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Ultrasound of tropical (parasitic) diseases

Christoph F Dietrich^{1,2}, Enrico Brunetti³, Nitin Chaubal⁴, Carmen Cretu⁵, Maria Teresa Giordani⁶, Beate Grüner⁷, Tom Heller⁸, Adnan Kabaalioglu⁹, Kerstin Kling¹⁰, Joachim Richter¹¹, Francesca Tamarozzi¹²

¹Department Allgemeine Innere Medizin in Hirslanden Kliniken Bern, Beau Site, Salem and Permanence, Switzerland. ²Johann Wolfgang University Frankfurt, Germany. ³Department of Infectious Diseases, San Matteo Hospital Foundation- University of Pavia, Pavia, Italy. ⁴Thane Ultrasound Centre, Thane, India. ⁵University of Medicine and Pharmacy "Carol Davila" Parasitology Department Colentina Teaching Hospital, Bucharest, Romania. ⁶Infectious and Tropical Diseases Unit, San Bortolo Hospital, Vicenza, Italy. ⁷Sektion Klinische Infektiologie, Comprehensive Infectious Diseases Center, Klinik für Innere Medizin III, Universitätsklinikum Ulm. ⁸Lighthouse Clinic Trust, Lilongwe, Malawi. ⁹Department of Radiology, Koç University Hospital-İstanbul, Turkey. ¹⁰Department of Infectious Disease Epidemiology, Robert Koch-Institute, Berlin, Germany. ¹¹Institute of Tropical Medicine and International Health, Charité Universitätsmedizin, Berlin, Germany. ¹²Center for Tropical Diseases, IRCCS Sacro Cuore Don Calabria Hospital, Negrar, Verona, Italy.

Corresponding author:

Prof. Dr. Christoph F. Dietrich, MBA, Department Allgemeine Innere Medizin (DAIM), Kliniken Hirslanden, Beau Site, Salem and Permanence, Bern, Switzerland. Schänzlihalde 11, CH-3013 Bern. T +41 31 337 88 70. christophfrank.dietrich@hirslanden.ch

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Introduction

This chapter addresses the clinical and ultrasound findings for the major parasitic diseases, including amoebiasis, ascariasis, toxocariasis (visceral larva migrans), fascioliasis, small Asian liver flukes (*Clonorchis sinensis*, *Opisthorchis spp*), cystic and alveolar echinococcosis, schistosomiasis, and melioidosis.

Amoebiasis**Introduction**

Amoebiasis is a parasitic infection caused by the protozoon *Entamoeba histolytica*. It is the third most frequent parasitic cause of death after malaria and schistosomiasis in developing countries, with an estimated 40,000 to 100,000 fatalities every year. Amoebic infection has been reported to affect approximately 12% of the world's population; in tropical and subtropical regions up to 50% of the population are affected although the majority of these infections are caused by the non-pathogenic *E. dispar*, which is morphologically indistinguishable from *E. histolytica*.

Infection is acquired by the faecal-oral route through ingestion of mature cysts passed in the faeces of infected individuals, this result from the poor sanitation, often found in resource-limited settings. After ingestion of mature cysts, excystation occurs in the small bowel. The trophozoites colonize the large intestine where they remain confined (non-invasive infection), multiplying and producing cysts that are passed in the faeces. In some patients, the trophozoites invade the intestinal mucosa (intestinal invasive disease), which causes characteristic flask-shaped ulcers, and may disseminate through the bloodstream to other sites such as the liver, lungs and brain (extra-intestinal disease) to cause amoebic abscesses.

These are usually located in the right lobe of the liver and are known as amoebic liver abscesses (ALA).

ALAs develop in less than 1% of *E. histolytica* infected patients. Adult males are affected 10 times more often than women (1). Abscesses form by coalescence of small foci of hepatic necrosis, and are made up of a central area of colliquation (“amoebic pus”) surrounded by a rim of liver tissue and inflammatory cells in which the trophozoites feed and multiply. No capsule is present.

Clinical presentation

In non-endemic areas, symptoms of ALA typically begin a few months after the patient has travelled to an endemic region and include weight loss, high fever, chills and right upper quadrant abdominal or pleuritic pain.

