

## Cystic and alveolar echinococcosis of the hepatobiliary tract – the role of new imaging techniques for improved diagnosis

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### Abstract

Cystic echinococcosis (CE) or hydatidosis (hydatid cysts) is an infection with a wide spectrum of manifestations, from asymptomatic infection to fatal disease. Ultrasound (US) allows screening, diagnosis, differential diagnosis, treatment guidance and follow-up of CE under many circumstances. Hydatid cysts are predominantly observed in the liver. Herewith we present a review to demonstrate established and innovative imaging features of CE of the hepatobiliary tract.

**Keywords:** Tropical medicine; parasites; guidelines; contrast enhanced ultrasound; elastography

### Introduction

Cystic echinococcosis (CE) or hydatidosis (hydatid cysts), is an infection caused by the larval stage (metacystode) of the cestode (tapeworm) *Echinococcus granulosus*. In humans, it may result in a wide spectrum of manifestations, from asymptomatic infection to fatal disease. Correspondingly, the imaging characteristics are broad.

Imaging is useful to stage disease in differing organs, including the location and number of cysts, along with more detailed characterization of CE. Local experience influences the choice of preference for ultrasound (US), computed tomography (CT), or magnetic resonance imaging (MRI), though basic portable ultrasound devices have been adequate to screen patients in endemic areas with *E. granulosus* infections [1,2]. The early descriptions have been published by Gharbi et al [3-11]. Recent publications on the epidemiology, anatomical locations, cyst structure, US classification, diagnostic imaging and clinical work up, discuss in detail the advantages of established imaging modalities [12].

The liver (predominantly the right lobe) is the most commonly affected organ by *E. granulosus* infection in adults and is most often asymptomatic. Symptoms occur

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when the cyst becomes larger than 10 cm or infiltrates surrounding structures. If this includes portal vein thrombosis, signs of portal hypertension or the Budd-Chiari syndrome may result. Infiltration of bile ducts may cause colicky pain, obstructive jaundice, cholangitis and abscess formation. Infiltration of the diaphragm and pleural cavity may cause peritoneal-pleural (bronchial) fistula, whilst rupture into the peritoneal cavity may lead to a life threatening peritonitis.

Most recently we summarized the current knowledge on hepatic echinococcosis, focusing particularly on defining stages via standard imaging modalities [12]. In brief, the WHO imaging categories include the active parasitosis stages CE1 (unilocular) and CE2 (multilocular with daughter cysts) and the inactive stages CE4 and CE5. These frequently non-viable stages (CE4 and CE5) are echogenic with increasing degrees of fibrosis and calcification. Category CE3 cysts are in the process of degenerating and so defined as “transitional active” and can be further subdivided by morphology; CE3a is morphological characterized by the so-called “water-lily” sign representing floating membranes, whilst subgroup CE3b is characterized predominantly by solid daughter-cyst components. The presence of daughter cysts, whether ruptured or calcified, guides decisions regarding local ablative treatment [13–20]. Unfortunately, morphological signs may not distinguish between vital and avital echinococcosis, which is key to differentiation of stages CE3a and CE3b.

Alveolar echinococcosis (AE) results from infection with *Echinococcus multilocularis*; taxonomically from the same genus as *E. granulosus* but with different manifestations and disease course. It presents as infiltrative mass lesions almost exclusively within the liver, varying in size from sub-millimeter to 3 cm [21], but needs to be considered in the differential of atypical cystic lesions.

