



A simple sonographic scoring system combined with routine serology is useful in differentiating parasitic from non-parasitic cysts of the liver[☆]

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KEYWORDS

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Abstract In the absence of a detached endocyst, unilocular echinococcal cysts of the liver may be difficult to distinguish from non-parasitic cysts. In an attempt to identify sonographic features that could help distinguish these two types of cysts, we retrospectively analyzed 64 cases of fluid-filled hepatic cysts whose parasitic nature was ultimately excluded. This experience allowed us to develop a simple scoring system that quantifies the likelihood that hepatic cysts are non-parasitic. Sonographic criteria, together with the results of standard serological testing for cystic echinococcosis, proved to be sufficiently specific to allow definitive diagnosis without resorting to further tests.

Sommario In assenza di distacco dell'endocistio, le cisti epatiche da echinococco uniloculari, possono essere difficili da distinguere dalle cisti non parassitarie. Allo scopo di definire meglio le caratteristiche ecografiche che possano aiutare a distinguere questi due tipi di cisti, abbiamo esaminato retrospettivamente 64 casi di cisti epatiche a contenuto liquido, che si sono rivelate essere non parassitarie. Abbiamo quindi realizzato un sistema a punteggio in grado di predire la probabilità di una cisti di essere non parassitaria. In conclusione, i criteri ecografici associati ai test sierologici per echinococcosi sono sufficientemente specifici per ottenere una diagnosi, senza ricorrere ad ulteriori indagini.

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Introduction

Clinicians who deal with cystic echinococcosis (CE) are often asked to determine the nature of abdominal cysts. Ultrasound (US) is the first-line imaging tool for the

diagnosis of abdominal CE. The sonographic appearance of these cysts varies at different stages of their natural history or in response to therapy. The WHO Informal Working Group on Echinococcosis has grouped these cysts into three categories: active, transitional, and inactive [1]. Five types

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have been identified drawing from the previous Gharbi classification [2] (Fig. 1). Whereas CE2 and CE3, and to a lesser extent, CE4 and CE5, have specific features, CE1 cysts may be difficult to distinguish from non-parasitic cysts. Indeed, a CL (cystic lesion) type has been added in the WHO classification that was not included in Gharbi's classification, for those cysts whose parasitic nature cannot be determined based on solely on the results of the US examination.

To identify sonographic criteria that are specific to non-parasitic hepatic cysts, we retrospectively analyzed a series of patients referred to our center for diagnosis of hepatic cysts. This experience allowed us to develop a scoring system for differential diagnosis of these cysts that are based on epidemiological data and sonographic features.

Materials and methods

From January 1994 through September 2006, our staff saw 64 patients (50 females, 14 males, mean age: 56.8 years, range: 30–80 years) with fluid-filled hepatic cysts that were suspected to be parasitic. These cases were retrospectively analyzed by our group.

All patients had undergone abdominal US at our institution. Examinations were performed with an ultrasound scanner equipped with a 3.5–5-MHz probe (H21, Hitachi, Singapore; AU5 Harmonic, Esaote, Genova, Italy). Blood samples were routinely drawn for indirect hemagglutination assays (IHA) (Cellognost Echinococcosis Dade Behring, Marburg, Germany) and ELISA determination of IgG antibodies against *Echinococcus* spp. (*Echinococcus* IgG, Ridascreen, Darmstadt, Germany). Immunoblotting assays (*Echinococcus* Western Blot – Lobio Diagnostics, Lyon, France) and ultrasound-guided fine-needle aspiration (FNA) of cysts were also performed in selected cases. Fluid was aspirated with a 20–22-G Chiba needle and examined after

centrifugation by an experienced parasitologist for the protoscolices of *E. granulosus* or their hooklets.

Based on our experience and data available in the literature, we developed a scoring system to predict whether a hepatic cyst was parasitic or non-parasitic (Table 1). The criteria used for all cysts included presence or absence of a wall sign and calcifications, regular and clear-cut borders of the cyst, patient sex, and stable US appearance at follow-up. For septated cysts, two additional features were considered: the number and regularity of the septa. The higher the score, the lower the likelihood of the cyst being parasitic. Unilocular cysts were considered non-parasitic (NP) if their total scores fell between 6 and 10. Septate cysts were classified as NP if their total scores were ≥ 10 .