Hepatomegaly and jaundice may be present, as well as atelectasis, pleural effusion and an elevated hemidiaphragm. Rupture into the pleural cavity presents with cough, pleuritic pain and dyspnoea. Occasionally, expectoration of brown amoebic material can occur if there is erosion of a bronchus. Abscesses located in the left hepatic lobe may rupture into the pericardium causing pericardial effusion and tamponade. In the abdominal cavity, rupture into the peritoneum occurs in 2–7% of cases, more often with abscesses located in the left lobe, but many other structures can be involved including bowel, large vessels, bile ducts and retroperitoneum. Finally, infection may spread to the skin and the central nervous system.

Diagnosis

The diagnosis of ALA is based on clinical findings, laboratory tests including antigenic and/or serologic testing and the identification of the parasite in fresh stool and abscess material and imaging techniques. Absent history of diarrhoea does not rule out ALA. The examination of the stool for ova and parasites is often negative in extra-intestinal amoebiasis. Leucocytosis without eosinophilia, hypoalbuminaemia and elevated alkaline phosphatase are common laboratory findings. Trophozoites are occasionally observed in abscess material. Serological tests are highly useful for the diagnosis of invasive amoebiasis. Antibodies are detectable 7–10 days after the onset of symptoms and gradually decrease in the 2 months following treatment; however, they may persist for years, which limits their diagnostic value in patients

from endemic areas. Other tests like RT-PCR and antigen detection on pus are available but their role is not yet established.

Ultrasound

Liver

Ultrasound is reported to be as sensitive as CT and MRI, but very early pre-colliquative stages cannot be detected. On ultrasound, ALA lesions are typically single (in over 60% of cases), located in the right hepatic lobe near the surface of the organ, round or oval in shape. They appear hypoechoic, with initially irregular and ill-defined margins (first 4–5 days); occasionally they are hyperechoic. Later, with the progressive colliquation of necrotic material, the lesion assumes a homogeneous hypoechoic pattern, with regular, well-defined margins [Figure 1] (2, 3). This appearance typically occurs within 2 weeks. In immunocompromised patients, the amoebic abscess can assume a tumour-like or honeycomb appearance. In the healing phase, a slow progressive evolution can be observed with the lesion increasing in echogenicity and showing an irregular and ill-defined margin. Sometimes a sterile cystic cavity can persist for months or years (4-6).

Figure 1 Different sonographic appearance of ALA. Well-defined margins with almost echo-free content in a quasi-cystic ALA (a). Hypoechoic with centrally located necrotic areas (b). Large hypoechoic lesion with almost solid content (c).

a



b



c

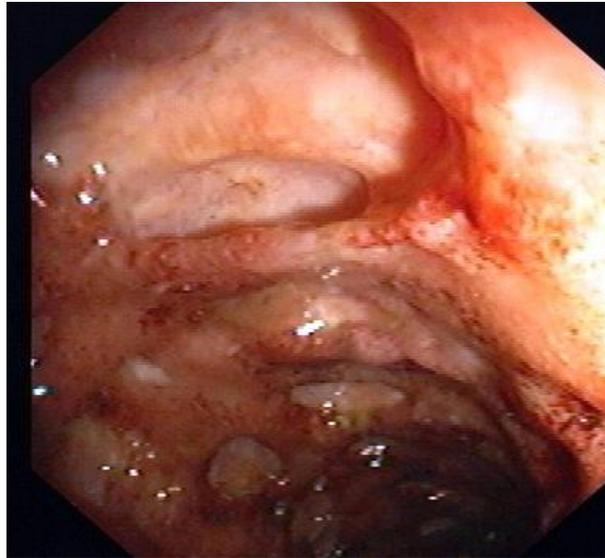


Gastrointestinal tract

Besides ALA, amoebic colitis is also often found on ultrasound where the colon wall is typically thickened and hypoechoic. Ultrasound may show the signs of severe ulcerative colitis including loss of layer structure, transmural inflammation and surrounding peri-intestinal inflammatory reaction, which are shown in Figure 2 (7).

Figure 2 Amoebic colitis. Endoscopy reveals typical ulcerations (a). Ultrasound shows the signs of severe ulcerative colitis including loss of layer structure, transmural inflammation and surrounding peri-intestinal inflammatory reaction (b).

