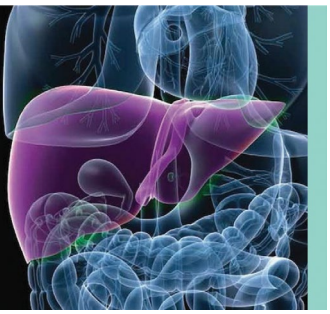

Liver Abscess: Complications and Treatment

Sanchit Sharma, M.D., D.M., and Vineet Ahuja, M.D., D.M.

Liver abscess is an inflammatory space-occupying lesion of the liver caused by infectious agents. Amoebic liver abscess (ALA) and pyogenic liver abscess (PLA) are its two predominant causes. Rarely, liver abscess can be caused by fungi, mycobacteria, and other atypical organisms. ALA is the predominant cause of liver abscess in India, seen in more than 60% of cases.[1] It is caused by *Entamoeba histolytica* with feco-oral route, the predominant mode of transmission. In this review, we describe the overview of ALA and PLA, along with its complications and management.

AMOEBIC LIVER ABSCESS

Overview

Amoebiasis is endemic in India and primarily affects the gastrointestinal tract. ALA is the most common extraintestinal involvement in amoebiasis, seen in 3% to 9% of cases.[2] The disease usually occurs in male patients in the 20 to 45 years age group. Risk factors include chronic alcohol use, diabetes, cirrhosis, and retroviral disease. The clinical presenting features include fever, pain in the abdomen, and anorexia. Jaundice can be seen in about 15% of patients with ALA and is usually associated with a large and/or multiple abscesses and compression of biliary tree by an abscess near porta hepatis or caused by concomitant alcoholic hepatitis.[1] Although classically described as a solitary abscess in the right lobe of the liver, 35% of patients may have a left lobe liver abscess with or without a right lobe abscess, and 15% of patients can have multiple liver abscesses.[3] Recognizing the unusual variants of ALA is important because these are generally associated with complications (Table 1).[2] The clinical course of ALA is usually benign in the absence of poor prognostic markers (Table 2).[1,4]

Diagnosis

Clinically and radiologically, ALA may be difficult to distinguish from PLA. Classically, aspiration of ALA reveals anchovy sauce–like aspirate. Microbiologically, trophozoites are rarely demonstrated in aspirate. In addition, serology for *E. histolytica* may be relevant in travelers returning from high-endemic areas, being of limited value in residents of highly endemic areas. Molecular and antigen testing, if available, may be useful. Noninvasive testing, such as use of polymerase chain reaction, is increasingly being used for detection of *E. histolytica* DNA in other body fluids, such as blood, pus, saliva, and

Abbreviations: ALA, amoebic liver abscess; IV, intravenous; PCA, percutaneous aspiration; PCD, percutaneous catheter drainage; PLA, pyogenic liver abscess; PO, orally.

From the Department of Gastroenterology and Human Nutrition, All India Institute of Medical Sciences, New Delhi, India.

Potential conflict of interest: Nothing to report.

Received February 25, 2021; accepted April 25, 2021.

View this article online at wileyonlinelibrary.com

TABLE 1. COMPLICATIONS OF ALA

Local complications
- Pleural effusion
- Rupture*
  - Pleural cavity: empyema
  - Peritoneal cavity: peritonitis/abdominal collection
  - Pericardial cavity: pyopericardium
  - Biliary tree: spontaneously or after catheter drainage

Compression
- Biliary tree: jaundice
- Inferior vena cava: ascites, pedal edema

Vascular thrombosis
- Hepatic venous thrombosis
- Portal venous thrombosis

Systemic complications
- Systemic inflammatory response syndrome
- Encephalopathy
- Shock
- Acute kidney injury
- Acute respiratory distress syndrome

*Risk factors for rupture include left lobe liver abscess and abscess with a thin rim (<10 mm) of hepatic parenchyma.

urine.[5] Newer tests such as lateral flow assays using markers in serum can potentially be used for rapid noninvasive diagnosis of ALA if available on a widespread basis.[6]

Management

Management of ALA comprises medical management, radiological drainage, and surgical management (Fig. 1). In the absence of formal guidelines on management, evidence for guiding treatment decisions, such as timing and indications of radiological intervention, is limited.

