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Review Article

Liver Abscess Versus Verminosis: A Review

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Abstract

The objective of the present review was to update the understanding of the types of liver abscesses, namely: pyogenic, amoebic and fungal and relate this pathology with verminosis, in general. Liver abscesses remain a challenge in clinical medicine throughout the world, whether in its diagnosis and or even in its therapy. In "short" it is a serious disease that affects 8-22 individuals per group of 100,000 inhabitants. In recent decades, there have occurred changes in epidemiology, advances in diagnostics and the emergence of new therapeutic alternatives; however some causes for such pathology are still common. Medical literature discusses that parasitism is still a common cause and salutary in the understanding of liver abscess. However, in recent literature it's been evidenced that the presence of gastrointestinal helminth parasites in preschool aged children has a direct relationship with pyogenic liver abscess. It's concluded that the pyogenic liver abscess is the most common type and has verminosis as one of its main causes.

INTRODUCTION

Liver abscesses were already identified in the time of Hippocrates (40 A.C.), but, to date, remain a challenge in diagnosis and therapy. In "short" it is a serious disease that affects 8-22 individuals per group of 100,000 inhabitants and further comprises a rare clinical entity, but which presents challenges in diagnosis and treatment [1].

Microbial contamination of the liver parenchyma leading to hepatic abscess (HA) can occur via the bile ducts or vessels (arterial or portal) or directly, by contiguity. Infection is usually bacterial, sometimes parasitic, or very rarely fungal. In the Western world, bacterial (pyogenic) HA is most prevalent; the mortality is high approaching 15%, due mostly to patient debilitation and persistence of the underlying cause. In South-East Asia and Africa, amebic infection is the most frequent cause [2].

Hepatic abscess (HA) can be defined as an encapsulated collection of suppurative material within the liver parenchyma, which may be infected by bacterial, fungal, and/or parasitic micro-organisms [2]

In the early 1900s, the most common cause of HA was pylephlebitis secondary to appendicitis. In the late 1900s, biliary tract disease emerged as the most frequent culprit [3] and it remains the most common cause of HA today. More recently, there has been an increase in the incidence of HA arising in association with malignancies and their treatment [2].

In recent decades, there have been changes in epidemiology, advances in diagnostics and the emergence of new therapeutic alternatives. The overall incidence of pyogenic liver abscess remained constant with an average of six to ten cases per 100,000 hospital admissions [2].

The three major forms of liver abscess, classified by etiology, are as follows: Pyogenic abscess, which is most often polymicrobial, accounts for 80% of hepatic abscess cases in the United States, Amebic abscess due to *Entamoeba histolytica* accounts for 10% of cases and Fungal abscess, most often due to *Candida* species, accounts for fewer than 10% of cases [4].

The first liver abscess description was performed by Bright in 1836 [5]. Ochsner et al., observed that 0.0008% of hospitalized patients presented liver abscess [6], while Branum et al., reported an incidence of 0.022% [7]. Attributing, among other factors, to the increase in diagnostic features such as ultrasound and computed tomography, during the 70s, as well as to changes in the etiological pattern, particularly when related to pyogenic liver abscess. Branum et al., continued to state that, from there, the mortality also decreased, however the incidence increased [7]. In this sense, pyogenic abscesses generally represent a bacterial infection complication elsewhere in the body. The pathogens reach the liver by: the portal vein; arterial blood supply; ascending infection in the biliary tract (ascending cholangitis); direct invasion of the liver from a nearby source, a traumatic lesion [8]. However, it is important to know the etiopathogenesis for proper treatment in which, in addition to antibiotic therapy, includes abscess drainage. The two main types of liver abscesses

are pyogenic and amoebic. The pyogenic is responsible for about 90% of the cases and the amoebic represents only a tenth of the cases [8]. Furthermore, gastrointestinal helminth parasites depending on the infection can produce mechanical obstruction and cause liver abscesses [9].

The objective of the present review was to update the understanding of pyogenic, amoebic, and fungal liver abscess, and correlate them with verminosis in general.

LIVER ABSCESS: REVIEW

Pyogenic liver abscess

The pyogenic abscesses present generalities of polymicrobial infections and the most frequent agents are of enteric origin [10]. Some literatures indicate that 50 to 70 percent of pyogenic liver abscess presented gram-negative and another percentage of 40 to 50, anaerobes [11]. The current treatment for pyogenic liver abscess includes intravenous antibiotic therapy associated with drainage in which can be percutaneous or surgical [12].