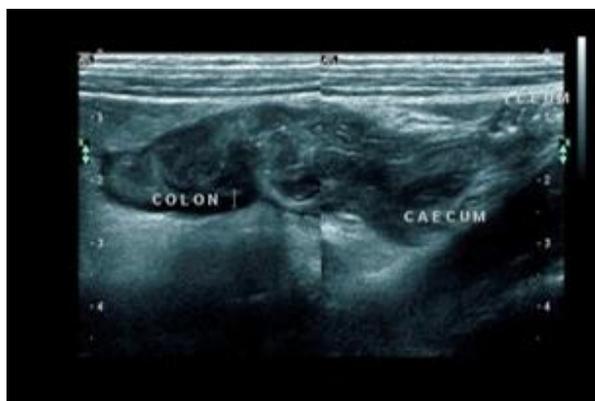
a



b



c



Amoebic colitis with its diverse clinical appearances and extraintestinal manifestations cannot be sonographically differentiated from colitis of other aetiology. Superinfection in ulcerative colitis is differential diagnosis. Attention should be paid to concomitant sonographic findings (ameboma, liver abscess) since they can be suggestive of amoebiasis despite the fact that multiple (pyogenic) liver abscesses can also occur in all acute and chronic inflammatory intestinal diseases (8, 9).

Differential diagnosis

The differential diagnosis includes pyogenic liver abscesses (PLA) (10-12), echinococcal cysts (13) and hepatic neoplasia (14, 15). Patients with pyogenic liver abscesses tend to have more severe forms of the disease; they have positive blood cultures, are often older with significant co-morbidities such as diabetes, and have a history of recent biliary disease or surgery. On ultrasound, PLA tend to be multiple with irregular and faded margins. Their echogenicity varies depending on the stage of the disease, from hypoechoic (pre-suppurative and resolution phase) to anechoic with floating or stratified echoes, or hyperechoic (suppurative phase). In the chronic phase, PLA walls may be hyperechoic with a thick fibrous capsule; they are sometimes surrounded by a thin hypoechoic halo. Echinococcal cysts are typically asymptomatic. The appearance is rarely misleading (13). However, infected or complicated echinococcal cysts may not be easily differentiated. Malignant cystic or metastatic hepatic tumours can present as cystic lesions and should be considered in the differential diagnosis of ALA (16).

Treatment

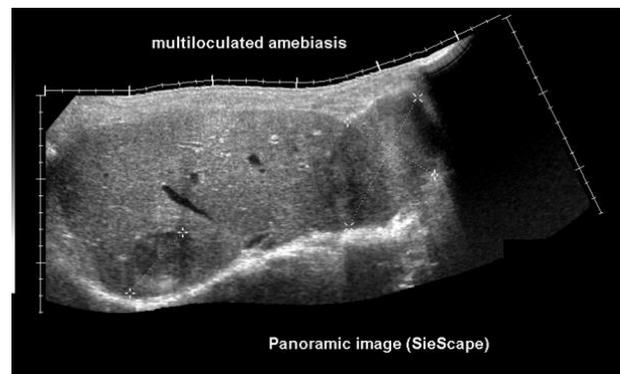
In ALA, medical treatment is the mainstay of therapy and puncture and drainage rarely required. Ultrasound-guided percutaneous drainage of abscesses followed by microscopic examination is diagnostic and therapeutic (5, 6). Amoebic “pus” has a typical “anchovy paste” appearance [Figure 3], the sonographic appearances of the punctured liver abscesses are shown in Figure 4.

Figure 3 “Anchovy paste” appearance of amoebic material drained from a liver abscess.

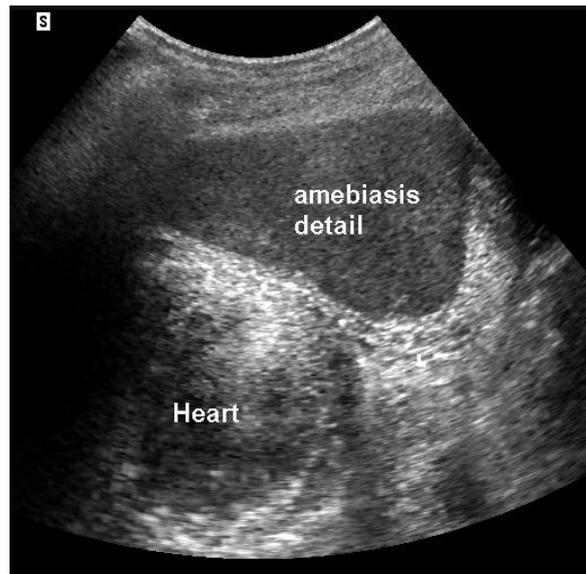


Figure 4 Amoebic abscesses. Incidental finding of multiloculated liver abscesses with liver like parenchyma echogenicity using panoramic imaging (a). Detail of the left liver lobe (b). Two hypoechoic amoebic liver abscesses; after CEUS, there is no enhancement of the lesions (c).