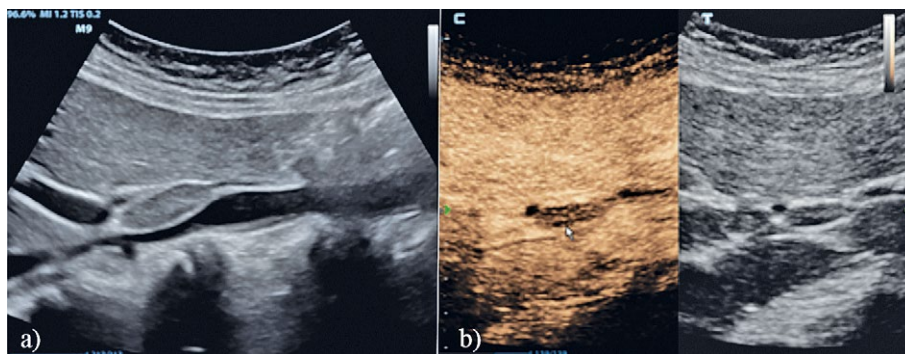
In this paper we feature images demonstrating the wide variety of imaging features but also include typical findings when newer imaging modalities are utilized – contrast enhanced ultrasound (CEUS), elastography, imaging fusion or positron emission tomography.

#### **Differentiating vital and avital echinococcosis**

The optimal method to differentiate between viable and sterile echinococcosis remains uncertain. CEUS (case of the month, [www.efsumb.org](http://www.efsumb.org)) [22–26], positron emission tomography (PET) and MRI [27] may have potential to differentiate. In principle, demonstration of concurrent inflammation suggests viable echinococcosis but it may be also a sign of superinfection of the cyst. Inflammatory reactions in the liver can be displayed by perihepatic lymphadenopathy [28–37], focal changes to vascularity and perfusion in the surrounding liver parenchyma [38–40], or by demonstrating increased metabolic turnover using PET technology. The role of artificial intelligence in the imaging of CE is promising but has not been evaluated so far [41,42].

#### **Perihepatic lymphadenopathy**

The inflammatory process within organs frequently leads to hyperplasia of draining regional lymph nodes. Lymph node enlargement within the hepatoduodenal ligament may be present in patients with acute [34] or chronic liver and pancreatic diseases including chronic virus hepatitis C [30,36,37,43], autoimmune hepatitis [44], primary biliary cirrhosis [45], primary sclerosing cholangitis [35] and other liver [32] and pancreatic [46] diseases. Lymph node enlargement in the liver hilum may reflect inflammatory activity and/or the immunological response of the host [37]. Lymph nodes in the hepatoduodenal ligament can be non-invasively detected using modern imaging techniques such as US [28,29,31,33,34]. In our personal experience, enlarged perihepatic lymph nodes are a typical sign of viable echinococcosis (fig 1).



**Fig 1.** An asymptomatic 51 y/o female, is found to have presumably avital endstage echinococcosis. Signs of concomitant inflammatory reaction, perihepatic lymphadenopathy, are demonstrated by B-mode imaging (a). The use of Contrast enhanced ultrasound (CEUS) demonstrates early wash out from the lymph nodes, consistent with the inflammatory reaction. CEUS is useful to demonstrate the architecture of pathological lymph nodes. Here, normal architecture is displayed, and no circumscribed malignant infiltration could be shown.

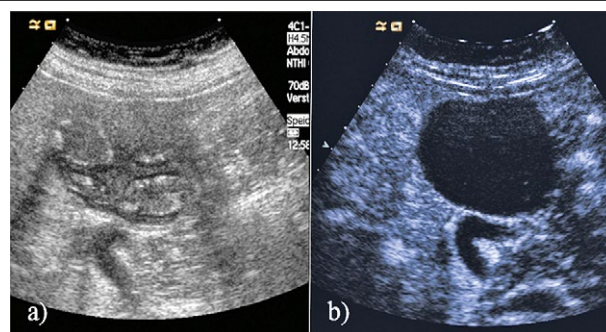
### Contrast enhanced ultrasound (CEUS)

Contrast enhanced ultrasound (CEUS) has been available for more than twenty years, with guidelines and recommendations published for its use in liver imaging [38,39,47], non-liver applications [48] and US guided procedures [13,20,49-53]. CEUS in echinococcosis has not been evaluated to date but to our experience it may show a hyperenhancing rim in the surrounding parenchyma as a sign of inflammation. Commentaries elaborating on these recommendations are also published [15,54-57]. In the context of hydatid cysts, there is only scarce data available. CEUS may distinguish hydatid cysts from neoplasms; the absence of contrast enhancement in CE due to fluid-filled avascular cysts (fig 2) may be demonstrated.