We did not include a control group of patients harboring known CE1 and CE2 parasitic cysts because, although the area served by our hospital includes some zones with a high prevalence of CE, only a small number of these cysts are generally found in the population. Therefore, enrollment of a control group would have prolonged the study to an unacceptable extent.

Results

The patients analyzed in this study harbored a total of 116 fluid-filled cysts with transverse diameters ranging from 3 to 180 mm (mean, 45 mm). Eighty of the cysts (69%) were unilocular and 36 (31%) were septate (Table 2).

Simple cysts appeared on US as round or oval space-occupying lesions (multiple or single), with well-defined borders and acoustic enhancement, surrounded by normal hepatic parenchyma. The absence of the wall sign was suggestive of non-parasitic cysts. Septate cysts appeared as round echo-free lesions with regular borders and the presence of regular or irregular septa (sometimes with small hyperechogenic spots).

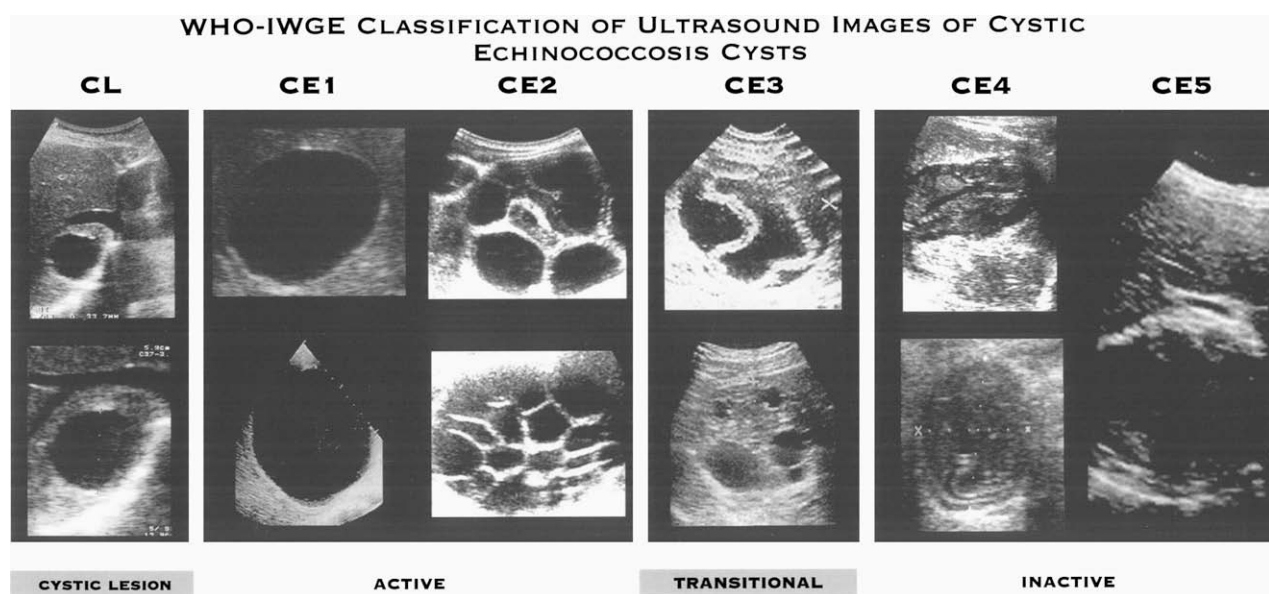


Fig. 1 WHO IWGE standardized classification of Echinococcal cysts. Transitional cysts are subdivided into CE3a (upper row) and CE3b (lower row). © World Health Organization, all rights are reserved by the Organization.

Table 1 Ultrasound scoring system for diagnosis of unilocular and septate hepatic cysts.

Unilocular and septate cysts		
1. Double-layer sign	Present	0
	Absent	3
2. Regular borders	Present	1
	Absent	2
3. Regular shape (round/oval)	Present	0
	Absent	1
4. Calcifications	Present	0
	Absent	1
5. Patient Sex	F	1
	M	0
6. Stable US appearance at follow-up	Present	2
	Absent	1
Septate cysts only ^a		
7. Number of septa	Single	2
	Multiple	1
8. Appearance of septa	Regular	1
	Irregular	3

^a Items 1–6 are evaluated for all cysts (unilocular and septate). Items 7 and 8 are additional criteria assessed only in septate cysts. A total score of 6 or more (for unilocular cysts) or 10 or more (for septate cysts) indicates that the cyst is non-parasitic.

