure has shown excellent results, reducing the odds for surgical intervention[24].

Recurrence of the disease, either in the peritoneal cavity or locally in the liver, represents a significant complication of surgery for hepatic hydatidosis often requiring hazardous reoperations[25,26]. This is caused either by intraoperative spillage of hydatid fluid in the peritoneal cavity or by incomplete removal of the cyst or cysts. Almost 30% of patients with operative dissemination are expected to develop secondary peritoneal echinococcosis[27], while between 5 and 10% of all operated patients are expected to develop postoperative recurrence[28]. The problem of satellite cysts has been addressed by Magistrelli et al[18] and their incidence has been reported to reach 29.5%[29]. They are vesiculations of daughter cysts beyond the pericyst layer, not identifiable at the operation. These cysts as well as small "occult" liver cysts, not detectable during the procedure seem to be responsible for local, hepatic recurrence. Low recurrence rates have been reported after pericystectomy in several series[30,31] and many authors consider drainage operations associated with higher recurrence[16,18]. However, rates of less than 6% have been reported with carefully performed drainage operations[17]. Careful preoperative evaluation of the patient's CT-scans by experienced radiologists allows the exact location of all the primary cysts, including the satellite cysts. Operative Ultrasound also seems to be very helpful in detecting these small satellite cysts, particularly when performed through the remaining cavity[32]. We consider operative Ultrasound absolutely necessary in cysts highly suspicious for harboring satellite cysts, such as multilocular, infected or multiple liver cysts.

Initial conservative treatment of asymptomatic recurrent small cysts seems to be effective[33]. On the other hand, symptomatic or exceptionally large peritoneal cysts should be treated surgically before complications develop, and surgery in such cases has to be repeated several times until permanent eradication is achieved[25]. Total cystectomy, whenever possible represents the treatment of choice for peritoneal cysts, except when they are firmly attached to intraperitoneal viscera, when drainage and wide deroofing is safer and equally effective[34].

Radical treatment of disseminated peritoneal echinococcosis is not possible. In such cases, only large, symptomatic cysts should be surgically removed, anthelminthics should be administered continuously and the patient should remain under closed follow-up. This therapy seems to be effective in keeping the disease asymptomatic for prolonged periods[25,33].

Cystic hepatic hydatidosis is a world wide disease, mostly found in areas with hospitals sub-optimally equipped, and doctors not particularly experienced in major hepatic surgery. It is of great importance to propose a safe operation such as the one described, offering equally good results as major resections, with significantly less mortality and morbidity. The application of endoscopic techniques, for prevention or treatment of unavoidable complications, offers additional safety and eliminates the need of the major and complex operations of the past, even in more specialized centres, with significant experience in extended liver surgery[35].

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