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A review of the diagnosis and management of liver hydatid cyst

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ABSTRACT

Hydatidosis is a zoonosis caused by Echinococcus in the larval stage. Humans are accidental intermediary hosts where cystic lesions develop, primarily in the liver and lungs. It is usually asymptomatic, hence it is usually incidentally identified. Symptoms result from cyst expansion and/or host inflammatory reaction. Hepatomegaly is the most common sign.

Hydatidosis induces no specific changes in lab tests, but immunodiagnostics are available that may complement its study, with antibody detection being the method of choice. While ultrasound is the main diagnostic technique, tomography offers more accurate
information regarding characteristics and anatomical relations.

A number of therapy options are presently available. Treatment with albendazole, whether combined or not with praziquantel, is useful for smaller, uncomplicated cysts (< 5 cm). Only 30 % of cysts disappear with medical treatment alone.

Surgery is indicated for bigger liver cysts (> 10 cm), at risk for rupture and/or complicated; the laparoscopic approach is scarcely widespread. The radical technique (total cystopericystectomy) is preferable because of its lower risk for postoperative abdominal infection, biliary fistula, and overall morbidity. Conservative techniques are appropriate in endemic areas where surgery is performed by nonspecialist surgeons.

PAIR (puncture-aspiration-injection-reaspiration) is an innovative technique representing an alternative to surgery. It is indicated for inoperable cases and/or patients who reject surgery, for recurrence after surgery, and for lack of response to medical treatment.

Active surveillance without treatment may be indicated for quiescent or inactive, uncomplicated liver cysts.

1. INTRODUCTION

Hydatidosis is a cestozoonosis caused by larval-stage flatworms in the genus *Echinococcus*. Only 2 types affect humans: *E. granulosus* (cystic hydatidosis) and *E. multilocularis* (alveolar hydatidosis). While virtually all organs and tissues are fit for harboring metacestodes, the most commonly affected organ is the liver (70%), followed by the lungs (20%), and less commonly the kidneys, spleen, muscles, and skin, among others. A primary characteristic is high infestivity in case of rupture, fissuration, or intraoperative contamination. The parasite is characterized by slow growth (1-5 cm/year), and may remain latent for 10-15 years.
2. **DIAGNOSIS**

Hydatidosis is usually asymptomatic or nonspecific,\textsuperscript{1,10,11} hence most cases are incidentally identified during imaging for other issues or because of complications.\textsuperscript{3,12} Symptoms result from cyst expansion or the host’s inflammatory response, with irritation of the adjacent parietal peritoneum and pain in the right upper quadrant of the abdomen.\textsuperscript{10} Hepatomegaly is the most commonly found sign.\textsuperscript{13}

No specific changes in liver function tests support diagnosis.\textsuperscript{2} Immunodiagnostics play a supplementary role\textsuperscript{12} when imaging studies are inconclusive.\textsuperscript{14} Serological testing is used for differential diagnosis, epidemiological surveillance, and post-treatment follow-up.\textsuperscript{3,14} Antibody detection remains the modality of choice.\textsuperscript{3,4}

When results are inconclusive (false negatives in 20-40%), fine-needle aspiration or even biopsy may be used to complete diagnosis.\textsuperscript{2}

Ultrasound is the primary technique for the diagnosis of hydatid cyst.\textsuperscript{3,9} Furthermore, it is particularly useful for screening in endemic areas, staging, interventionist treatment, intraoperative exploration, and follow-up. Lesions are seen as well circumscribed, anechoic areas, round or polylobulated in shape.\textsuperscript{1} The presence of daughter vesicles, which give the lesion a rosette-like appearance, and/or wall calcifications supports the diagnosis. Additional signs that may be found include a germinate membrane, inner wall invaginations, hydatid membrane detachment, or hyperechoic hydatid sand.