Hepatic abscesses result from a bacterial infection of the hepatic parenchyma and subsequent infiltration by neutrophils and polymorphonuclears with the consequent formation of pus. A large number of pyogenic liver abscesses were diagnosed and treated through aspiration and/or percutaneous drainage [10,13]. "This technique, guided by US or CT, is suggested when there is an apparent diagnosis of pyogenic liver abscess or when there is an imprecision in the differential diagnosis between a pyogenic and an amoebic abscess" [14].

Surgical drainage was widely used in the mid-seventies and still suggested in the early 80's [15-17]; however, with improved radiological techniques, there was a gradual replacement of this approach by others, through aspiration and/or drainage guided by US or CT. The effectiveness of such techniques has been confirmed by several studies [18], demonstrating a lower morbidity and mortality, by aspiration, as well as by percutaneous drainage particularly [19].

The use of isolated antibiotic therapy has been successful [20] as occurred in two cases, in treatments with multiple small hepatic abscesses [14]. Thus, open drainage has been reserved for patients in which failure of less invasive methods occurs or when a determining factor preventing the realization of a percutaneous drainage process lasts. Additional indications for surgical drainage are: fistula association, cholecystitis, appendicitis or abscess [12,18].

Epidemiology: During the first half of the twentieth century, the pyogenic liver abscess was described as a condition that affected mainly young men. In 1938, the first major series of studies on liver abscesses was published, observing a peak incidence in the fourth life decade. In this first series, a mortality rate of 60 to 80% was observed and all the non-operated patients died. Over the past 60 years, with access to antibiotic therapy, evolution in microbial identification, the development of new radiological techniques and advances in drainage techniques, the mortality rate decreased to about 30% [21]. Peak incidence is in the fifth life decade, with the biliary tract as a starting point [21].

A potent "effort" to identify an underlying pathology is an important component in the evaluation of these patients and several research strategies are proposed. Despite the effort, in many cases, no predisposing pathology is found [22].

In a study involving patients diagnosed with pyogenic liver abscess in the service of a Spanish university hospital, in the period from 1992 to 2005, an incidence of 44.9/100,000 admissions was found, with a M:F relation of 1:1 and an average patient age of sixty-four [23].

Pathogenesis: According to a survey of seven studies conducted from 1970 to 1995, of all cases, 40% of patients were diagnosed with pyogenic liver abscess via cryptogenic infection. However, when the route is known, the biliary tree is the most responsible, followed by the portal vein, hepatic artery, trauma and direct extension [24].

The biliary tract is the main source currently responsible for the formation of pyogenic abscesses, mainly due to stasis due to bile duct obstruction caused by parasites, helminths in children, especially, calculus or expansive processes in adults, providing an ideal medium for bacterial colonization and its possible ascension to the liver [24].

Pathology: Pyogenic liver abscess is a serious disease with a mortality rate of up to 80%. It is most often located in the right hepatic lobe in 83.8%; the left, in 14.5% and in both lobes in 1.7%. It is more common in men in the fifth decade, and the mortality is higher in multiple abscesses and in the immunocompromised [22].

In developing countries, the pathogens which cause diarrhea of both bacterial (mainly by *Shigella*), and amoebic dysentery (*E. histolytica*), leads to the death of one in every thirty children before the age of five. In developed countries, the main concern is with the use of these organisms as bio-agents [25,26].

Pyogenic liver abscesses in children are rare indeveloped countries. The predisposing factors are immunodeficiencies, alterations in innate defensemechanisms, appendicitis, cholecystitis, and, less frequently, skin and respiratory infections [27]. In developing countries, reports of pyogenic liver abscess are uncommon, although some observations indicate that they are more frequent than in developed countries, even those countries where invasive amoebiasis is frequent [28].

Little is known about preexisting lesions in livers of children with pyogenic liver abscess (PLA). Study of these lesions may elucidate possible predisposing factors for the disease [29]. In Vitoria (state of Espirito Santo, Brazil) it has been reported that pyogenic liver abscesses are frequent in children from poor socioeconomic conditions and are often associated with peripheral eosinophilia and intestinal parasites [30].

In children, in particular, a common cause of pyogenic liver abscess is biliary tract obstruction caused by helminth parasites, congenital diseases and umbilical infection in newborns. Moreira-Silva and Pereira reported that eosinophilia and intestinal helminths are frequent in children with pyogenic liver abscess diagnosed in the city of Vitória, ES, Brazil. [31].

