*Review*

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# Comments and illustrations of the WFUMB CEUS liver guidelines: Rare focal liver lesion – infectious parasitic, fungus

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**Abstract**

In this series of papers on comments and illustrations of the World Federation for Medicine and Biology (WFUMB) guidelines on contrast enhanced ultrasound (CEUS) the topics of parasitic and fungus infections are discussed. Improved detection and characterization of common focal liver lesions (FLL) are the main topics of these guidelines but detailed and illustrating information is missing. The focus in this paper on infectious (parasitic and fungus) focal liver lesions is on their appearance on B-mode and Doppler ultrasound and CEUS features. Knowledge of these data should help to raise awareness of these rarer findings, to think of these clinical pictures in the corresponding clinical situation, to interpret the ultrasound images correctly and thus to initiate the appropriate diagnostic and therapeutic steps in time.

**Keywords:** Liver lesions; candidiasis; parasitic diseases; ultrasonography; CEUS

## Introduction

The World Federation for Ultrasound in Medicine and Biology (WFUMB) has published guidelines on the use of contrast-enhanced ultrasound (CEUS) for the evaluation of focal liver lesions [1-5]. Improved detection and characterization of common focal liver lesions (FLL) are the main topics of these guidelines. In recent years, conventional ultrasound (US) and CEUS features of less common FLL and vascular have been described in detail [6-10]. In this current paper series, we aim to summarize the US and CEUS features of very rare FLL where there are limited reports and figures published in order to create a library of these rare lesions [10-19]. Parasites and fungal diseases have manifestations in the liver that pose a diagnostic challenge. Often they are incidental findings

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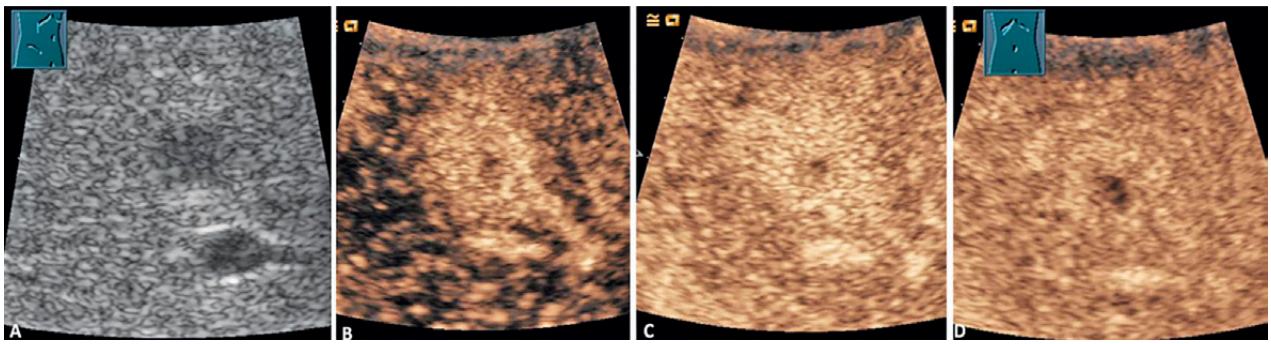

**Fig 1.** A 23-year-old patient with a hypoechoic hepatic mass after aggressive chemotherapy for acute myeloid leukemia (A). On contrast-enhanced ultrasound, the lesion shows arterial rim hyperenhancement after 15 s (B) and after 20 s (C). After 1 min, the small central non-perfused area is unchanged. Clinically, a diagnosis of hepatic candidiasis was made. The FLL resolved after treatment.

or are detected in the context of unclear clinical scenario. Knowledge of such sonographic findings leads to an expansion of the differential diagnostic repertoire.

In various endemic regions of the world for parasitic diseases, liver lesions are part of the disease spectrum [20-26]. For some parasites, typical changes present themselves, on which a targeted diagnosis is based. For example, the diverse picture of liver lesions in echinococcus or the presentation of ascarids in the biliary system and the pancreatic duct.

It is important to evaluate the entity in the context of its occurrence. Pathogens in high-endemic areas of Africa and South-East Asia need to be known as well as infestations of immunocompromised individuals. This paper describes the sonomorphological changes and CEUS appearance of focal liver lesions in candidiasis, parasitic diseases in different endemic regions of the world or immune incompetent patients.

## Hepatic candidiasis

In acute leukemia in the neutropenic patient, newly diagnosed hypoechoic liver lesions suggest candidiasis [27,28]. On CEUS, lesions that are similar on the B-scan can then be further differentiated. Mycotic abscesses can be differentiated from leukemic infiltrates, Pneumocystis carinii infections or hemophagocytosis syndrome manifestations. Hepatic candidiasis (HC) is seen in the course of chronic disseminated candidiasis [29]. It is most commonly observed in acute leukemia, at the stage of regeneration after therapy-induced neutropenia, with an incidence of 6.8% [30].