Routine serological testing (IHA and ELISA IgG) was performed in 62 patients (95%). The immunoblotting (IB) test was also performed in 37 patients (56%). All serologic tests were negative. Computed tomography (CT) was performed in 1 patient (1.5%) and 8 (12%) had FNAs. No protoscolices, viable or otherwise, were found upon microscopic examination of the aspirated fluid.

When our score was applied to these cysts, all those that were unilocular had scores of ≥ 6 , and 28 of the septated cysts (77%) had scores ≥ 10 . The 8 cysts with scores of 8 and 9 were confirmed to be NP by the results of FNA or IB.

Discussion

The different structures of NPC and EC account for their different appearances on US and provide elements that are useful for differential diagnosis.

Non-parasitic cystic lesions are cavities containing a transparent, citrine fluid. They are lined with a biliary-type epithelium and do not communicate with the biliary ducts.

Table 2 Hepatic cyst types and scores in the retrospectively analyzed series.

Cysts reviewed (N = 116)			
Structure	No.	%	Score indicative of NP cysts ^a
Unilocular	80	69	80 (100%)
Septate	36	31	28 (77%)
	116		

^a Scores ≥ 6 for unilocular cysts or ≥ 10 for septate cysts.

They are thought to originate from excess biliary ducts that have not undergone evolution. Slow dilation of these ducts produces cystic lesions. Non-parasitic cysts are generally solitary, but multiple cysts may be observed, especially in polycystic liver disease. Simple cysts of the liver are a relatively frequent condition. Although the exact frequency is unknown, autopsy and sonographic surveys indicate that the prevalence is between 1% and 2.5%. Ultrasound examinations reveal cysts in 4–5% of the general population [3] but only 10–15% of these patients have symptoms. They appear on US as single round or oval echo-free masses with well-defined borders and acoustic enhancement, surrounded by normal hepatic parenchyma. Less frequently, they must be differentiated from neoplastic lesions (cystadenoma, cystadenocarcinoma), post-traumatic fluid collections, abscesses, inflammatory lymphatic cysts.

Echinococcal cysts consist of an inner germinative layer of cells supported externally by an acellular, laminated membrane of variable thickness. The parasitic cyst is surrounded by a host-produced, granulomatous, adventitial reaction that varies widely in intensity. Small secondary cysts called *brood capsules* bud internally from the germinative layer and produce multiple protoscolices (Fig. 2). The sonographic appearance of EC changes as the cyst undergoes involution, and these changes are the basis for all ultrasound classifications.

Unilocular cysts (CE1) appear as round, echo-free masses with a distinct double-layer wall sign (endocyst, inner line, and the pericyst, outer line) (Fig. 4). Inside the cyst, small echogenic spots may be found. These are consistent with the so-called *hydatid sand* formed by brood capsules and free scolices. The next stage is represented by the cavity with detached endocyst (CE3a). From this stage,

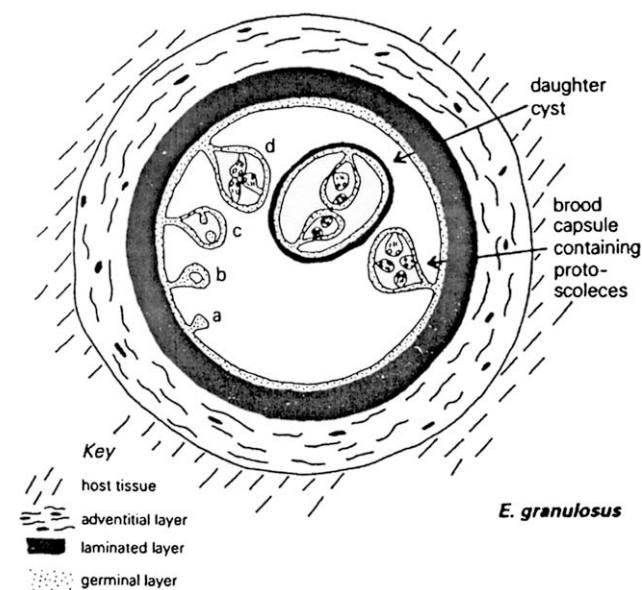


Fig. 2 Diagrammatic representation of the metacestode of *Echinococcus granulosus* (reproduced with permission from the WHO/OIE Manual on Echinococcosis in Humans and Animals: A Public Health Problem of Global Concern (Eds: J. Eckert, M.A. Gemmell, F.-X. Meslin and Z.S. Pawłowski). Paris, France 2001.



