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REVIEW ARTICLE

Amebic Abscess—Is it still a Common Entity?

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ABSTRACT

Amebic liver abscess is the most common extraintestinal manifestation of amebiasis. It is seen most frequently in the fourth and fifth decades of life and is more common among adult men and alcoholics. The infection is primarily transmitted by food and water contamination. It presents commonly with fever and right hypochondriac pain but can present with complications like rupture into the pleural and peritoneal cavity or with abdominal vein thrombosis. The infection still responds well to nitroimidazoles, which remain the mainstay of treatment. In India, the epidemiology and presentation of amebic abscess have not changed over the years and it still is the major cause of liver abscesses.

Keywords: Amebic, Liver abscess, Metronidazole.

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INTRODUCTION

Amebic liver abscess is the most common extraintestinal manifestation of amebiasis. It still accounts for less than 1% of *Entamoeba histolytica* infections.[1]

Epidemiology

Amebic liver abscess (and other extraintestinal disease) is seen most frequently in the fourth and fifth decades of life.[2] It is 7 to 10 times more common among adult men though there is equal gender distribution of colonic amebic disease. Suggested mechanisms for this gender difference are alcohol consumption causing Kupffer cell depression and protective effect of estrogen.[3] Areas with high rates of amebic liver abscess include India, Africa, Mexico, and parts of Central and South America. Indian studies have reported amebic liver abscess to account for three-fourths of all cases of liver abscess, with a mean age of presentation of 40 years with an alcoholic male predominance.[4-6] In a recent Indian study of 200 patients of liver abscess, amebic liver abscess accounted for 69% of the cases.[4] Another study reported a high rate of complications (~30% pleuropulmonary and intraperitoneal rupture) but this could be due to referral bias to a surgical unit.[5] A study in the emergency unit showed a mortality of 5.8% with number of pigtail catheters inserted correlating with mortality.[6] Data from our institution where 200 patients with liver abscess were analyzed over a period of 3 years, amebic liver abscess accounted for 72% of the cases, with a male to female ratio of 8:1 and an average age of presentation of 42 years. Most of our patients were alcoholic (62%); however, the incidence of liver cirrhosis was low among these patients (4%). A high content of iron (present in country liquor) and carbohydrate in the diet predisposes to invasive amebiasis.[7] In developed countries, amebiasis is generally seen in migrants from and travelers to endemic areas. Sexual oral–anal contact may also account for acquisition of infection.[8] The mortality rate has been estimated to be around 0.2 to 2.0% in adults and up to 26% in children.[9]

Pathogenesis

The infection is primarily transmitted by food and water contamination. Rarely transmission via oral/anal sex or direct colonic inoculation during colonoscopy has occurred. *Entamoeba histolytica* exists in two forms. The cyst stage is the infective form, and the trophozoite stage causes invasive disease. The cyst wall is broken down by trypsin in the small intestine. Trophozoites are released and colonize the cecum. To initiate symptomatic infection, *E. histolytica* trophozoites present in the lumen must adhere to the underlying mucosa and penetrate the mucosal layer.

Liver involvement occurs following invasion by *E. histolytica* into mesenteric venules. Amebae then enter the portal circulation and travel to the liver where they typically form one or more abscesses. The *E. histolytica* galactose/N-acetyl-D-galactosamine lectin is an adhesion protein complex, which sustains tissue invasion.[10] The abscess contains acellular proteinaceous debris, which is thought to be a consequence of induced apoptosis and is surrounded by a rim of amebic trophozoites invading the tissue. The right lobe of the liver is more commonly affected than the left lobe. This is because the right lobe

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portal blood flow is supplied predominantly by the superior mesenteric vein, whereas the left lobe portal blood flow is supplied by the splenic vein.

Risk factors for amebic liver abscess are alcoholism, malignancy, human immunodeficiency virus (HIV) infection, malnutrition, corticosteroid use, disorders of cell-mediated immunity, and homosexual activity. Alcohol suppresses function of Kupffer cells (specialized macrophage) in liver, which clear the amebae. Defects in cell-mediated immunity are attributed to cause unchecked invasive amebiasis.[11]

Clinical Manifestations

Patients with amebic liver abscess usually present with 1 to 2 weeks of right upper quadrant pain and fever (38.5–39.5°C). Pain may be referred to the epigastrium, the right chest, or the right shoulder. The pain is usually dull but may be pleuritic or aching. Other symptoms may include cough, sweating, malaise, weight loss, anorexia, and hiccoughs. Concurrent diarrhea is present in less than one-third of patients, although some patients report history of dysentery within the previous few months. Jaundice occurs in less than 10% of patients.[2] Physical examination reveals hepatomegaly and point tenderness over the liver in approximately 50% of cases. Localized tenderness in the region of the abscess, most commonly at the lower right intercostal spaces, is frequently seen. Hepatomegaly may not be detected in patients with abscess at subdiaphragmatic location. Movement of the right side of the chest and diaphragm may be restricted with dullness on percussion.