*Imaging*

The diagnosis is usually made clinically and on imaging, where B-mode US demonstrates multiple small-focal, <2 cm hypoechoic lesions in the liver and other solid organs [31]. However, the B-mode US appearance is non-specific and a definitive diagnosis can only be made histologically, with evidence of granulomatous inflammation and evidence of fungi [29]. In clinical practice, this diagnostic confirmation is rarely performed, because patients usually have significant thrombocytopenia, and antifungal therapy is usually administered for the neutropenic sepsis [32]. As a result, biopsies are usually negative with respect to the detection of vital fungal organisms.

Basically, leukemic recurrences and other rarer syndromes, such as hemophagocytosis syndrome or *Pneumocystis carinii* infection, present identically on B-mode US [32]. Owing to the diagnostic uncertainty in these cases, CEUS plays an important role in patients with suspected HC allowing differentiation of these lesions from leukemic infiltrates and other disease entities by their enhancement characteristics [32]. A pathological/histological explanation for the variable ultrasound pattern remains undetermined [32]. It can only be speculated that the presence of a margin of hyperenhancement is indicative of florid inflammation. Another CEUS characteristic is the obligatory detection of a non-perfused central area of variable size (fig 1).

### *Hepatic alveolar echinococcosis*

Alveolar echinococcosis (AE) is a rare chronic zoonosis caused by the larval stage of *Echinococcus multilocularis*, a cestode parasite. In humans, the disease typically presents with liver involvement. Extrahepatic manifestations are rare (13% of cases affect the lung, spleen, or brain). Patients complain of unspecific symptoms such as right upper quadrant discomfort (hepatomegaly), weight loss, or malaise. Infrequent manifestations include obstructive jaundice, cholangitis, and portal hypertension due to vascular invasion (portal or hepatic veins). Although AE is a non-neoplastic disease, the inflammatory tissue growth induced by the parasite resembles that of slow-growing malignant tumors, progressively exhibiting infiltrative growth, invasion of adjacent organs and vessels, and distal metastasis [33]. If left untreated, the

prognosis of the disease after the onset of symptoms is poor, with a mortality rate of over 90% at 10 years [34]. Therapy options dramatically improve the prognosis and include (curative) surgery and benzimidazoles (e.g., Albendazole, Mebendazole). The diagnosis is usually made via imaging in combination with serology.

*Imaging*

On US, AE lesions can be indistinguishable from malignancy (particularly cholangiocarcinoma and hepatocellular carcinoma), especially since the vessels can be invaded. Notably however, the general conditions of patients with AE are usually much better than those with malignancy. The described US imaging features of AE are either of a hyperechogenic (around 50% of published cases), hypoechogenic, or heterogeneous solid lesion with irregular and poorly defined margins. Small calcifications in the periphery have been described in 50–70% of the cases, and this can help with the diagnosis. The size of the lesions varies from several centimeters to involving most of the liver, often the right liver (fig 2, fig 3). The following imaging classification system describes five types of sonographic changes in hepatic alveolar echinococcus [35] (fig 4).

- Type 1: A hailstorm pattern appearing as heterogeneously echogenic areas with irregular contours and visibly scattered hyperechoic areas; calcifications can be observed in some cases.
- Type 2: A pseudocystic pattern with an irregular hyperechoic rim that is not vascularized on power Doppler and CEUS imaging.
- Type 3: A metastasis-like pattern.
- Type 4: A hemangioma-like pattern.
- Type 5: An ossification pattern with calcification features.

In a separate study, the most frequent patterns of AE lesions in the liver were the hailstorm and pseudocystic patterns. There was no correlation between the clinical stage of the disease and the US appearance of the lesions [36]. Few studies have evaluated the CEUS behavior of AE [37-41]. Research using first-generation ultrasound contrast agent (UCA) (Levovist) have suggested an absence of enhancement in AE [42]. However, more recent data with second-generation UCAs have revealed that enhancement is frequent (78% in the most recent series). A recent study indicates several changes with CEUS: 23 lesions (53.5%, or 23 out of 43) display no enhancement