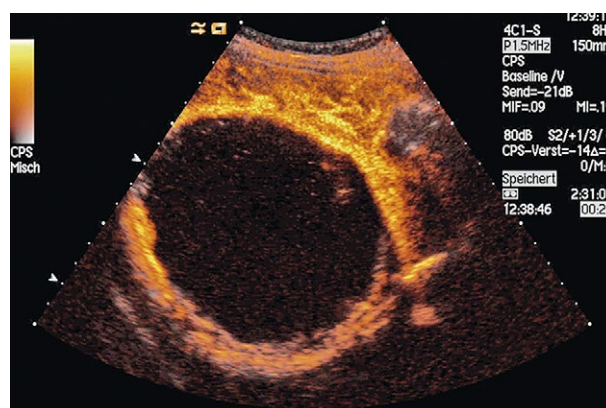
CEUS demonstrates perifocal inflammatory reactions, as nodular zones of peripheral ring enhancement [22] (fig 3) are seen. Thus, echinococcal cysts can be differentiated from dysontogenetic cysts under some circumstances [47,58]. Future prospective studies are required to refine the characteristics and utility of CEUS for hydatid disease. In addition to serological tests and grey scale US, CEUS imaging could be integrated as an easily accessible tool helping to describe hypervascularization due to active perilesional inflammation of echinococcal manifestations. CEUS may further help to differentiate between CE and alveolar echinococcosis (AE) and also to evaluate treatment outcome [59]. Previous study results revealed that CEUS and PET-CT have good inter-rater reliability in determining the activity of hepatic alveolar echinococcosis [60]. The metabolic activity in alveolar echinococcosis as assessed by FDG-PET has been found to correlate with CEUS vascularity in lesions of the liver, suggesting CEUS may represent a cost-effective tool in resource allocation to FDG-PET examination [61]. CEUS images of large hepatic AE lesions are more complex than that of the small lesions. Large AE lesions can be hypoechoic with mixed content with or without circular rim enhancement or as lesions with no internal area enhancement with circular rim enhancement. The small lesions generally present circular rim enhancement and non-enhancement internal area [62]. CEUS is regarded as an important tool in monitoring hepatic alveolar echinococcosis. Dimensions of the parasitic lesions are displayed more precisely through CEUS than in B-mode. With currently available methods however, CEUS quantification has no benefit in monitoring hepatic alveolar echinococcosis lesions in daily clinical practice [63].

### Shear wave elastography (SWE)

SWE was introduced more than ten years ago to liver imaging [64-67] and non-liver applications [66,68-70].



**Fig 2.** Hydatid cyst displayed by B-mode (a) and CEUS (b). CEUS allows differential diagnosis to solid tumours



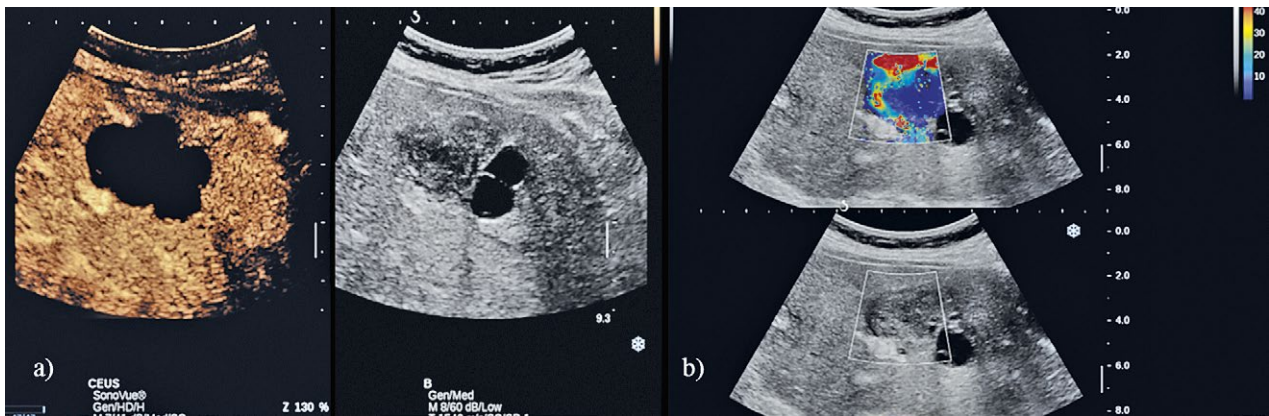
**Fig 3.** Contrast enhancement of the capsule and surrounding liver parenchyma are seen, consistent with a concomitant inflammatory reaction to the hydatid cyst.