According to Pereira et al. [29], in Vitória, state of Espirito Santo, Brazil, PLA in children is frequently associated with

helminthic infections and eosinophilia. Your hypothesis is that nematode infection with larvae migrating through the liver is a predisposing factor for PLA, because the infection induces immunomodulation and likely trapping of bacteria in liver granulomas. That nematode infections, in which the larvae migrate through tissues including the liver would be a predisposing factor for pyogenic liver abscess in children. Immunomodulation induced by helminthic infections may reduce the microbicidal activity of phagocytes, thus enhancing the growth of bacteria trapped in granulomas induced by nematode larvae in the liver.

Lee and Block [32], proposed that lesions in liver tissue could be areas of bacterial colonization. These authors suggested that infection of focal areas of necrosis or scars of granulomatous hepatic lesions is a predisposing factor for the development of liver abscess.

In another study, Ferreira et al. [22], reported that sixty-five cases of pyogenic liver abscess were observed, during a period of three years, from May 1991 to April 1994 (average of 2,800 children admissions/year). Forty-seven cases occurred in males (average age of 8.1 ± 3.5 years, median of 8 years) and 18 girls (average age of 6.1 ± 3.3 years, median of seven years) with a male/female ratio of 2.7. Among the predisposing factors, these authors discriminated: skin infections (23 cases), ascariasis (six cases), trauma (two cases), and in another thirty cases predisposing factors were not diagnosed. However, helminth infections were also observed (especially with *Ascaris* and *Toxocara*), whose larvae migrate to the liver and can produce modulation of the immune response and granulomas around the larvae and antigens, which can propitiate the localization of bacteria, increasing the risk of pyogenic liver abscess, according to Lambertucci et al. [33].

Pereira et al. [29], described observations of 22 cases of PLA in children studied at autopsy (16 cases) or in surgical biopsies (6 cases), including 17 boys and 5 girls ranging in age from 1 to 13 years. Multiple abscesses in both lobes were found in 13 cases and a single abscess was found in the right lobe in 10 cases. All cases showed histologically classical pyogenic inflammation without morphological evidence of amoebiasis. In six cases there were granulomas similar to those caused by larva migransvisceralis (from *Toxocara* or other nematodes) in liver tissue not affected by the abscess. Nematode antigens in central areas of necrosis of granuloma in all six cases and fragments of a larva, possibly of *Toxocara*, were found on samples immuno histochemically stained with polyclonal anti-Toxocara antibodies. Eosinophils were found frequently in portal triads far from the abscess wall. In four cases, in which bile duct ascariasis was found, worms were noted in the bile ducts, and eggs were found in liver parenchyma surrounding the abscess in two cases. At the end of the study it can be concluded that the observation of six cases of granuloma similar to larva migransvisceralis (or produced by other nematode larva) in liver tissue not directly affected by the abscess supports the hypothesis that helminth infections with larva migrating through the liver are a predisposing factor for pyogenic hepatic abscess in children.

Macroscopically, *in vivo*, the abscess has a bronzed aspect compared to normal liver parenchyma and is fluctuating to the touch. When they are deeper, only phlogistic signs in its surroundings, are observed. Microbiology of liver abscesses is varied, in which they may be polymicrobial or represented by only one bacteria. The polymicrobial abscesses are usually derived from the biliary tree (cholangitis) or portal vein (pylephlebitis), with a microbiota prevalent in gram-negative microorganisms. The most commonly found bacteria are *Escherichia coli* and *Klebsiella* in two thirds of the cases, followed by anaerobic bacteria, which account for about 40 to 60%. Among the anaerobes, *Bacteroidesfragilis* predominates. Gram-positive pathogens are also found, mainly *Enterococcus faecalis*, *Sthaphylococus*, and *Streptococcus* [22].

Clinical manifestations: Occurrence of the pyogenic type of liver abscess is variable. Rarely asymptomatic, and may have a short duration or extend for weeks. The patient usually has a high fever (84.5%), intermittent and with shivers, abdominal pain (77.4%), especially in the right hypochondrium (39.3%) and leukocytosis with a left deviation (81%), being most often insidious, occurring for about two weeks [34].

The classic triad consists of pain in the right hypochondrium, hepatomegaly and fever with shivers [35].