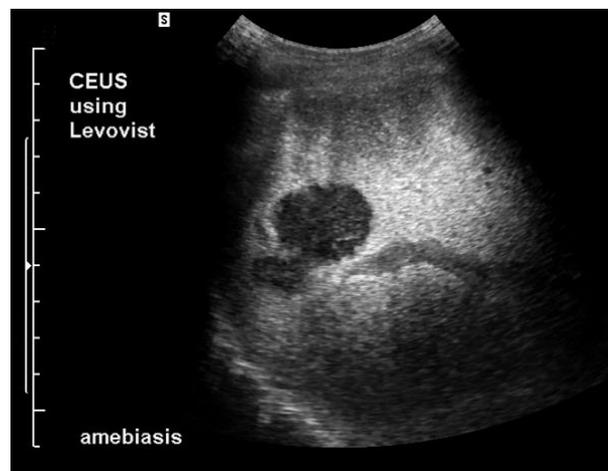
a



b



C



Primary treatment of uncomplicated amoebic liver abscess consists of a tissue agent and a luminal agent to eliminate intraluminal cysts.

Metronidazole

Patients with uncomplicated amoebic liver abscess are traditionally treated with metronidazole orally 3 x 500 mg for 7 to 10 days (17). The cure rate is >90%. Shorter duration of treatment is not recommended. Intravenous treatment generally offers no advantage since metronidazole is well absorbed from the gastrointestinal tract. In case of slow response to metronidazole or relapse following therapy, percutaneous catheter drainage, and/or a prolonged course of metronidazole may be warranted. In pregnancy, metronidazole

treatment should be considered in severe disease, but its use should be carefully evaluated since it crosses the placenta and enters the foetal circulation. Tinidazole, as compared to metronidazole in a randomized prospective study, has proven early clinical response, shorter treatment course, favourable rate of recovery, and high tolerability (18). Thus, tinidazole maybe preferred over metronidazole in ALA, at the dosage of 2 g once daily for 5 days.

Luminal agents

Following systemic treatment for invasive amoebiasis using tinidazole or metronidazole, treatment to eliminate intraluminal parasites is recommended, even if stool microscopy is negative. The most commonly used drug is paromomycin 3 x 750 mg (25 to 30 mg/kg) for 7 days if no severe colitis is present (also in pregnant women). Severe colitis is treated as mentioned above with metronidazole. As less effective alternatives, diloxanide furoate 3 x 500 mg p.o. for 10 days or chloroquine 600 mg base for two days, followed by 300 mg daily for three weeks can be used (19, 20), which are also active against the parasites in the gut lumen.

Abscess drainage

In uncomplicated amoebic liver abscess, there is no benefit for drainage in addition to medical therapy. Ultrasound-guided percutaneous drainage, and less frequently surgical drainage, is indicated in cases of imminent rupture or risk of rupture into the pericardium, treatment failure, large cysts (>10 cm) or in pregnant women. Although size is often cited as the main reason to drain ALA percutaneously, the evidence on which this decision is made is still weak and prospective studies are needed (5, 6, 21). Aspiration may be recommended for patients with lack of clinical response within 5 – 7 days, in patients with uncertainty about the diagnosis (22) and in large abscesses located in the left liver lobe (5, 6). In patients of recurrent or large abscesses drainage with pigtail catheter is preferred.

Follow up and prognosis

Ultrasound is useful for follow-up because the abscess resolution generally occurs between 10-300 days and correlates directly with the initial size of the abscess cavity (23). In approximately 5% of ALA patients' resolution is not complete and post-ALA residual lesions may be found. These are usually hypo- to isoechoic compared to liver tissue and show a

hyperechoic wall. The residual lesions have been found to persist for more than a decade and may pose differential diagnostic problems (24).

Ascariasis

Introduction

An estimated 1.2 billion people are infected by *Ascaris lumbricoides*, making ascariasis the most common human helminthic infection (25). Although most infections are asymptomatic, over 250 million people are estimated to suffer from associated morbidity, and more than 200,000 deaths are attributed to ascariasis every year. Ascariasis is a significant cause of biliary disease in areas where the rate of infection is high and *Ascaris*-infections account for up to 10-19% of all hospital admissions. Ascariasis is found throughout the world, but it is more common in warm climates and overcrowded rural communities with inadequate sewage systems (26). The infection is more common and severe among children, whereas biliary ascariasis is more common in adults (27, 28).