Additional clinically relevant commentaries to supplement the published recommendations are also available [28,31]. There are however no published data on the use of SWE in hydatid cysts. Like CEUS, SWE is a new method which needs to be evaluated in CE. Elastography techniques may be helpful to characterize hydatid cysts though do not differentiate stages [71] and may differentiate hepatic neoplasms from ‘tumor-like’ hydatid cysts. Type I HC has a similar echo pattern to a simple cyst. The elastography value of the cysts is zero in SWE. Type V is pure calcific and very heterogeneous. The other types have heterogeneous internal components [71]. Further research is required. The combined approach is shown in figure 4.

### Fusion imaging

Fusion imaging is a technique which combines a new US transducer with a dynamic volume navigation system, integrating a patients’ previously acquired MRI DICOM image data into a real time volume navigation. It thus displays synchronized side-by-side MRI and US images in the same plane, allowing a precise position tracking of the US transducer, which facilitates accurate localization





**Fig 4.** Hydatid cyst displayed by CEUS (a) and SWE (b). Note the additional information with localisation next to a portal vein branch (b) and the stiffness values which may reflect the stage of diseases (b).

of target lesions, with a high degree of confidence during real time US scanning [72–74]. In recent years, fusion imaging methods have been widely used in percutaneous ablation treatment of liver malignancies [72,75,76]. During the local ablative or medical treatment of hydatid cysts, fusion images might be helpful to correctly identify focal liver lesions and to realize real time monitoring of treatment (fig 5).

#### **Positron Emission Tomography (PET)**

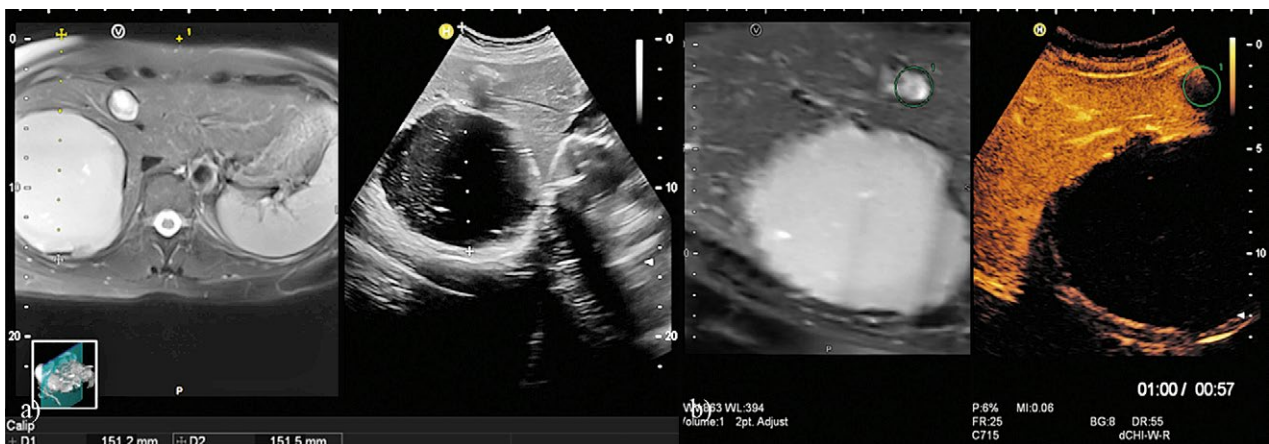
$^{18}\text{F}$ -FDG PET/CT demonstrates metabolic activity and so can effectively determine the biological boundary of liver AE along with the metabolic activity of surviving liver following autologous liver transplantation [77] and is, therefore, recommended for the initial assessment and follow-up of human AE [78]. In a recent study, CEUS and  $^{18}\text{F}$ -FDG PET showed good inter-rater reliability in determining the activity of hepatic AE [60]. Combining FDG-PET/CT with anti-EmII/3-10 antibody