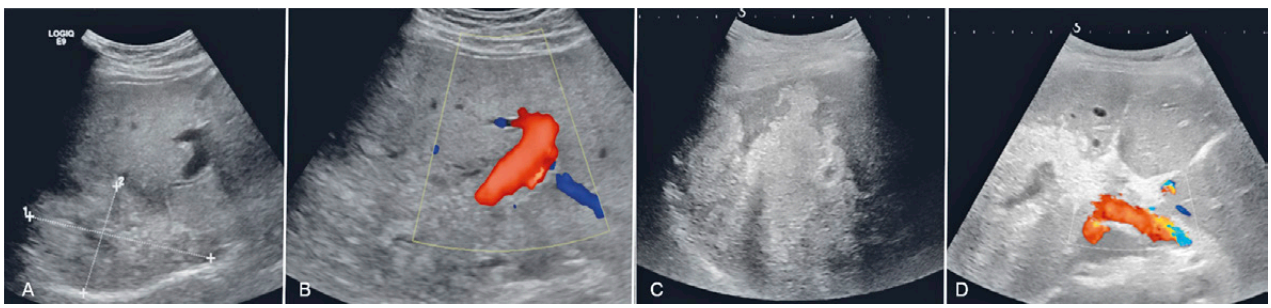


**Fig 2.** Hepatic Alveolar Echinococcosis (HAE): A – a large heterogenous lesion (about 12 cm) with solid aspect is visualized in the right liver in B-mode ultrasound. Note the small hyperechoic spots that correspond to microcalcification. B – the lesion infiltrates the right posterior branch of the portal vein, which has a truncated aspect (arrow); C and D - another example of a very large hepatic alveolar Echinococcosis. Note again the solid aspect, in this case mostly hyperechoic; at the periphery of the lesion very small hyperechoic spots corresponding to microcalcifications are visualized. Also in this case, there is infiltration of the portal vein.

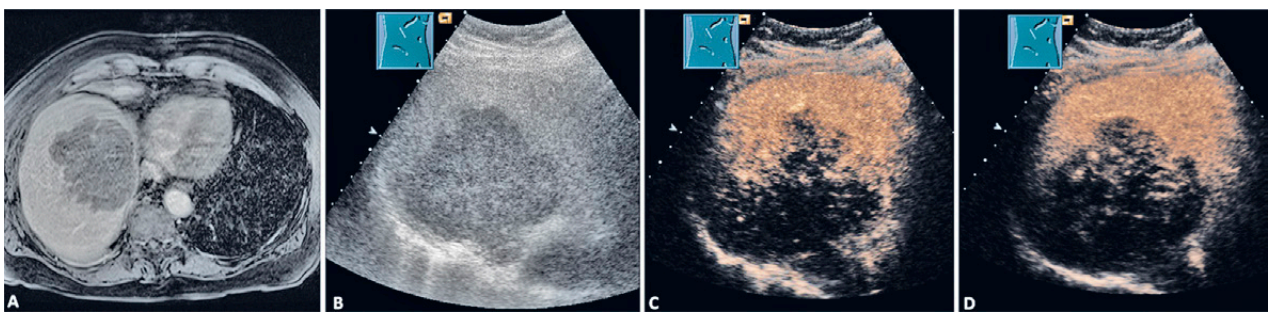


**Fig 3.** A 49-year-old patient with hypointense hilar liver lesion on computed tomography (courtesy of Prof. Dr. Mahnken, Department of Radiology, University Hospital Marburg) (A) and B-mode ultrasound (B). On contrast-enhanced ultrasound, the lesion showed an absence of enhancement after 20 s (C) and 1 min (D). Histologically and serologically, the diagnosis of alveolar echinococcosis was confirmed.