Fig. 3 Septate NPC. Note the slightly irregular septum.

the cyst can be infiltrated by inflammatory material, which gives it a pseudo-solid appearance that may have a “ball-of-wool” aspect (CE4). The next stage is characterized by the presence of peripheral calcifications (CE5).

A different pattern of involution involves the transformation of type CE3a cysts type CE2 as a result of the growth of several daughter vesicles from the germinal layer.

Type CE3b cysts may be the result of partial pseudo-solidification of a CE2 cyst or of re-growth of a previously solid (CE4) cyst.

Though all these types may have aspects that are pathognomonic – at least to the experienced sonologist – the wall sign is not always seen. Moreover, the presence of echogenic spots is inconstant and non-specific. (Indeed, similar findings can be caused by debris within an abscess or necrotic tumor, or by infection or hemorrhage within an NPC.) For CE2/septate cysts, differential criteria also exist. As we observed, NPCs tend to have one or two septa, whereas EC is characterized by more numerous septa,



Fig. 4 The double-line sign is clearly visible on the left side of this dumbbell-shaped echinococcal cyst.

which are produced by the daughter vesicles’ walls adjacent to one another. We also occasionally observed small irregularities (Fig. 3) of the septa in NPCs, a feature that was never observed in ECs.

The characteristics of the cysts we used to develop our scoring system are as follows:

- *Ultrasound wall sign*: produced by the distinct appearance of the endocyst (inner line) and the pericyst (outer line), the wall sign is the most characteristic feature of a CE1 cyst (Fig. 4). Caremani et al. investigated this sign in ECs and reported that a wall sign can always be demonstrated when a 7.5-MHz probe is used [4]. Their study is flawed, however, since a probe of this type is of no use with deep-seated lesions, which include the majority of liver cysts. In addition, their series included CE2 type cysts, which have clear pathognomonic features without resorting to the wall sign. In a descriptive study attempting to elucidate US and CT findings typical of a CE1 cyst, the authors claimed that in approximately two thirds of patients the wall and the content of the cyst should be sufficient to allow reliable identification. In the remaining third, serological tests, with or without needle aspiration, are usually required for a definitive diagnosis [5].

Therefore, to the best of our knowledge, the presence of a wall sign in the different types of liver cysts, the vast majority of which are likely to be deep-seated lesions, has never been systematically studied.

Working on the assumption that, given its structure, a NPC has no wall sign (Fig. 5), we retrospectively evaluated all suspected ECs that were shown to be NPC on the basis of serological testing and FNA, looking for other elements that could help in the differential diagnosis.

- *Borders*: we attributed a higher score to non-regular borders because the endocyst is a linear structure with a well-defined cleavage plan from the pericyst



Fig. 5 Unilocular NPC: no double-layer sign is seen.

- Shape: NPCs may be irregularly shaped, but the same is occasionally true of ECs.
- Calcifications: these are seen in ECs, especially in CE5 and CE4 and occasionally in CE3b cysts [6], but they are rarely observed in NPCs.
- Sex: in certain studies, females harbor NPCs more frequently than males, while CE affects males and females with more or less equal frequencies.
- Stable US appearance at follow-up: the appearance of an EC changes over time, as a result of treatment or as part of its natural history. The latter aspect has still not been fully investigated, and only a few accounts have been published [7]. NPCs can also evolve although the pattern of change is less predictable and it usually involves only an increase in size. Occasionally, NPCs may grow very rapidly [8].
- Septa: NPCs tend to have only one or two septa, which may show some irregularities.

Conclusion

We attempted to define sonographic criteria that could help distinguish NPCs from unilocular ECs. Our objective was to make sonographic diagnosis of CE less operator-dependent, to limit or avoid the need for further diagnostic procedures, and to identify diagnostic elements that can be used in field studies.

While others have dealt with the issue previously, to the best of our knowledge ours is the first attempt to use a semiquantitative method to diagnose NPCs based on US characteristics and routine serology.

Our data show that when US findings are coupled with routine serology (IHA, ELISA), FNA is seldom required. The

reliability of our scoring system needs to be verified in prospective studies of larger series (with observers blinded to the results of serological tests and conducted in different epidemiological settings).

Conflict of interest statement

The authors have no conflict of interest.

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