TABLE 2. POOR PROGNOSTIC FACTORS IN PATIENTS WITH ALA

Clinical
- Encephalopathy
- Jaundice

Biochemical
- Serum bilirubin > 3.5 mg/dL
- Serum albumin < 2 g/dL

Sonographic
- Large volume of abscess
- Multiple abscess

Underlying chronic liver disease

Medical Management. Tissue amebicides such as nitroimidazoles form the mainstay of management of all patients with ALA (Table 3). Oral or intravenous (IV) administration (in patients unable to take orally [PO]) of metronidazole results in resolution of fever, toxemia, and pain in 80% of 90% of patients with uncomplicated ALA within 48 to 72 hours of treatment. Tinidazole is better tolerated and has the advantage of shorter duration of treatment. Other options include nitazoxanide, which has an advantage of being both tissue and luminal amebicide. The treatment with tissue amebicides should be followed with luminal amoebicidal agents to eradicate the luminal

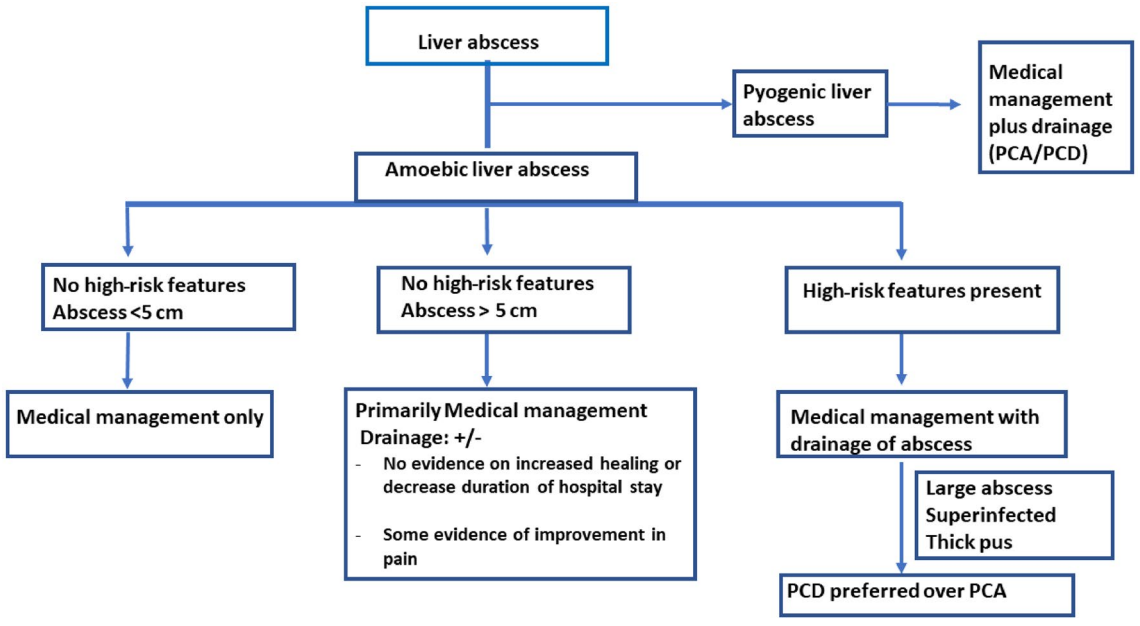

FIG 1 Suggested algorithm for the management of liver abscess.

TABLE 3. DRUGS USED IN THE MANAGEMENT OF ALA

Drugs	Dose and Duration	Adverse Events
Tissue amoebicidal drugs		
Metronidazole	800 mg three times a day PO or 500 mg IV three times a day for 7-10 days	Gastrointestinal: anorexia, nausea, vomiting, metallic taste Neurological: dizziness, peripheral neuropathy, seizures
Tinidazole	1.2 g PO per day for 7 days	Gastrointestinal-like metronidazole
Luminal amoebicidal drugs		
Diloxanide furoate	500 mg three times a day for 20 days	Gastrointestinal: nausea, vomiting
Paromomycin	30 mg/kg for 10 days (in 3 divided doses)	Gastrointestinal: diarrhea, nausea
Tissue plus luminal amoebicidal drug		
Nitazoxanide	500 mg twice a day for 10 days	Gastrointestinal: nausea, vomiting

TABLE 4. OVERVIEW OF PLA

Causative organism
- *Klebsiella pneumoniae*
- *Escherichia coli*
- *Pseudomonas*
- *Enterobacter*
- *Proteus*
- *Streptococcus**
- *Staphylococcus**