Rupture of liver abscess can occur into any adjoining space or organ; extension into the chest occurs almost four times as often as extension into the peritoneal cavity. In up to 7% of cases, the abscess ruptures into the peritoneum, causing peritonitis.[12] Hepatic vein and inferior vena cava thrombosis secondary to amebic liver abscess have also been described.[13] Occasionally, patients have a more chronic presentation with months of fever, weight loss, and abdominal pain with or without hepatomegaly. No differences in clinical manifestations or radiographic findings in HIV-infected individuals as compared with seronegative individuals with liver abscess have been observed.[11] Uncommonly, patients with amebic hepatic abscesses may also have localized colonic infection resulting in a mass of granulation tissue forming an ameboma, which may mimic colon cancer.[14] Patients with secondary cardiac or pulmonary involvement may present with symptoms primarily due to these complications.

Diagnosis

Amebic liver abscess should be suspected in the setting of fever and right upper quadrant pain together with relevant epidemiology (resident in, migration from, or travel to an endemic area). In such circumstances, the diagnosis may be supported by radiographic imaging of the liver. In the setting of suggestive findings on imaging studies, confirmatory serologic or antigenic testing should be pursued, perhaps supplemented with stool microscopy or antigenic testing of stool, with or without evaluation for the parasite in liver abscess fluid. However, simultaneous liver abscess and amebic colitis are uncommon, so stool microscopy and polymerase chain reaction (PCR) are usually negative in the setting of liver abscess.

Laboratory Investigations

General findings

Raised bilirubin, leukocytosis (75% cases), raised transaminases and alkaline phosphatase (nonspecific), and raised markers of acute inflammation may be seen.

Imaging

Radiographic imaging of the liver can be pursued with ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI). Ultrasonography (USG) usually demonstrates a cystic intrahepatic cavity. Amebic liver abscesses are most commonly found in the right lobe; 70 to 80% are solitary subcapsular lesions, although multiple lesions can be present.[15] Localization in the left lobe predisposes to extension into the pericardial sac. On ultrasound, the abscess appears as a round, well-defined hypoechoic mass without significant wall echoes. On CT scan, it appears as a low-density mass with a peripheral enhancing rim. On MRI, the abscess appears as low signal intensity on T1-weighted images and high signal intensity on T2-weighted images. After healing, the periphery of the abscess may calcify as a thin, round ring.

A chest radiograph abnormality will be observed in approximately 50% of patients with an amebic liver abscess, most commonly elevation of the right hemidiaphragm. This finding does not necessarily signal pulmonary involvement in the infection.

On gallium citrate and technetium-labeled sulfur colloid radionuclide liver scans, amebic abscesses are "cold" (with a bright rim in some cases), whereas pyogenic abscesses are "hot."[15]

Serial imaging is generally not helpful since lesions may appear to increase in size or number on ultrasound following initiation of treatment, even with appropriate therapy and clinical improvement. Treated lesions may become anechoic, calcified, or may persist as cystic-appearing lesions. Complete radiologic resolution may take 2 years or more. Therefore, persistent abnormalities

on ultrasound imaging should not prompt retreatment or additional testing in a patient who is clinically well.[16]

Serology and Antigen Detection

Approximately 99% of patients with amebic liver abscess develop detectable antibodies, but serologic testing may be negative in the first 7 days. Serum antibodies are detectable in 92 to 97% of patients at the time of presentation.[17] In endemic areas, up to 35% of uninfected individuals have antiamebic antibodies due to previous infection with *E. histolytica*. Therefore, negative serology is helpful for exclusion of disease, but positive serology cannot distinguish between acute and previous infection.[18]

New serologic tests based on recombinant *E. histolytica* antigens have been developed. In these tests, patients lost seroreactivity with the recombinant antigens more rapidly than with conventional serologic tests; such assays may be especially useful in endemic areas.[19]

Aspiration

Needle aspiration under ultrasound or CT guidance or insertion of a pigtail catheter is not routinely required but may be warranted if the cyst appears to be at imminent risk of rupture (particularly for lesions in the left lobe), if there is clinical deterioration or lack of response to empiric therapy, or if exclusion of alternative diagnoses is needed. In some cases, aspiration may be therapeutic as well as diagnostic.