Adult worms live in the small intestine, usually the jejunum, in which the females produce eggs that are passed into the faeces. In the environment, the larva develops within eggs in approximately 3 weeks. Infection occurs through ingestion of material (soil, food or water) contaminated with larva containing (i.e. fertile) eggs. Once swallowed, the larvae hatch and invade the intestinal mucosa. They then migrate through the portal and then systemic circulation to the lungs. Here the larvae penetrate the alveolar walls, ascend the bronchial tree to the throat and are swallowed again. On reaching the small intestine, they develop into adult worms [Figure 5] within 2–4 weeks.

Figure 5 Adult *Ascaris lumbricoides* worm.



Clinical presentation

Although infection is commonly asymptomatic or causes only few symptoms, actively motile adult worms can migrate to different segments of the gastrointestinal tract, into the oropharynx and the nose. The most common complication of ascariasis is mechanical bowel obstruction caused by a large number of worms, which may also cause volvulus, intussusception or intestinal perforation. They can enter the appendix and cause appendicular colic and gangrenous appendicitis (27). Severe pathology is associated with the migration of the worms through the duodenal papilla into the biliary system or the pancreatic duct, resulting in obstruction, perforation or pancreatitis. In addition, the intestinal bacteria carried by the worm can induce pyogenic cholangitis and empyema of the gallbladder (28). The adult worms usually migrate out of the biliary tract shortly after inducing symptoms; however, dead worms or their fragments in the bile duct can serve as a nidus for stone formation causing obstruction, and on-going inflammation can result in the development of strictures.

Diagnosis

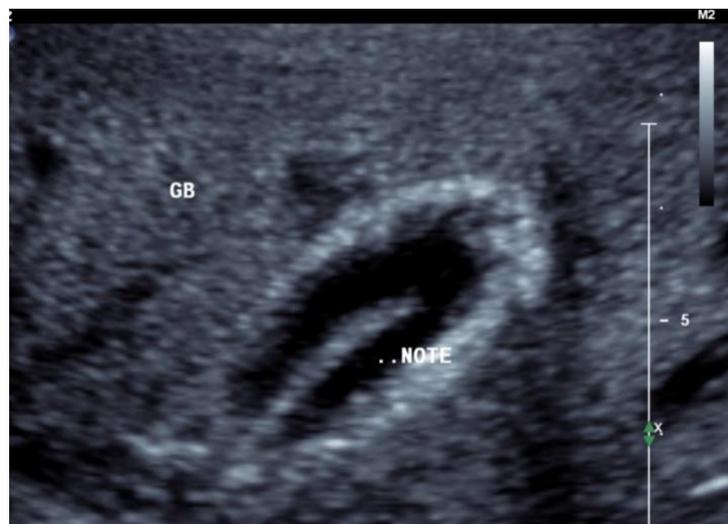
Diagnosis of intestinal ascariasis is usually achieved by parasitological stool examinations with visualization of the eggs. In patients with high worm burden the worms can be also excreted as a whole.

Ultrasound

Ascaris lumbricoides worms in the intestinal tract may be missed by ultrasound because of bowel gas. Ultrasound is a highly sensitive and specific non-invasive method for the detection of worms in the biliary tract [Figure 6], although the diagnosis of biliary ascariasis requires a high index of suspicion because the worms move in and out of the biliary tract and can be missed on biliary imaging (27, 28).

Figure 6 Ultrasound images of *Ascaris lumbricoides* in the gallbladder (a) in the common bile duct (b) and in the intrahepatic bile ducts (c) as well in the appendix (d) and the gut (e, f).