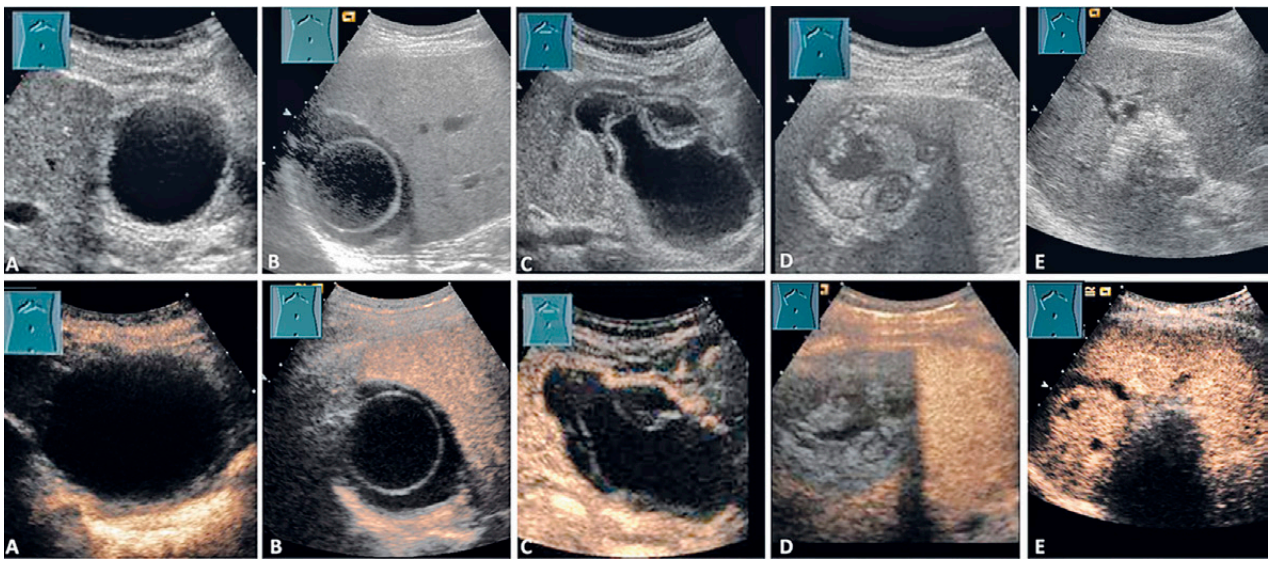


**Fig 4.** A 67-year-old patient with serologically confirmed cystic echinococcosis and with corresponding patterns of liver involvement on B-mode and contrast-enhanced-ultrasound: (A) type I (pure cyst); (B) type II (cyst within cyst); (C) type III (water lily sign); (D) type IV (solid impinging); and (E) type V (calcifications).

in the arterial, portal, and delayed phases with CEUS imaging. Meanwhile, 11 lesions (25.6%, 11/43) display a slight rim-like hyperenhancement in the arterial phase and hypoenhancement in the portal and delayed phases, and 6 lesions (14%, 6/43) display hyperenhancement in the arterial phase and hypoenhancement in the portal and delayed phases. Two lesions (4.7%, 2/43) exhibit isoenhancement in the arterial, portal, and delayed phases, whereas one (2.3%, 1/43) showed slight hypoenhancement in the arterial, portal, and delayed phases [43]. From a structural point, the most common aspect is circular rim (i.e., peripheral) enhancement, with a lack of central enhancement, and this has been described in about one-third of the published lesions. Early arterial enhancement is seen in some patients (circa 30%), while enhancement in the portal venous phase only was observed in the remaining cases.

The correlation between pathological and CEUS findings remains controversial. Based on one study performed with an animal model [44], larger lesions may have more pronounced peripheral and central enhancement due to the development of small neoangiogenic vessels in the inflammatory tissue surrounding the parasitic vesicles. Whether contrast enhancement corresponds to more active lesions has not been fully elucidated. In one study [40], CEUS using SonoVue® was compared to three-phase helical CT and positron-emission tomography with 18F fluorodeoxyglucose (FDG-PET). Lesions with enhancement on CEUS are also metabolically active on FDG-PET, suggesting that CEUS could be useful in this regard. However, FDG-PET reveals significantly more active lesions than CEUS, and more data is needed before recommending its routine use in patients on drug therapy. Previously, CT was considered the method of choice [45]. In CT scans, lesions are most often hypodense (70% of cases), and calcifications have been identified with higher sensitivity using this technique than via US. Disease activity, meanwhile, is better studied using FDG-PET. Since hydatid cysts have been recently summarized in detail by the authors, they have not been included as part of this paper [22,23,25].

**Fascioliasis**

Fascioliasis is a zoonotic disease caused by two main liver fluke species of the *Fasciola* genus: *Fasciola hepatica* and *Fasciola gigantica* [46]. Fascioliasis is typically a rural distomatosis that commonly affects livestock such as sheep, goats, buffaloes, and cattle; humans are accidental hosts of the parasite [47]. The most common symptoms are abdominal pain, weight loss, and fever. One study suggests that the mean duration starting from the onset of symptoms to a definite diagnosis is 44.3±39.1 days. In physical examinations, the most common clinical signs are tenderness in the epigastrium or the right side of the abdomen, followed by hepatomegaly and fever. Jaundice is relatively uncommon in this condition [48]. The treatment of choice for fascioliasis in humans is a single oral dose of 10 mg/kg triclabendazole.

*Imaging*

US findings are nonspecific (fig 5-7) and include focal hypoechoic or hyperechoic lesions or diffuse in-