Computed tomography (CT) offers more accurate information by identifying small cysts, providing a detailed view of lesion characteristics and of anatomical relations involving both intra- and extra-hepatic vascular and ductal structures, as well as extrahepatic lesions.\textsuperscript{1,9} These appear as hypodense, heterogeneous lesions in 90% of cases.\textsuperscript{17} Such images are vital for surgical planning,\textsuperscript{18} as well as for differential diagnosis and the analysis
of postoperative results.³

Magnetic resonance imaging (MRI) may be indicated for cysts with biliary complications; cholangio-MRI is more specific, and provides a more detailed view of cysto-biliary communications.³,⁹

3. STAGING

Gharbi’s classification of 1981 represents the first and most commonly used attempt at staging.¹¹ Based on an ultrasound categorization system, it covers the natural history of hydatid disease, allowing classification of hydatid cysts into five types.³,¹³ Classification is useful for guiding clinical management when based on cyst stage and size.¹²,¹⁴ This classification is now being replaced by the one the WHO developed back in 1995.¹³ These staging protocols based on ultrasonographic findings bear correlation with CT and MRI results³ (Table 1).

4. COMPLICATIONS

They develop in 20-40% of cases² as a result of various mechanisms:

- **Compression and displacement:** These are most common. Bile duct compression results in obstructive jaundice or cholangitis; hepatic, portal or cava vein compression results in portal hypertension and Budd-Chiari syndrome.²,³

- **Rupture:** This may result from trauma, spontaneously, or from iatrogenic causes.¹ Rupture may be contained in case of fissure or communicating in case of fistula,² with communication between the cyst and the biliary tree, pancreatic ducts, adjacent veins, gut lumen, abdominal wall (Figure 1) or lungs.² They may rupture into the peritoneum or pleural space, with implantation of protoscolices in these cavities, resulting in secondary hydatidosis (incidence of 1-8%),¹,¹¹ which augments morbidity and mortality exponentially.²
Diagnosis is challenging since symptoms are nonspecific and polymorphic.\textsuperscript{2} It may cause acute hypersensitivity reactions associated with the release of antigenic material.\textsuperscript{3} Severe anaphylactic events occur in 1% of cases.\textsuperscript{1,3}

- **Bacterial overinfection:** As a result of fissures or hematogenous spread.\textsuperscript{2,3} It develops in 7% of cases.\textsuperscript{2} Presentation is similar to that of pyogenic liver abscess (pain in the upper quadrant of the abdomen, fever, leukocytosis, and C-reactive protein elevation).\textsuperscript{3}

- **Biliary tree involvement:** The most common event, representing 40%-60% of complications.\textsuperscript{2} It has an incidence of 1%-42%, but some authors state that up to 90% have some type of communication during cyst evolution.\textsuperscript{3} A biliary communication is considered major when the size of the intrabiliary rupture is larger than 5 mm, and minor when is smaller than 5 mm. In major ones cyst contents may be seen inside bile ducts in 65% of cases (in up to 79% for communications > 75 mm), whereas this is exceptional in minor communications.\textsuperscript{3} The passage of intracystic material into bile ducts may result in colic, intermittent obstructive jaundice, or overt cholangitis, which suggests the passage of vesicles to the main biliary tract.\textsuperscript{1,3} Imaging tests show cyst membrane detachment in association with dilation of intra- and/or extra-hepatic bile ducts.\textsuperscript{3}

- **Respiratory tract involvement:** Postero-superior liver cysts may fistulize through the diaphragm.\textsuperscript{3} Cysto-bronchial fistulas (manifesting as purulent, bilious expectoration and/or right basal pneumonitis) or cysto-pleural fistulas (manifesting as right pleural effusion with bile and hydatid contents).\textsuperscript{1,3}

- **Malignization:** Although parasitic infestations with trematodes have been related to malignization, its relationship with hydatidosis has not been demonstrated beyond a
few isolated case reports.20

5. TREATMENT
It is based on surgery (conservative or radical), PAIR (puncture-aspiration-injection-reaspiration), antiparasitic drugs, and active surveillance in some cases.3,21,15,11 (Table 2).

5.1. SURGICAL TREATMENT
Objectives include: parasite destruction, cystic cavity treatment, avoidance of spillage, management of potential complications, and prevention of recurrence.13 Relapse rates range from 1% to 20%, morbidity rates from 12% to 84%, and mortality rates from 0.5 to 6.5%.22

Surgery indications include:2,3,11
- Large liver cysts with a diameter > 10 cm (especially when associated with multiple daughter cysts) and/or isolated liver cysts superficially located at risk for rupture.
- Complicated Quistes complicados (overinfection, biliary communication, compression of neighboring structure or obstruction).