levels, better predicts echinococcosis-larval activity after long-term benzimidazole therapy for non-resectable alveolar infection, than either parameter alone [79]. Delayed  $^{18}\text{F}$ -FDG PET facilitates differentiation of active and inactive liver lesions in AE patients [80].

PET/MRI also provides comparable diagnostic information for AE management. The reduction in radiation exposure compared to PET/CT may be of particular importance for children and young patients not amenable for curative surgery requiring repeated long-term follow-up with dual imaging modalities [78].

#### **Differential diagnosis**

The clinicians should be aware of the changing epidemiology of hepatic cystic lesions, as echinococcosis has spread to previously non-endemic Western European countries [81]. Accurate diagnosis of CEs is essential because the mortality of these lesions is higher than for simple cysts, estimated between 2–5% [82]. US is the first



**Fig 5.** Fusion imaging using RVS with magnetic resonance imaging (a, left), conventional B-mode ultrasound (a, right) and magnetic resonance imaging (a, left) with contrast enhanced ultrasound (b, right). The images can be overlaid to correctly identify focal lesions and to monitor before and after local ablative or medical treatment.

Table I. Ultrasound features for the diagnosis of monocytic diseases of the liver (after [87], adapted)

	<b>Cystic echinococcosis</b>	<b>Alveolar echinococcosis</b>	<b>Cystadenoma and cystadenocarcinoma</b>
Border	Laminated	Irregular	Irregular
Shape	Round or oval	Irregular	Round or oval
Echo pattern	Anechoic or atypical	Hyperechogenic outer ring and hypoechogenic centre	Hypoechogenic with hyperechogenic septations
Appearance	Multiseptated	Multivesicular	Septated and/or solid structures (papillary projections)
Wall			Wall enhancement
Posterior acoustic shadow		Present (calcified areas)	Present (calcified areas)

choices of imaging in the diagnosis of CE, with a specificity near 90% [83]. Typical US features are observed in 70% of echinococcosis and include an irregular shape and border, hyperechogenic outer ring, hypoechogenic center, multi-vesicular appearance and acoustic shadowing due to calcified areas. Atypical US features include small hyper-echogenic nodules (amorphous AE), large lesions with massive necrosis (pseudocyst) which might be confused with neuroendocrine tumour metastases [84] or sarcoma [85,86], small calcified lesions (inert AE) [87] and liver cystadenoma or cystadenocarcinoma [88].

The US features useful for differentiating between CE, AE and cystadenoma and cystadenocarcinoma are summarized in table I [89].

#### ***Haemorrhagic hepatic cysts***

Echinococcosis should also be differentiated from haemorrhagic hepatic cysts, which is aided by serial imaging. Features of the later include decreasing cyst size, progressive centrifugal enhancing pattern on dynamic contrast-enhanced CT or MRI, a hypointense rim with central hyperintensity on T2-weighted MRI, and cyst wall calcification [90].