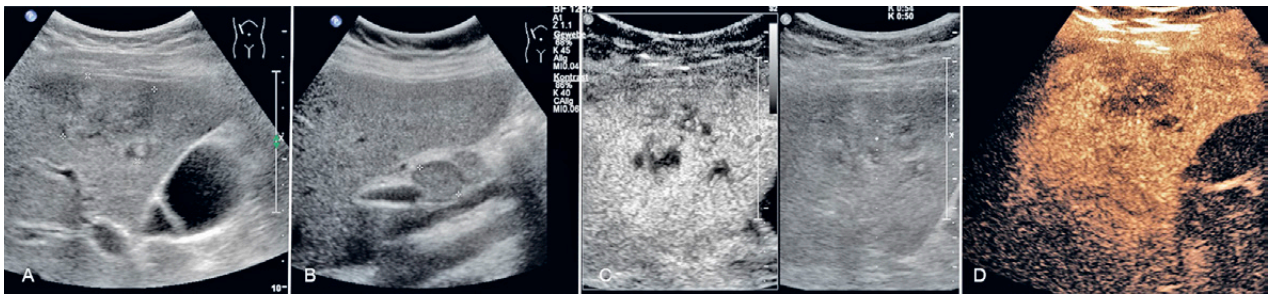

**Fig 5.** Fasciolosis hepatica (serological proven) in a 19-year-old woman with abdominal feeling of pressure and eosinophilia of 30%. The grey scale ultrasound displays confluent hypoechoic lesions up to 4 cm in the right liver lobe, which were blurred and without a halo (A). In the porta hepatis, enlarged and rounded lymph nodes up to 2.2 cm were detected (B) CEUS demonstrates arterial contrast enhancement in the outer areas (C) and increasing washout in the late phase (3:49 minutes, D).

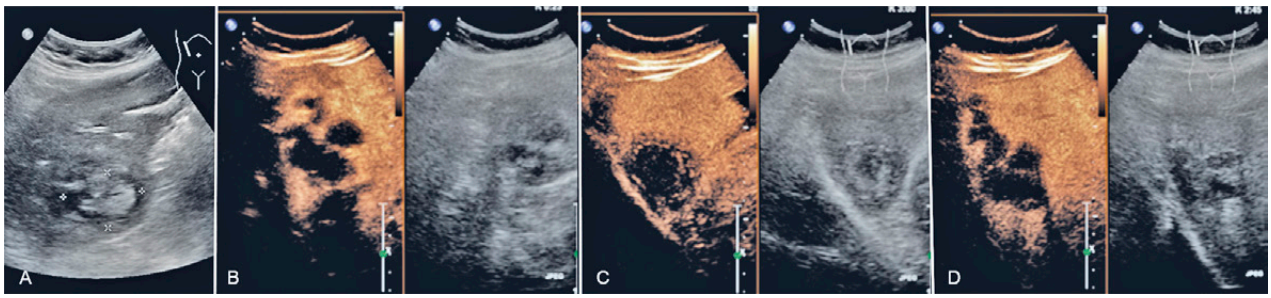

**Fig 6.** Fasciolosis (serological and histological proven). 76 y/o female from Eastern Turkey presenting with subfebrile temperature, weight loss and eosinophilia. B-mode ultrasound showed a heterogeneous lesion in liver segment VI (A). Contrast enhanced ultrasound CEUS revealed a rim-like peripheral enhancement during the arterial phase (B) with slight washout during the delayed phase (C) and confluent unenhanced central areas correlating to the eosinophilic abscess caused by the fluke´s migration (D).

volvement of the liver. CEUS reveals rim-like peripheral enhancement during the arterial phase, with a slight washout during the portal venous and delayed phases. Most striking are the confluent unenhanced central areas associated with the eosinophilic abscess and the migration route of the fluke [21,49]. It is worth noting that due to scar tissue, unenhanced areas may persist for years after successful treatment. An abdominal CT scan demonstrates a conglomerated hypodense lesion (89%), rim-enhanced lesion (71.4%), subcapsular or peripheral location (72.3%), and tubular branching track described as a serpiginous track resulting from parasitic migration (64.6%). Other findings include single hypodense lesions (10.9%), cystic lesions (8%), centrally located lesions (14.3%), scattered lesions in both lobes (10.6%), and localized perihepatic fluid accumulation (10.3%). Portal vein thrombosis was observed in 17 patients (9.7%). The associated extrahepatic findings include intra-abdominal lymph node enlargement (40.6%), ascites (13.7%), and presence of an abdominal wall abscess (4%). Bile duct dilatation was found in 40 patients (22.9%) [48].

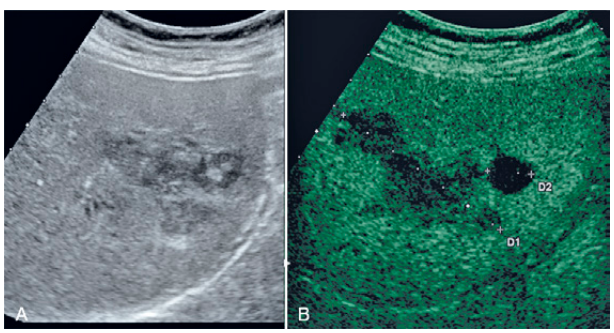

**Fig 7.** Fasciolosis (serological proven). Abscess formation can be proven only by CEUS (a, b).

### Clonorchis and opisthorchis

The liver fluke *Clonorchis sinensis* is a high-risk, pathogenic parasitic helminth that is endemic to and actively transmitted predominantly in Asian countries, including Korea, China, Taiwan, Vietnam, and the far eastern parts of Russia. Clonorchiasis and opisthorchiasis are characterized by chronic infection that induces hepatobiliary inflammation, especially periductal fibrosis, which can be detected by US. To reduce hepatobiliary morbidity, the primary intervention measures focus on control and elimination of the liver fluke [50]. The short-term goal of liver fluke control can be achieved by praziquantel chemotherapy. US reveals various findings,