Preventing intraoperative spillage is vital, as is protecting surgical wound borders and any exposed intra-abdominal structures with protoscolicide-soaked drapes (mainly with 20% hypertonic saline solution).1,3,11

Perioperative benzimidazole use is controversial. Its goal is to reduce cyst size, to sterilize cysts, and to prevent relapse.23

Two types of surgical approach may be differentiated:
- OPEN: a thoraco-abdominal approach may be used for combined lung-liver hydatidosis when one-time surgery is feasible.3
- **LAPAROSCOPIC**: it offers advantages for selected cases: less morbidity, shorter hospitalization, and improved identification of biliary fistula.\textsuperscript{24,25} On the other hand, this approach is not widespread because of limited space for instrumentation, difficulties in aspirating contents from thick cysts, a need for special instruments, and suspicion of increased risk for secondary spread to pneumoperitoneum.\textsuperscript{3,19}

The findings of most recent meta-analyses suggest that radical surgery is superior to conservative surgery, with less morbidity and mortality.

Radical surgery is preferable given its lower risk for postoperative abdominal infection, biliary fistula, and overall mortality.\textsuperscript{6,21,13} It allows removal of the pericystic area and all parasites, thus solving the issues of residual cavity persistence, complications, and likelihood of relapse.\textsuperscript{1,3}

Radical techniques include total cystopericystectomy or capsulectomy, of choice when technically feasible, and hepatic resection.

Closed total cystopericystectomy is the technique of choice.\textsuperscript{1} The cyst is resected en bloc, creating a surgical plane between the pericystic wall and liver parenchyma\textsuperscript{1,3} (Figure 2). In high-pressure cysts intraoperative fissuration represents a serious complication, hence the technique is restricted to peripheral, smaller cysts.\textsuperscript{1} It also should be avoided in cysts endangering the main hepatic veins, inferior vena cava, or hepatic hilum.\textsuperscript{3}

Furthermore, in open total cystopericystectomy, prior to resecting the lesion’s wall, the cyst is punctured and its contents are drained with a thick needle or trocar connected to an aspirator.\textsuperscript{1} Withdrawal of 50-60 mL of fluid beforehand is useful to relieve the cyst pressure.\textsuperscript{1} Then a scolicidal agent is injected into the cavity, and left there for 10 minutes before moving on to capsulectomy.\textsuperscript{1}
Indications for liver resection are uncommon\textsuperscript{1,3} and the available evidence is sparse.\textsuperscript{6} It is usually reserved for cases with severe biliary tract involvement, vascular involvement with lobar atrophy, or recurrence.\textsuperscript{21} Recurrence rate is low since the cyst is never opened and management of any smaller satellite lesions is ensured.\textsuperscript{6}

In contrast with the conservative technique, all or most of the pericystic wall is excised.\textsuperscript{1}

It is indicated for unilocular cysts with a thin, non-calcified wall, peripheral location, and no overinfection, and for cysts with overt or foreseeable complexity for complete resection intraoperatively.\textsuperscript{1} Technical difficulty is lower with higher rapidity and feasibility,\textsuperscript{6} high recurrence rates (15-25 \%), and a high incidence of postoperative biliary morbidity.\textsuperscript{1,6,19}

In subtotal cystopericystectomy the risk for secondary echinococcosis from spread is higher.\textsuperscript{3} It begins with puncture-aspiration of the contents, followed by injection of a scolicidal solution that is left to rest for several minutes and then aspirated. Hydatectomy is then performed, wherein cystic contents are removed through a needle. Subsequently the cyst is unroofed, the cavity is washed with saline solution, and potential bile leaks are inspected\textsuperscript{3} (Figure 2).