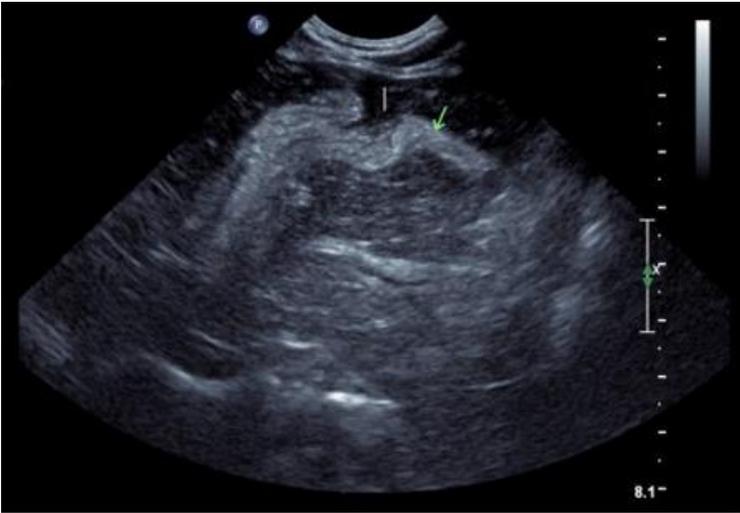
a



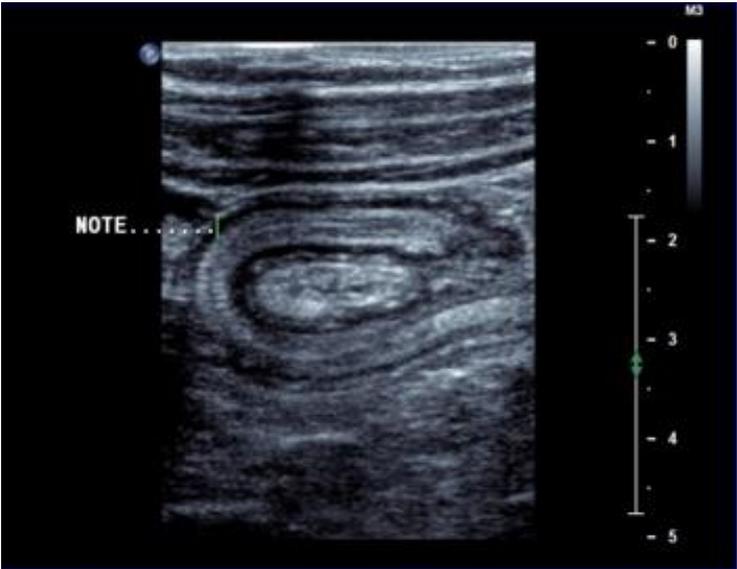
b



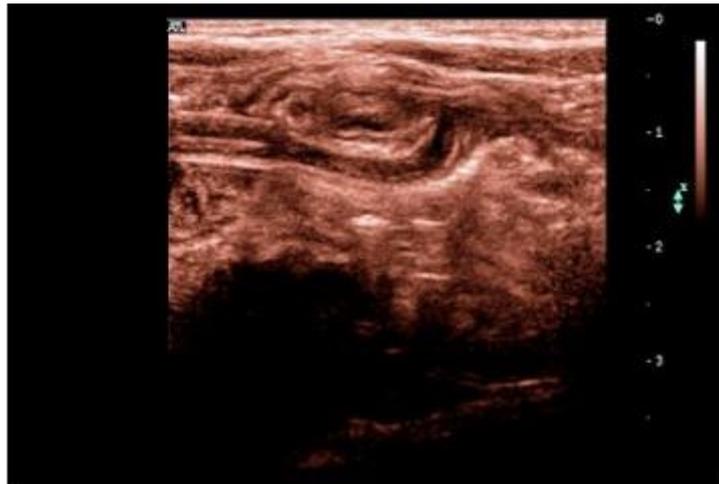
c



d



e



f



g



Adult *A. lumbricoides* are 15–35 cm long and 2–6 mm in diameter, with a peculiar sonographic appearance (29). In longitudinal sections, they have an echogenic non-shadowing tubular

structure with a hypo- or anechoic centre, and can be seen moving with a slow-waving pattern. Multiple worms in the bile duct produce a spaghetti-like image, with alternating echogenic and anechoic strips or, if densely packed in the bile duct, can appear as an hyperechoic pseudotumour. On transverse sections, a “bull’s eye” echo can be seen owing to the presence of a worm in the dilated bile duct.

Treatment

The management strategy for patients with biliary ascariasis depends on the clinical situation; it can include conservative management, endoscopic extraction or surgical intervention. In most cases, pathology resolves with pharmacological treatment and response to treatment can be monitored by ultrasound (30). Conservative treatment includes the use of analgesics, antibiotics for pyogenic cholangitis and oral administration of albendazole, which paralyses the worms so that they can be expelled. Symptoms resolve within 3 days in 60–80% of patients, accompanied by the disappearance of worms on ultrasound. Endoscopic intervention is indicated in cases of acute severe pyogenic cholangitis, recurrent biliary colic non-responsive to analgesics, high amylasaemia, and when the worms persist in the bile duct for longer than 3 weeks (probably because they are dead). Endoscopic extraction of worms across the papilla leads to rapid resolution of symptoms and can be performed using grasping forceps or a Dormia basket (31). Surgical intervention is required when endoscopic treatment fails, or if the worms are located in the intrahepatic bile ducts or in the gallbladder.

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