most commonly small- and medium-sized intrahepatic bile duct narrowing, with subsequent pre-stenotic bile duct dilatation. Depending on the stage of the disease, hypoechoic periductal edema or hyperechoic periductal fibrosis may be found [26]. Furthermore, fluke aggregates may be detected as hyperechoic spots within the bile ducts. Over the time, such aggregates may cause hypo- to isoechoic nodules, which coalesce and lead to heterogeneous echogenicity of the liver.

**Ascariasis of the liver**

Ascariasis is a common cause of hepatic abscesses in certain regions of the world. Imaging sometimes reveals pathognomonic features such as the typical morphology of an adult worm in the diagnosis of hepatic ascariasis. However, it is not sensitive, and most infections do not manifest such characteristic features. This means that a lack of imaging abnormalities does not confirm the absence of ascariasis. Moreover, the infection can be easily diagnosed through a parasitological stool examination. Imaging is therefore indicated only when diagnosis is difficult or if complications are suspected [51].

Fine-needle aspiration cytology from the liver abscess could display an ascariasis-associated result. Patients with hepatic abscesses develop pain in the right hypochondrium, high fever, point tenderness in the first intercostal space, and edema of the right lateral chest wall [52]. Ascarides are localized in the intrahepatic ducts in most of these patients. Pus from the abscess often indicates *Ascaris* ova and/or fragments of dead ascarides [53]. In US images, hepatic ascariasis may contain single or multiple long, linear or curved echogenic structures without acoustic shadowing. A long, thick linear or curved non-shadowing echogenic strip containing a central longitudinal anechoic tube (i.e., a 4-line sign) represents the digestive tract of the worm [51]. While gallbladder ascariasis (GB) has been abundantly described in the literature, this is a relatively rare manifestation constituting only 2.1% of all hepatobiliary manifestations. Its characteristics are writhing movements of the echogenic strips within the ducts. Other signs include gallbladder and cystic duct distension, gallbladder wall edema, sludge within the gallbladder, and multiple liver abscesses [53]. Retained worm fragments can serve as a nidus for biliary stones. Other rare conditions such as microgallbladder in cystic fibrosis have to be ruled out (34). Compared to B-mode US, CEUS can be used to differentiate between GB tumors and GB ascariasis debris with a higher degree of confidence [54]. Furthermore, GB ascariasis debris may present with solid solitary hyperechoic lesions in the gallbladder in conventional B-Mode US with no mobility in the standing position. Zigzag and multiple parallel echogenic lines were detected in the lumen of the gallbladder. After an injection of 2.4 ml US SonoVue, no enhancement could be observed throughout the entire enhancement period (non-published data).

**Schistosomiasis**

Schistosomiasis remains a public health problem in many parts of the world, particularly in Africa, where 93% of the total population require chemotherapy to prevent the complications of the disease, namely hepatic fibrosis and portal hypertension, urinary tract obstruction, hydronephrosis and bladder cancer, as well as sequelae involving the reproductive tract [55]. Since eradication of schistosomiasis is difficult, the WHO has focused on morbidity control. Consequently, morbidity assessments are crucial. Ultrasound is a pivotal method to assess the morbidity due to schistosomiasis and its complications in endemic countries [47,56-58]. In general, US examination of patients with schistosomiasis should refer to the WHO Niamey-Belo Horizonte protocol so that the data can be compared on an international scale. Although estimates are not available, schistosomiasis must be considered to be the most frequent cause of liver fibrosis worldwide [59].

The typical US features of schistosomal Symmers' fibrosis include echogenic bands, streaks, and areas accompanying portal branches compared to standard images [60,61]. Portal fibrosis may be graded by comparing the liver sonomorphology with standard imaging patterns. Furthermore, *S. japonicum* may cause portal fibrosis and/or interseptal hepatic fibrosis, which by imaging techniques resemble "network-" or "tortoise-back"-like liver aspects [57,58,62]. Portal hypertension is indicated by portal vein dilatation. Doppler US may be misleading in cases where the flow is not reduced and can even be increased from the enlarged spleen to the liver. In well-equipped hospitals, endosonography, CT, and especially MRI may contribute to further assessment of liver fibrosis and the associated hemodynamic abnormalities [63]. Gallbladder abnormalities usually occur in patients with advanced hepatic portal fibrosis due to a *Schistosoma mansoni* infection. Gallbladder abnormalities have occasionally been observed in children, and they may occur without associated overt liver abnormalities. The specific *S. mansoni*-induced gallbladder abnormalities detectable by US include typical hyperechogenic wall thickening with external gallbladder wall protuberances whereby the luminal wall surface is smooth [64].