Other important symptoms can be present: icterus (17.9%), anorexia (27.4%), weight loss (22.6%) and non-specific symptoms such as nausea and vomiting (17.9%, 36.9%), diarrhea, malaise and cough. Pulmonary involvement may also be observed at times, such as coughing, dyspnea, pleural effusion, atelectasis and pneumonia [34].

Diagnosis: Diagnosis is obtained by clinical manifestations, image examinations (X-ray, Ultrasound, and Computed tomography), as well as confirmation by the appearance and analysis of secretions obtained through percutaneous aspiration and surgical drainage. It is characterized classically by localized pain in the right hypochondrium, fever (moderate to high) and hepatomegaly. Shivers, malaise, anorexia, weight loss, and non-productive cough can also be associated [6,23,24].

In the physical examination, the patient presents toxemia with mucocutaneous pallor, feverish, with pain during palpation in the right hypochondrium, and hepatomegaly. The Torres-Homem sign (acute pain during liver percussion) may be present. In the lungs, crackles or diminished vesicular murmurs in the right base may be found [36].

Clinical demonstration of liver abscess is often unspecific [10,18].

Signs and symptoms most often presented are: pain in the upper right quadrant of the abdomen, fever, shivers, nausea, vomiting and anorexia. Among the laboratory findings, leukocytosis, and liver function abnormalities, particularly high alkaline phosphatase, are invariably present [10,33].

Early diagnosis or exclusion of infection and inflammation is of utmost importance for the optimal management of patients with such common disorders. However, in certain settings, these diagnoses can be made without difficulty; in most others, clinicians encounter substantial challenges in detecting and localizing the exact sites of infection [37]. The radiological image examinations, such as ultrasound (US) and computed tomography (CT) increased diagnosis capacity accuracy, where

the US is more used in first attendance, because far from being more understandable, it has a reduced value [25,11,29]. However, the CT has more accuracy than the US in the diagnosis of these lesions (sensitivity 95 to 100%); while for the US indexes are lower (85 to 95%); [14,33,38]. Magnetic resonance does not seem to offer more information than the US and CT, while the liver scintigraphy has become obsolete in the definition of the infirmity [14,33].

Modern imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) provide excellent structural resolution for visualizing advanced diseases including those related to infection and inflammation. However, these modalities are generally of limited value in detecting early disease regardless of the cause. Therefore, functional and metabolic imaging techniques are often needed to complement the role of anatomic imaging modalities in most clinical settings [37].

It is of fundamental value to note the importance of imaging procedures for a more perfect diagnosis, for they are the most valuable information for the diagnosis of a liver abscess. Chest X-rays may show diaphragm addition, pleural effusion, atelectasis, air-fluid levels below the diaphragm, commonly attacking the right side (this change may also occur in the left side, when the left lobe is affected) [33,35]. Computed tomography (CT) is the method of choice, with a sensitivity of 95 to 100%. However, due to lower cost, ultrasound (US) is the main exam responsible for the diagnosis, with a sensitivity of up to 95% [23]. The concept of positron emission tomography (PET) with 18F-fluorodeoxyglucose (FDG) was born in 1973 [39]. In spite of the great successes achieved by FDG-PET imaging in the evaluation of malignant disorders, the test is nonspecific for cancer. In fact, soon after the introduction of this technique for human studies, it was noted that lesions with substantial numbers of inflammatory cells also take up FDG. Therefore, in the appropriate settings, FDG-PET imaging can be effectively employed to detect and characterize infectious and inflammatory processes. The enhanced uptake of FDG in activated inflammatory cells such as lymphocytes or macrophages is related to significantly increased levels of glycolysis as a result of increased numbers of cell surface glucose transporters, particularly after cellular stimulation by multiple cytokines [40].

Radionuclide imaging (SPECT-CT) has been frequently used for detection and localization of infectious and inflammatory diseases for over five decades. Although there are many infection seeking agents available and currently being used but there is a general consensus that none of them is ideal. In fact, presently, the clinical utility of radionuclide infection imaging varies under different circumstances and clinical scenarios; but with the incorporation of hybrid imaging systems, the fusion of functional and anatomical data in form of SPECT-CT and PET-CT has certainly improved the sensitivity and specificity of detecting and localizing an infectious process. Ga-67 citrate, bone seeking radiotracers, radiolabelled leukocytes, antibody and antibody fragments labelled white cells are used in different clinical situations such as osteomyelitis, diabetic foot, infected vascular grafts, infected hip or knee prostheses, intra-abdominal infections including acute appendicitis, cardiovascular, pulmonary infections, malignant otitis externa with variable sensitivity and specificity. The role of radionuclide imaging in the evaluation of the patient suspected of harboring an infection varies with the situation. At the moment, in immunocompetent patients, labeled leukocyte imaging is the radionuclide procedure of choice for detecting most infections. Several tracers are available for imaging infection: 99mTc-diphosphonates, 67Ga-citrate, and 111In- and 99mTc-labeled leukocytes [41].