#### ***Complications of hydatid cysts in the liver***

Growing hydatid cysts may be asymptomatic or may cause secondary effects through local compression, erosion into local structures or rupture e.g., into the peritoneal space (fig 6). Direct rupture of a hydatid cyst occurs

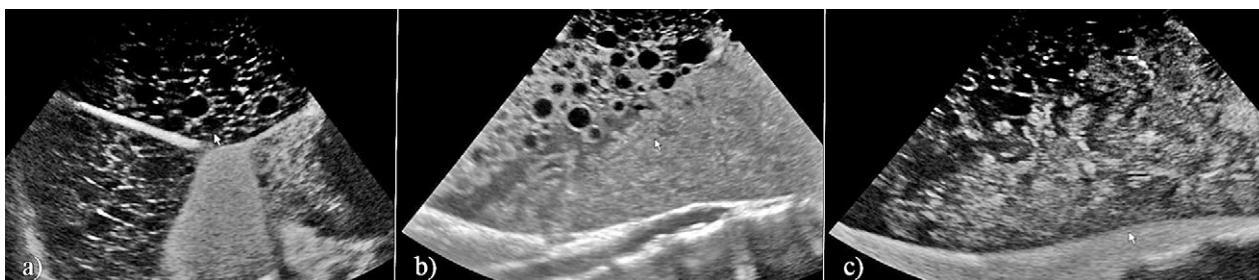
when both the pericyst and endocyst break, allowing free spillage of hydatid material into the surrounding anatomical channels, adjacent organs, or free body cavities [91]. There are several types of direct rupture, including into the gastrointestinal tract, peritoneal cavity, diaphragm, pleural space, bronchi (with development of cystobronchial fistula), pericardium, and skin [91,92].

#### ***Rupture into biliary tree (communicating rupture)***

Compression and displacement of the biliary ducts are frequent. At the point of contact with a biliary duct, a rupture may occur. Communication of a CE with the biliary tree occurs in up to 90% of cases. This high frequency is due to incorporation of the small biliary ducts into the pericyst during cyst growth [92]. A communicating intra-biliary rupture may be occult, usually through small fissures (seen in 10-37% of patients), or frank (3-17%) [93,94]. Occult rupture is usually silent but may be accompanied with signs of suppuration or evolve into frank rupture. In a frank rupture, daughter vesicles and fragmented membranes escape into the biliary tree causing obstruction, cholangitis or septicemia [94]. Acute pancreatitis and acute cholecystitis caused by hydatid material have been described [94-97].

There are several US criteria to diagnose intrabiliary rupture of a hydatid cyst [91,94,98-100] (fig 6).

- The ruptured cyst is often multivesicular, has a polycyclic shape, septa or irregular echogenic areas in its interior.



**Fig 6.** Hydatid cyst of the liver, ruptured. CEUS allows differential diagnosis of enhancing (solid tumour) and non-enhancing (e.g., parasitosis) pathology. The images show the contrast enhancing liver to the right (a,b) and the enhancing aorta distally (c). In all images non-enhancing hydatid vesicular material is shown in the peritoneal space.

- A loss of continuity of the cyst wall adjacent to the bile duct representing the site of communication is a pathognomonic direct sign of cyst perforation in the biliary tree but is very rarely seen
- Dilatation of the biliary tree occurs with biliary obstruction
- The presence of small cystic images in the biliary ducts may represent daughter cysts, and is a very specific sign of rupture but poorly sensitive. Linear hyperechoic images and non-shadowing material may be found in biliary ducts and are the expression of hydatid membranes and hydatid sand respectively.
- Thickened, double layered bile ducts wall are expression of cholangitis.