**Toxocariasis**

Toxocariasis is caused by ascarids in dogs known as *Toxocara canis*; it leads to eosinophilic inflammation such as eosinophilic abscesses or granuloma in the liver and lungs. Due to the slow movement of the lesions, the disease is known as visceral larva migrans. In CT or MR imaging, hepatic lesions are observed as multiple ill-defined oval lesions that measure 1.0–1.5 cm in diameter [65]. Sometimes, they may be angular or trapezoidal. The lesions are usually best seen in the portal venous phase via dynamic contrast-enhanced CT and MR imaging. They are either invisible or only faintly visible in the arterial and equilibrium phases; either with an enhancing rim or occasionally enhancing nodules can be observed. Sonographically, the lesions appear as multiple small, oval hypoechoic lesions in the liver parenchyma. They differ from metastatic nodules in that they have fuzzy margins, are uniform in size and non-spherical, and are best observed during the portal venous phase. In follow-up images, the lesions may improve or sometimes change positions, reflecting migration of larva in the liver, supporting the phenomenon of visceral larva migrans [66].

**Paragonimus**

Paragonimiasis is a parasitic lung infection caused by lung flukes of the *Paragonimus* genus, with most cases reported in East Asia and caused by *P. westermani* following the consumption of raw or undercooked crustaceans. Ectopic infection may occur and most commonly involves the brain and striated muscle. Involvement of the liver is rare with only case reports and no larger studies reporting liver involvement [67]. Drug therapy such as praziquantel is the first choice for hepatic paragonimiasis.

*Imaging*

Hepatic Paragonimus (HP) lesions are often incidentally detected on routine US. Typically, HP presents as subcapsular hyperechoic lesions with irregular, tract-like, non-enhancing areas of necrosis on CEUS [68]. Liver biopsy is usually performed for diagnosis distinguish it from other liver lesions [69]. In addition to more invasive methods, US, CT, and serum laboratory studies can be used to establish the diagnosis of HP. Abdominal CT reveals multiple low-density lesions (poorly circumscribed with inhomogeneous enhancement, suggestive of areas of necrosis), formation of visible partitions, and absent invasion of adjacent vessels [70]. The presentation of Paragonimus in MRI may mimic hepatocellular carcinoma with a mass of inhomogeneous signal intensity. The lesion may exhibit mild enhancement and restricted diffusion [71].

**Lepra**

Leprosy is a systemic infectious disease affecting several parenchymal organs to varying extents. Next to the neurocutaneous system, the liver is the most common organ involved. Hepatic granulomas have been reported predominantly in patients with lepromatous leprosy and are rare in those with tuberculoid leprosy. Abnormal US findings include an inhomogeneous echo texture of the hepatic parenchyma in all cases [72]. However, hepatic sonography was conducted on 36 patients with lepromatous leprosy and 3 with borderline lepromatous leprosy. No definite abnormal sonographic findings were observed in the liver for a large majority of these patients [73].

**Primary toxoplasmosis of the liver**

Hepatic toxoplasmosis is associated with elevated serum alkaline phosphatase activity and minimally elevated lactate dehydrogenase levels [74]. Liver pathologies and infection with *Toxoplasma gondii* are widespread among HIV-infected patients. Among these patients, *T. gondii* is a weak, nonspecific adjunct that supports chronic liver inflammation and the progression to cirrhosis, but it does not influence the degree of hepatitis activity regardless of the etiology.

**Focal pneumocystis carinii**

*Pneumocystis carinii* is a frequent cause of interstitial pneumonitis in patients with cell-mediated immunodeficiencies. Extrapulmonary *P. carinii* infection is a rare manifestation of disease caused by this organism. Nevertheless, reports of such infections are increasing in the setting of the acquired immunodeficiency syndrome (AIDS; [75]. *Pneumocystis carinii* pneumonia (PCP) is an opportunistic infection associated with morbidity and mortality in solid-organ transplant recipients [76].