Similarly, the ability of F-18 FDG PET to detect infection, inflammation and granulomatous diseases due to their increased glycolytic activity has provided us with another effective agent especially in cases of fever of unknown origin, vasculitis, chronic osteomyelitis, sarcoidosis, inflammatory bowel disease and assessing response to therapy. New advances in the form of SPECT-CT have now also incremented the diagnostic capability of conventional scintigraphic procedures to localize infection. Finally, many investigational new infection seeking agents are in the process of being developed in search of an ideal. These include Tc-99m ubiquicidin, Tc-99m labelled Interleukin-8, N-formyl products, chemotactic cytokines etc. Therefore, with on going research in development of infection specific agents and the advent of hybrid imaging the future offers definite hope for better infection detection and localization in our patients [41].

Laboratorial alterations are frequent, especially leukocytosis with left deviation, and anemia. Liver function is usually affected, altering the albumin, TAP, and bilirubin parameters. AST and ALT are often high (60% of cases), as well as alkaline phosphatase and gamma GT. These laboratory tests are nonspecific, but suggest some liver disorders [35].

A positive blood culture is found in half the patients, while the aspirate culture can be positive in up to 90%. The differential diagnosis is done with liver cancer, nephrotic abscess, subphrenic abscess, acute cholecystitis, acute appendicitis, cholangitis, pleurisy, lung abscess, and general serious infectious diseases (typhoid fever, tuberculosis, mononucleosis, malaria). The transmural diagnostic puncture has therapeutic orientation function [42].

Treatment: The open drainage was the only treatment for liver abscess with a not very satisfactory result. However, with the advent of antibiotics and minimally invasive methods, there is a better prognosis in these patients. In the 70s and 80s, this drainage was open, but, with the advent of accurate radiological methods, doctors opt for a less invasive drainage, the percutaneous [22].

Antibacterial therapy should begin as soon as blood has been obtained for identification of organisms [2] and the patients are typically treated initially with IV antibiotics, followed by a course of oral (PO) antibiotics. Treatment is based on broad-spectrum antibiotics for three to six weeks (can be extended up to twelve weeks). Treatment duration depends on both response to treatment, as determined by repeat US imaging, and resolution of fever and leukocytosis [43]. The drainage can be surgical or percutaneous. Several antibiotics schemes are proposed, including: Ciprofloxacin+metronidazole or ampicillin+sulbactam [42]. Empiric coverage for gram-negative *bacilli*, gram-positive cocci, as well as anaerobic bacteria has been recommended. This is usually accomplished with a third-generation cephalosporin

plus metronidazole or piperacillin/tazobactam [43]. In liver abscess due to *Ascaris*, the approach is clinical with intravenous antibiotic therapy; if evolution is not satisfactory, there will be surgical indication [44-47]. However, some common pathogens associated with HA are resistant to both ampicillin and the fluoroquinolones. Treatment is becoming complicated as the incidence of a hyper-resistant *K.pneumonia* increases in some parts of the world [43].

Biskup et al. [48], proposed that smaller abscesses in difficult anatomical positions, such as in the caudate lobe, may be best treated conservatively due to the increased risks associated with invasive management. In a larger study of 176 patients, an 81.2% success rate after antibacterial treatment was reported [49]. In other study the management with antibiotics alone has been shown to be effective for small abscesses, <3-5 cm in diameter [2]. Hope et al. [5], reported a 100% success rate for eight patients with unilocular abscess measuring <3 cm in diameter with antibiotics alone.

Table 1 summarizes the therapeutic options facing a pyogenic liver abscess situation. The percutaneous drainage, guided by ultrasound or CT can be used in several cases, except in multiple microabscesses, when ATB intravenous therapy is opted.

Indications for percutaneous drainage:

1. Abscesses.
2. Patients with sepsis and hemodynamic instability when there is no time to wait for blood cultures and serologic test results.
3. In association with ATB (drainage after two days of treatment with antibiotics).
4. Patients with culture and serology that do not respond to established therapies.
5. Malnutrition, failure in clinical treatment, superinfection. Important to remember that the obstruction of the biliary tree, if present, should be treated with ERCP (Endoscopic retrograde cholangiopancreatography) the most appropriate choice.