5.2. **PUNCTURE, ASPIRATION, INJECTION, AND REASPIRATION (PAIR)**

This alternative to surgery consists of puncturing the cyst under imaging (US or CT) guidance, aspirating the cyst’s fluid (with a fragmenting instrument that removes daughter cysts and laminated membrane), injecting a protoscolicidal agent, and reaspirating after 15-20 minutes.\textsuperscript{1,15} Therapy with oral antiparasitic drugs may be used to supplement PAIR (4 h before puncturing, and 30 days afterwards).\textsuperscript{1,3}
A drain catheter may be left in the cavity to facilitate drainage and control of potential biliary fistulas.³

It is indicated for inoperable patients and/or patients who refuse surgery, in case of relapse after surgery, and in the setting of no response to medical therapy.³,¹³ It is contraindicated in: cysts inaccessible to puncture, cysts with non-aspirable thick contents, when at risk of damaging vascular structures, peripheral cysts with inadequate liver tissue for safe trans-hepatic puncturing, inactive and/or calcified cysts, and presence of biliary, peritoneal, or pleural space communications.³,¹¹

Unilocular CE1 and CE3a lesions respond well to percutaneous treatment (> 80%), whereas multilocular CE2 and CE3b cysts display a lower success rate, inferior to 40%.¹¹ Relapse (1.6%-5%), morbidity (0.9%), and mortality (2.5%) rates are low, and hospital stays are shorter.²

5.3. MEDICAL

It is based on the administration of anthelmintics in the benzimidazole class.²³ The most widely used drug is albendazole,¹⁸ which is dosed per os (10-15 mg/kg/12 h) for 3-6 months; in case of intolerance mebendazole may be dosed at 40-50 mg/kg/24 h.³,¹¹

Praziquantel is an isoquinoline with protoscolicidal activity (25 mg/kg/24 h) that may be given alone and/or in combination with benzimidazoles,²,¹¹ the latter option being more effective and quicker.²³

With medical therapy exclusively, 30% of cysts disappear, 30-50% show evidence of degeneration or shrinkage, and 20-40% remain unchanged after 12 months.² Thus, fewer than half of treated patients achieve clinical and radiographical resolution in the absence of concomitant drainage.²³ It is appropriate as primary therapy for smaller cysts (< 5 cm) with no complications, CE1 or CE3, over 3 to 6 months, its success rate being 74%.³,⁹
Relapse has a 9-25% rate, and mostly occurs at 2-8 years after treatment completion.\textsuperscript{9}

Finally, these agents may be administered as preoperative supplementation of surgery (to reduce cyst viability, with administration 1 week before surgery) and postoperatively (to avoid intraoperative contamination of the surgical field, with dosing for 3-6 months).\textsuperscript{18} This has reduced the risk for anaphylactoid responses and prevents recurrence.\textsuperscript{23}

5.4. **ACTIVE SURVEILLANCE**

Non-complicated cysts deemed quiescent or inactive by imaging tests (CE4 and CE5) do not require treatment but simply regular follow-up,\textsuperscript{23} mainly with ultrasound since serology is not helpful in predicting reactivation.\textsuperscript{14}

These cysts tend to remain stable over time, and have a low reactivation rate (0-6%), mostly within 2 years.\textsuperscript{14} Cysts inactivated by therapy have a higher reactivation rate when compared to those spontaneously inactive.\textsuperscript{14} Treatment with albendazole does not prevent reactivation, which underscores the need to avoid overtreatment.\textsuperscript{14}

5.5. **MANAGEMENT OF BILIARY COMPLICATIONS**

Following perioperative imaging studies, when cysto-biliary communications are suspected cholangiography may be used to identify them.\textsuperscript{3} Cholangio-pancreatography (ERCP) is useful to confirm biliary obstruction secondary to hydatid material, and to allow its preoperative management with endoscopic sphincterotomy and removal of hydatid remnants with a balloon or basket.\textsuperscript{3}

Following a cyst’s surgical excision a methylene blue test may be performed through a transcystic duct to identify potentially overlooked biliary communications or leaks;\textsuperscript{3} intraoperative cholangiography, may also be helpful, but is often unnecessary when a
preoperative ERCP was conducted.
Any obvious biliary orifice must be sutured to prevent postoperative bile leakage, fistula, or cavity infection.\textsuperscript{3} Should communications involve a larger duct, placement of a Kehr tube may seldom be needed for suturing; it is useful to secure and decompress dangerous sutures, or to close any choledochotomy conducted to remove hydatid cyst remnants. In selected cases drainage with a Roux-en-Y hepatico-jejunostomy, and less commonly liver resection, may be indicated.\textsuperscript{3}

6. **FOLLOW-UP**

This is crucial to assess treatment effectiveness. Follow-up visits are usually scheduled every 3-6 months for the first 2 years, and then once a year for the next 5 years.\textsuperscript{11} Monitoring includes both ultrasounds and serology, and also CT or MRI when relapse is suspected.\textsuperscript{11}