**Leishmaniasis**

Leishmaniasis is a global infectious disease with obligatory intracellular protozoan parasites of the *Leishmania* genus. It is endemic in East Africa, Latin America, and Southeast Asia, areas in which malnutrition is associated with high concentrations of the parasite. However, foci of infection have also been found in the Mediterranean and the Middle East. The transmission takes place through the sand mosquito (genus *Phlebotomus*). Leishmaniasis has three manifestations: cutaneous, mucocutaneous, and visceral. Liver involvement is present in

the visceral form. Approximately 500,000 new cases of leishmaniasis occur each year, and an estimated 50,000 to 90,000 new cases of visceral leishmaniasis (VL) occur worldwide annually, of which only between 25 to 45% are reported to the World Health Organization (WHO; [77]. The pathogens of the disease take the form of *L. donovani* worldwide and *L. infantum* in Europe [78]. The most common symptoms and clinical signs are weight loss, fever, loss of appetite, hepatosplenomegaly, pancytopenia, and lymphadenopathy [79-81]. In the case of HIV infection, the risk of contracting leishmaniasis is increased significantly [82]. Visceral leishmaniasis is often atypical and fulminant in immunosuppressed patients [83]. The protozoa invade macrophages, which are found in the bone marrow, liver, spleen, and lymph nodes [84-86]. If visceral leishmaniasis is clinically suspected, microscopic detection of the pathogen in bone marrow is the method of choice. The pathogen can be directly detected through biopsy of the infected tissue, which is conducted by examining the bone marrow needle aspirates or from other affected organs with evidence of *Leishmania* amastigotes [79,84,87-89]. Alternatively, PCR from peripheral blood or serological diagnostics can be used [83]. The infection induces granulomatous inflammation [87,90-92], and therapy for visceral leishmaniasis is always systemic. Liposomal amphotericin B is the drug of first choice [83,93].

*Imaging*

Hepatosplenomegaly is a very common and detectable sonographic change in visceral leishmaniasis. In addition to observations of lymphadenopathy, small hypoechoic lesions are often detected in the spleen [78, 79,81,94-100]. Focal liver lesions are extremely rare [101]. Bükte et al report a case of visceral leishmaniasis with such lesions [97]. The liver was markedly enlarged, with heterogeneous, partly smooth-edged peripheral hypoechoic haloes of isoechoic or slightly hypoechoic structure, the largest of which measured 61x50 mm and contained multiple solid nodular lesions with hypoechoic necrotic regions. Microscopically, numerous intramacrophage *Leishmania* amastigotes were detected in the aspirate from the liver lesions. The authors considered the liver lesions to be abscesses [97].

Vascular changes in the liver have not been reported in visceral leishmaniasis. Since granulomatous inflammation has been histologically described in the liver in this disease, it is conceivable that imaging would find focal (granulomatous) lesions. However, such lesions have not been reported in the literature. A recent review of previous research regarding sonographic findings in visceral leishmaniasis includes 36 publications with 512 patients [102]. Among these, few publications report on focal liver lesions with a heterogeneous echopattern. As sonographic findings tend to resolve within several days to weeks after successful treatment, ultrasound can be a valuable, non-invasive tool for treatment monitoring. To the best of our knowledge, there have been no publications to date regarding the use of CEUS in the diagnostic work-up or the follow-up of visceral leishmaniasis.

## Conclusion

If focal liver lesions are detected, parasitic and, especially in immunocompromised patients, fungal diseases must be considered in the clinical context. New singular or multiple hypoechoic parenchymal lesions in patients with acute leukemia and neutropenia are highly suggestive of mycotic abscesses. In endemic areas of certain parasitic diseases again, these must be included in the differential diagnostic considerations from the beginning. This can also affect traveler returning from these areas. The manifestations on B-mode ultrasound are diverse. Parasitic liver lesions may be hypoechoic or hyperechoic lesions, complex solid or cystic lesions, well circumscribed lesions or infiltrative processes. The changes may be very bizarre in appearance, calcifications may be present. The parasitic diseases cannot be diagnosed from the sonomorphological B-scan alone. A disease such as hepatic alveolar echinococcus may manifest with multiple different appearances of focal lesions. CEUS may be helpful in parasitic abscesses to show inflammatory hyperemia of the surrounding area and non-perfused central areas. A contrast-enhancing rim has been described for quite a few echinococcal lesions. Important differential diagnoses of parasitic liver lesions are bacterial abscesses and tumors. Differentiation from tumors can be difficult in individual cases, as eosinophilic infiltrates or granulomatous changes also present as non-liver tissue on CEUS. Hepatobiliary complications caused by clonorchiasis and opisthorchiasis, such as strictures and cholangitis, can be visualised and, depending on the progression, show periductal changes as well as echogenic intraductal changes of the flukes themselves. Ascariasis can affect the entire hepatobiliary system and pancreas. The ascarids can be identified sonographically.

In the case of sonographic periportal changes, parasitic infections should be evaluated if there is a geographical prevalence of schistosomiasis. It is always important to see the lesions in the overall context. In appropriate regions of the world, parasitic diseases must be included in the differential diagnostic considerations and appropriate serological tests and stool examinations must be arranged.

**Conflict of interest:** none

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