Amebic liver abscesses contain acellular, proteinaceous debris, and a brown fluid likened to "anchovy paste," consisting predominantly of necrotic hepatocytes. Trophozoites are seen on microscopy of the aspirate in fewer than 20% of cases and are often present only in the peripheral parts of the abscess, invading adjacent tissue. Antigen testing and/or PCR on aspirated material may also be helpful in establishing the diagnosis.[20] In rare cases, amebic hepatic abscesses can become secondarily infected with enteric bacteria, so aspirated fluid should also be sent for bacterial culture.

Differential diagnosis: The differential diagnosis of amebic liver abscess includes pyogenic liver abscess, malignancy, and hydatid cyst disease, which can be differentiated from amebic liver abscess by radiology with reasonable accuracy.

Treatment: Management options include medical therapy (Table 1), USG-guided aspiration, percutaneous catheter drainage, and laparotomy. Uncomplicated abscesses may be managed by medical therapy. Nitroimidazoles are the drug of choice and should be given for at least 10 days. Relapses may be treated with the same drug for up to 3 weeks.[21] The response is seen within 48 to 72 hours with the disappearance of toxemia.

Aspiration is indicated in the following situations:[22]

- Lack of clinical improvement in 48 to 72 hours
- Left lobe abscess
- Large abscess having impending rupture/compression sign
- Subcapsular abscess (tissue rim <10 mm)
- Seronegative abscesses

Percutaneous drainage is indicated when the collection is not getting aspirated by needle or there is failure of USG-guided aspiration.

Table 1: Treatment of amebiasis

Medication	*Adult dose*	*Pediatric dose*	*Side effects*
Amebicidal agents	750 mg orally three times a day for 5–10 days	30–50 mg/kg/d for 5–10 days orally in three divided doses	Psychosis, seizures, peripheral neuropathy, and a metallic test
Metronidazole	500 mg intravenous (IV) every 6 hours for 5–10 days	15 mg/kg IV load followed by 7.5 mg/kg every 6 hours (maximum, 2250 mg/d)	
Chloroquine (base) (used as an alternative or adjuvant)	600 mg/d orally for 2 days, then 300 mg/d orally for 14 days	10 mg/kg of chloroquine base	Diarrhea, abdominal cramps, cardiotoxicity, seizures, and hypotension
Tinidazole (preferable to chloroquine)	2 gm/day for 3–5 days		
Luminal agents (used to eradicate intestinal colonization after amebicidal treatment)			
Paromomycin	25–30 mg/kg/d orally for 7 days in three divided doses	25 mg/kg/d orally for 7 days in three divided doses (maximum 2 gm/d)	Diarrhea
Iodoquinol	650 mg orally three times a day for 20 days	30–40 mg/kg/d for 20 days in three divided doses (maximum 2 gm/d)	Contraindicated in patients with hepatic insufficiency or hypersensitivity to iodine
Diloxanide furoate (indicated in patients who fail to respond to iodoquinol and paromomycin)	500 mg orally three times a day for 10 days	20 mg/kg/d in three divided doses	

Surgical drainage is rarely indicated and may be required in the following cases:[23]

- Large abscess with a poor yield on needle aspiration or percutaneous drainage
- Clinical deterioration despite attempted needle aspiration
- Ruptured abscess in peritoneal cavity with features of peritonitis
- Rupture in the pleural cavity/pericardial cavity/adjacent viscera

Long-term follow-up of patients: The mean time for the disappearance of the sonographic abnormality is 6 to 9 months. Relapses are very uncommon.

The patterns of resolution seen on sonographic follow-up include: Type I: Complete disappearance of the cavity occurs within 3 months (29.8%), Type II: A rapid reduction till 25% of the original cavity size, and then a delayed resolution (5.9%).[24]

Factors influencing healing time include the size of abscess cavity at admission, hypoalbuminemia, and anemia. The total abscess volume of all the cavities is the most important factor that influences resolution time in multiple abscesses. As clinical resolution does not correlate with USG resolution, it is suggested that the results of the therapy should be monitored by clinical criteria rather than USG.

Independent risk factors for mortality in amebic liver abscess are a bilirubin level >3.5 mg/dL, encephalopathy, volume of abscess cavity, and hypoalbuminemia (serum albumin <2 gm/dL).[25]

CONCLUSION

Amebic liver abscess still remains the most common cause of liver abscess in our country. The presentation and clinical profile remain unchanged to what was seen previously with a predominance in middle-aged alcoholic males. *Entamoeba histolytica* still remains sensitive to nitroimidazoles and can be treated effectively with a combination of medical and drainage techniques.

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