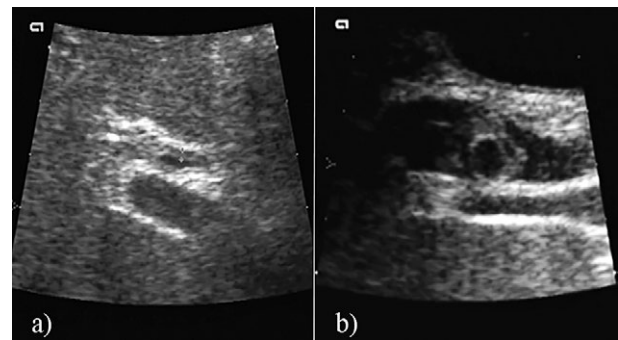
In a series of 15 cases, the sensitivity of US to diagnose intra-biliary rupture of a hydatid cyst was 66.7% [93]. Early evacuation of the cyst together with its germinal membrane and the involved biliary tract is important. Whilst avoiding spillage into the peritoneal cavity, treatment of the remaining cavity according to its location, size, and the presence of infection may be considered (fig 7). Decreasing the pressure in the biliary tract may be achieved by T-tube drainage [101].

#### ***Peritoneal hydatid cysts (peritoneal seeding)***

Peritoneal hydatid cysts (peritoneal seeding) are generally secondary to hepatic involvement and most common after previous surgery for hydatid cyst complication. They can also appear after a peritoneal cyst rupture. The prevalence of abdominal involvement with hydatid disease is approximately 10–13% [91,92]. The diagnosis can be made easily with US, because of the characteristic appearance of daughter cysts anywhere in the peritoneal cavity.

#### ***Involvement of the diaphragm and thoracic cavity***

Involvement of the diaphragm and thoracic cavity occurs in 0.6%–16% of cases of hepatic hydatid disease localized in the posterior segment of the right hepatic lobe.



**Fig 7.** Rupture of a hepatic hydatid cyst into the biliary tree. Linear echogenic material in the CBD on US is indicative of hydatid membranes. Ultrasound 2 days after endoscopic removal of hydatid membranes: common bile duct of normal size with thick, double layered walls (a). Intrabiliary masses with cystic areas inside, representing daughter vesicles (b).

Trans-diaphragmatic migration usually occurs at the level of bare area of the liver, with simple adherence to the diaphragm, then rupture into the pleural cavity, seeding into the pulmonary parenchyma, or chronic bronchial fistula [91,92]. US examination reveals the hepatic CE, pleural effusion, or basal consolidation of the liver [102, 103]. A diaphragmatic defect or fistula is rarely seen by US. Intracavity application of US contrast agents in the instance of CE drainage may depict the hepatic-bronchial fistula (Z.S., personal observation).

#### ***Secondary infection of the hydatid cyst***

Bacterial superinfection of a hydatid cyst occurs only after communication or direct rupture of a cyst with subsequent passage of bacteria. This occurs in 5%–8% of all HC cases and up to 25% of ruptured cysts [91,92,104]. The US features are similar to other hepatic abscesses: poor delimitation, mixed internal echoes, and air-air, air-fluid or fluid-fluid levels within the cyst [91, 92, 105]. However, as these US signs are the expression of a direct or communicating rupture, they do not necessarily imply



**Fig 8.** Infected hepatic hydatid cyst. US demonstrates a 3 cm cyst with detached membrane, echogenic internal echoes. The surrounding liver parenchyma is hypoechoic (a). A small volume of ascites near the liver surface was seen (b). CEUS arterial phase images reveal two zones around the cystic lesion: a non-enhancing circular area consistent with pericystic abscesses (→) and a hypervascular outer area representing peri-abscess inflammation (→) (c).



infection [91,104]. A hypervascular area around the lesion represents inflammatory liver parenchyma changes secondary to infection [92], which can be identified by contrast enhanced CT and CEUS (fig 8).

### **Compression of hepatic vessels**

Compression of hepatic vessels (portal branches or hepatic veins) is rarely seen. Imaging may reveal portal vein thrombosis with or without cavernous transformation (in lesions located mostly in the caudate lobe or near the hepatic bifurcation) or Budd-Chiari like changes (veno-venous collaterals) [92].

**In conclusion**, new imaging methods add important information for better understanding of the various manifestations of echinococcosis. Future studies should be performed to confirm the promoted additional value.

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**Conflict of interest:** none

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