Escherichia coli is the most common causative pathogen of PLA in most countries [7]. However, in the past three decades, *Klebsiella pneumoniae* has emerged as the single leading cause of PLA in East Asian countries, especially in Taiwan. A distinct syndrome of community-acquired pyogenic liver abscess, which is complicated by metastatic endophthalmitis or central nervous system (CNS) infections, has been reported since 1986, especially in patients with diabetes [51].

Taiwan is endemic for pyogenic liver abscess (PLA). Septic ocular or central nervous system (CNS) complications derived from PLA can result in catastrophic disability [52]. Lin et al. [52], indicate that septic ocular or CNS complications accounts for 2.1% of PLA patients in Taiwan. Septic ocular or CNS complications are more likely to develop in younger and diabetic, but otherwise healthy, patients.

According to Fang et al. [53], since 1986, researchers have noted a syndrome of *Klebsiella pneumoniae* pyogenic liver abscess that is complicated by endophthalmitis or central nervous system infections. There are limited data regarding the role of bacterial genotype in the pathogenesis of this syndrome. They did a retrospective cohort study that focuses on the predictors for the development of septic ocular or CNS complications in patients with *K. pneumoniae* pyogenic liver abscess. Of the 19 cases in which genotype K1 strains caused complications, 8 patients (42%) did not have identifiable underlying medical diseases and the Conclusion was that the *K. pneumoniae* genotype K1 is an emerging pathogen capable of causing catastrophic septic ocular or central nervous system complications from pyogenic liver abscess independent of underlying diseases in the host.

Prognosis: Prognosis is worse the younger the child, a statistically proven fact. As for multiple abscesses, hypoalbuminemia, associated malignant diseases, icterus, among others, poor prognostic factors are also implicated [33].

Some complications are feared, such as pulmonary alterations (atelectasis, bronchopleural fistula, and empyema), rupture to the peritoneal or thoracic cavity, and thrombosis in the portal vein, cava, or superior mesenteric and sepsis, which can worsenthe condition even more. Mortality due to liver abscess was great. With the development of diagnostic methods, treatment with surgical drainage and/or percutaneous drainage, broad-spectrum antibiotics, the mortality rate dropped to 31% [22,42].

Diagnosis delay and failure to establish a treatment may result in worsening the prognosis.

Amoebic liver abscess

In 1842, Miguel Jimenez described a case of liver abscess draining into the bronchus. It was a serious liver infection, abscessed secondary to intestinal amoebiasis [54].

Etiology: This type of abscess is an infection caused by a

Table 1: Liver abscess therapeutic options.

ANTIBIOTIC THERAPY Empiric According to blood culture results
PERCUTANEOUS DRAINAGE Transpleural Reserved for any abscess origin Transperitoneal If possible, the abscess must be maintained in external drainage until its debt is less than 10 mL/day (in which case the drain can be safely removed). Extra-peritoneal Monitor temperature: occurrence of fever for more than 14 days after the procedure may indicate the need for more aggressive drainage
Adapted from: FERREIRA et al., 2007

protozoan presented in two forms: cyst and trophozoite. This parasite can act commensal or cause tissue invasion, originating the intestinal and extra intestinal forms of the disease. The clinical condition varies from a mild form, characterized by mild or moderate abdominal discomfort, with blood and/or mucus in excrements, to an acute and fulminant diarrhea, of a bloody or mucoid character, accompanied by fever and shivers [55].

Remission periods may or may not occur. In severe cases, trophozoite forms spread through the blood stream, causing abscesses in the liver (most often), lungs, or the brain. When not diagnosed in time, they can lead to the patient's death [54].

The main sources of infection are ingestion of contaminated food or water by feces containing mature amoebic cysts. It occurs, more rarely, through sexual transmission due to oral/anal contact. Lack of household hygiene can facilitate the spread of cysts in the family components. Asymptomatic carriers, who handle food, are important disseminators of this protozoosis [54].

Epidemiology: More than 10% of the world population is infected with *Entamoeba dispar* and *E. histolytica*, which are species morphologically identical, but only the latter is pathogenic, being valued at fifty million invasive cases/year. In developing countries, the infection prevalence is high, being that 90% of those infected can eliminate the parasite for a period of twelve months. Infections are transmitted by cysts through the fecal/oral route. Cysts within the human host, release the trophozoites [45,46].