7. **CONCLUSIONS**

Liver hydatidosis remains a major public health issue in many countries despite being a preventable, treatable, and eradicable condition.\textsuperscript{12} Hydatid cysts must be managed as soon as they are diagnosed, and surgery is primarily the treatment of choice.\textsuperscript{21,13} CT scans are key for surgical planning, together with appropriate drug therapy, which will help reduce complications and relapse rates.\textsuperscript{18}

There is currently a tendency towards using minimally invasive approaches (laparoscopy, mini-laparotomy, PAIR) when cysts are accessible and visualization is good.\textsuperscript{3}
REFERENCES


FIGURES AND TABLES

*Figure 1: Computed tomography scan showing a hydatid cyst-to-abdominal wall fistula: hydatid cyst with thick walls and thin septa in the right hypochondrium, driving back the liver parenchyma, that extends caudally in contact with the anterior abdominal wall in the form of a fistulous traject, with compromise of muscle layers and subcutaneous tissue.*
Figure 2: **Left: Closed total cystopericystectomy:** en-bloc resection of a hydatid cyst, creating a surgical plane between the pericyst layer and surrounding healthy liver parenchyma. **Right: Subtotal cystopericystectomy:** aspiration of hydatid contents through a trocar connected to the intrahepatic cystic cavity, using a syringe filled with hypertonic saline; the surgical field is protected with gauze pads soaked in protoscolicidal agent.
Table 1: Staging: Correlation between Gharbi’s classification and the classification issued by the World Health Organization (WHO), according to ultrasound findings regarding the activity of liver hydatid cysts. This is used for treatment selection. Its findings are equivalent to those of magnetic resonance imaging and computed tomography.

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<th>US</th>
<th>MRI</th>
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<tr>
<td>GHARBI</td>
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<tr>
<td>I</td>
<td>Initial undifferentiated cystic lesions (CL): early stage consisting of a usually round, unilocular cyst with well-defined walls and anechoic fluid inside.</td>
<td>CE 1</td>
<td></td>
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<tr>
<td>II</td>
<td>Cyst with detached membrane</td>
<td>CE3a</td>
<td>CE3b</td>
</tr>
<tr>
<td>III</td>
<td>Multilocular, septated cyst, honeycomb sign. Daughter vesicles</td>
<td>CE2</td>
<td></td>
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<tr>
<td>IV</td>
<td>Cyst with heterogeneous content (no daughter vesicles)</td>
<td>CE4</td>
<td></td>
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<tr>
<td>V</td>
<td>Calcified wall</td>
<td>CE5</td>
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1. **Initial undifferentiated cystic lesions (CL):** early stage consisting of a usually round, unilocular cyst with well-defined walls and anechoic fluid inside.

2. **Cystic echinococcosis (CE) 1:** anechoic cyst with hyperechoic concentric halo. It may contain floating hyperechoic foci, which is known as “hydatid sand” or “snowflake sign.”

3. **CE2:** multilocular, multiseptated cysts that create a characteristic rosette appearance, where daughter vesicles may totally or partially fill the cyst’s space. Septa may give a “spoke wheel,” “rosette” or “honeycomb” appearance.

4. **CE3:** total or partial detachment of the laminated layer, which is visualized as floating, wavy hyperechoic membranes showing a dual wall, which is known as the “water lily” or “water snake” sign.
5. CE4: heterogeneous, hypoechoic cysts (with both cystic and solid components), or degenerative cysts with inhomogeneous contents, no daughter vesicles, sometimes exhibiting the “ball of wool sign.”

6. CE5 (least common presentation): solid- or semisolid-looking cyst with an amorphous matrix and thick walls, often with calcifications at the adventitious tissue border.
**Table 2: Treatment planning.** In case CE1, CE2, or CE3 cysts are < 5 cm in diameter, therapy with albendazole alone may suffice. For cysts larger than 5 cm in size, and in case of medical therapy failure in the above, the puncture, aspiration, injection of scolicidal agent, and reaspiration (PAIR) technique or a surgical procedure is indicated according to cyst characteristics. For inactive cysts, CE4 and CE5, monitoring is often adequate.