The transmission is maintained by cyst elimination in the environment that may contaminate food and water. These cysts remain viable in the environment away from sunlight and under favorable moisture conditions for about twenty days. Its occurrence is associated with inadequate sanitation, personal/environmental hygiene deficiency, and certain sexual practices. Amoebiasis is an infection caused by *E. histolytica*, a protozoan of universal distribution that predominates in tropical and developing areas, where the socioeconomic and sanitary conditions are poor. It can be associated with acute or chronic diarrheal infections, or even develop with severity and involve other organs such as liver, lungs, brain and skin. The most frequent manifestation of its extra-intestinal form is the liver abscess [56].

Unlike the pyogenic abscess, the amoebic abscess affects individuals aged between 20 and 40 years old, prevenient from an endemic area for amoebiasis (or travel history), mainly male, with a ratio of 19:1 (M:F) [45,46].

Regarding the amoebic life cycle, it is essential to remember that the protozoan has two life forms, cyst and trophozoite, the latter being responsible for human infection and disease development. Protozoa reach the liver via portal circulation, where they multiply causing obstruction of the small portal radicles. There is proteolytic enzyme synthesis, resulting in liver parenchyma destruction and necrosis, forming a cavity rich in cellular debris and trophozoites, marking the beginning of the amoebic liver abscess formation [57].

The macroscopic appearance is notorious as "anchovy paste". The liver parenchyma necrosis continues until reaching the Glisson's capsule. The patient's immune status is essential for the development of this disease. It became necessary to investigate immunosuppressive factors in patients from non-endemic areas, without travel history to endemic areas, who developed amoebic liver abscess. Some factors that reduce host resistance are known, such as pregnancy, alcohol abuse and immunosuppression [45,46].

Clinical manifestations: The typical disease condition consists of male patients, between 20 and 40 years old, from an endemic area, presenting fever with shivers (note that amoebic abscess is an important cause of fever of unknown origin in developing countries), anorexia, severe pain in the right hypochondrium, constant, especially during palpation, as well as hepatomegaly. Associated with the above, other symptoms may be present, such as nausea, weight loss, diarrhea, icterus, and cough. Some patients may have pulmonary involvement of the right base, such as pleural effusion, empyema, and elevation of the hemidiaphragm [57].

Diagnosis:

a) Laboratory exams**:** In amoebic liver abscesses, the complete blood count may show leukocytosis and anemia. The liver function tests may be altered.

The definitive diagnosis of amoebic abscesses is in the presence of *Entamoeba histolytica* trophozoites in the aspirated material. Since over 70% of patients do not have intestinal amoebiasis, laboratory evaluation of circulating anti**-**amoebaean antibodies, if performed, increase the specificity of the diagnosis since it can be detected in 90 to 95% of cases. The most used method is the indirect hemagglutination, with a sensitivity of 90%. This exam's disadvantage is the permanence of a high titling even after being cured, which may hinder the diagnosis in endemic areas [42].

b) Radiological exams: Radiological examinations are also fundamental for the diagnosis of amoebic liver abscess. Chest X-rays can show elevation of the right diaphragm, pleural effusion or atelectasis. Abdominal ultrasound is the most widely used method for the diagnosis and monitoring of patients with amoebic liver abscess, with a sensitivity of 90%. The characteristic feature is the presence of a rounded injury, near the hepatic capsule, without echoes in its periphery, representing the abscess's wall, with a hypoechoic and inhomogeneous content. According to the evolutionary stage, one can observe different sonographic patterns: *Amoebic hepatitis* (pre-suppurative phase), when normal hepatic parenchyma or mild hypoechoic zone without limit and with an adjacent normal parenchyma is observed, and *Amoebic necrosis*, presenting a cavity with hypoechoic necrotic content or even, later on, a cavity with a liquid content, anechoic and no true capsule Computed tomography (CT) is also widely used, with greater sensitivity, especially on small and multiple abscesses [45,46].

Complications: The main complications are abscess rupture (3 to 17%), which in 2/3 of cases occurs to the peritoneum, causing peritonitis, and 1/3 ruptures to the lungs, causing pleural empyema, pneumonia or lung abscess; and secondary infection which leads to significant worsening of the general condition [46].

Fungal liver abscess (FLA)

The liver abscess caused by fungus (FLA) is a rare condition and has a high mortality rate, especially in immunocompromised patients. The publications were investigated in LILACS and MEDLINE, being the inclusion criteria confirmation of the etiologic agent. One hundred and one articles were selected from literature, of which 61 (60.4%) were included and 40 (39.6%) excluded [47].

In the analysis of the 61 articles, there was description of 169 patients with FLA, and for each a standard questionnaire was completed. Attention was drawn to the lack of information in many cases. Of the 169 patients, 53.8% were female; and the mean age was 31.5 (± 18.8) years old. *Candida sp*. was described in 146 (84.6%) cases; and 84% had an associated neoplasia. Amphotericin B was the most used antifungal medication (95.4%) (Despite these results, almost all (98.8%) of FLA reports in literature were evaluated as low quality, with 8-49 points of the 92 possible. In conclusion, in addition to the scarcity and poor data quality, which greatly compromise literature publications, the lack of uniformity on the subject also indicates the need for further studies, and the existence of many gaps in FLA knowledge [45-47].

It is believed that helminth infections, especially those that produce larvae migrants that can pass through the liver, can also lead to pyogenic liver abscess and may cause modulation of the immune response; granulomas surrounding the migrant larva (or their antigens) can function as a localizing injury for bacteria in the liver, where high frequency of helminth infection in cases of pyogenic liver abscess is ascertained [45,58].

REPORT

In a retrospective study in a children's hospital in the state of Espírito Santo, southeastern Brazil, Morais et al. [58], demonstrated that a major cause of liver abscesses in those patients (2001-2012) was parasitism by *Ascaris lumbricoides*. In that study, the high prevalence, especially in poor populations and children, was due to poor sanitation, housing and education. These authors drew attention to the need for implementation of government programs that can reverse the municipalities' poor hygiene and health conditions issues.

Morais et al. [58], unpublished data, showed that in the period of 2001-2012 the results for stool analysis exams (SAEs), noted in the medical charts, were positive for helminths, especially for *Ascaris lumbricoides*. Also observing: (a) cases with elimination of this "worm", orally and/or anally, with negative SAEs; (b) positive SAEs (without elimination); and (c) elimination of the "worm" with positive SAEs. In the medical records used for the analysis, 90% presented an incidence of fever and only 10% had no fever. Of the total medical charts analyzed, 73% of them presented *A. Lumbricoides* and 27% of them did not. Of the records analyzed, it was found that 71% of them showed eosinophilia and 29% of them did not. Other data recorded by these authors and not yet published in the scientific community was the presence of *Toxocaracanis* in the SAEs.

Medical literature reports that the severity of the disease induced by the migratory phase of *Ascaris lumbricoides* correlates with the number of larvae that migrate simultaneously [44-46]. However, infection by this nematode, when in a mild degree, is usually unapparent.

Lastly, it is mentioned that gastrointestinal helminthiasis can be considered as one of the main causes of liver abscess, since they have high prevalence, especially in low-income populations and pre-school aged children. Thus, there is a clear need to implement government programs that attempt to reverse the poor hygienic and sanitary condition issues of the cities. It is known that health education for children is an essential factor for ascariasis control, especially considering the characteristics of the disease during childhood: high prevalence, high resistance percentage to treatment, high egg elimination rates and high levels of reinfection.

CONCLUSION

Hepatic abscess is a severe condition that can be life threatening. Diagnosis relies mainly on imaging (CT scan). The frequency of etiologies varies from one geographical region to another. In Europe, most classical HA is bacterial, arising as a complication of biliary disease. In Asia, but also more and more frequently in Europe, HA due to *K. pneumoniae* is being found, possibly arising from hematogenous seeding and capable of giving rise to ocular and/or meningeal septic metastases [2].

Despite its low incidence, HA is associated with a relatively high mortality rate and several serious complications. For these reasons, prompt recognition is important in instituting effective management and achieving good outcomes. Because of the nonspecific symptoms and laboratory findings, the presence of predisposing factors can be helpful in increasing the level of diagnostic suspicion [59].

For bacterial HA less than 3-5 cm in diameter, antibiotics alone should be adequate therapy, but needle aspiration helps to identify the responsible germ(s) and evacuate the contents as well as to identify biliary communication. For larger bacterial HA, antibiotics should be combined with radiological interventional or, more rarely, surgical management. Irrespective of the size of bacterial HA, it isimportant to determine the etiologic mechanism [2].

A comprehensive and collaborative management of PLA via the combined efforts of multiple medical subspecialties is necessary to tackle this problem in the future [52].

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