Diagnosis
- Imaging
- Microbiological

Associated conditions
- Biliary tract infection: cholangitis in biliary obstruction, acute cholecystitis
- Abdominal infections: diverticulitis, appendicitis
- Hematogenous spread: endocarditis, bloodstream infection, central venous catheter–associated infection
- Trauma
- Postoperative conditions

Treatment: combination of antibiotics and drainage of abscess and source control

Antibiotics (duration: 2-6 weeks)†
- Third generation cephalosporins
- Aminoglycosides
- Piperacillin tazobactam
- Carbapenems
- Vancomycin (if suspecting gram positive)
- Metronidazole (for anaerobic coverage)

Drainage (imaging guided)
- <3-cm abscess: antibiotics alone
- 3- to 5-cm abscess: percutaneous aspiration
- >5-cm abscess: PCD

Surgery
- Abscess not amenable to percutaneous drainage
- Rupture abscess
- No improvement with antibiotics and percutaneous drainage
- Underlying surgical cause of liver abscess

Source control
- Biliary tract obstruction: drainage of biliary tract
- Diverticulitis: drainage if associated with abscess
- Hematogenous spread: appropriate antibiotics, drainage if associated with abscess, removal of catheter (in cases of catheter-associated sepsis)

Predisposing host factors
- Diabetes
- Immunosuppression
- Malnutrition
- Advanced age

Outcomes

Mortality rate: 2%-15% across different series

Poor prognostic factors
- Advanced age
- Immunosuppression
- Comorbid medical conditions, such as cirrhosis, malignancy, etc.
- Abscess associated with systemic complications, such as acute kidney injury, shock, etc.

*Causative agents in case of bloodstream infections.
†Usual duration of 2 weeks of IV antibiotics followed by oral antibiotics.

amebae and to prevent subsequent tissue invasion and spread of the infection through cyst.[7]

Drainage of Abscess. The indications for drainage of liver abscess together with medical management are: (1) left lobe liver abscess, (2) abscess with thin rim of hepatic parenchyma (<10 mm) around it, (3) multiple liver abscesses, (4) impending rupture recognized on imaging, and (5) nonresponse to medical therapy after 3 to 5 days. In the absence of these high-risk features, the evidence for upfront drainage is controversial. Faster resolution of clinical and biochemical features is seen in some but not in other

TABLE 5. DIFFERENTIATING FEATURES OF ALA AND PLA

Variables	ALA	PLA
Etiology	*E. histolytica*	- *Klebsiella pneumoniae* - *E. coli* - *Pseudomonas* - *Enterobacter* - *Proteus*
Risk factors	- Alcohol consumption - Immunosuppression - Retroviral disease	- Advanced age - Diabetes - Biliary tree and other abdominal infections
Radiological features	Usually solitary and situated in right lobe	Multiple abscesses in either lobe
Management	Amebicides ± drainage	Antibiotics and drainage

randomized trials comparing the strategy of combination of drainage and medical management with that of medical management alone. A recent systematic review found a combination strategy to be effective in reducing the abdominal pain and local tenderness, but not in resolution of fever, healing of abscess, and length of hospital stay, with benefits limited to abscesses of more than 5 cm.[8] Hence routine drainage of abscess is not recommended in patients with ALA but may be used in selected patients with size greater than 5 cm. Percutaneous catheter drainage (PCD) is preferred over percutaneous needle aspiration, particularly in larger abscess (>10 cm), subcapsular location, high risk for rupture, and if superinfected. Even for complications such as rupture into peritoneum, there is evidence that conservative management with PCD results in better outcomes than surgery.[9] Catheter removal is usually recommended when the drainage output is less than 10 mL/day.[10] Duration of catheter removal may vary; however, earlier removal is not associated with a higher healing rate.[11] The higher mortality associated with surgery combined with the widespread availability of image-guided drainage has limited the role of surgery in the management of ALA. Surgery can be considered in those with no response to appropriate antibiotics and PCD drainage. Clinical and biochemical resolution occurs rapidly in patients with ALA with optimal management. Radiological resolution is often delayed and does not warrant additional therapy. Relapses are uncommon in ALA.[12]

PYOGENIC LIVER ABSCESS

PLA occurs in the setting of abdominal/biliary tree infections or in the presence of systemic bloodstream infections. Patients with PLA usually have more pronounced systemic features with multiple liver abscess on imaging compared with those with ALA. Unlike ALA, the principles of treatment of PLA involve drainage of abscess, use of appropriate antibiotics, and control of primary source of infection (Table 4).[13] The differentiating features of ALA and PLA are summarized in Table 5.

CONCLUSION

Recent advances in interventional radiology, intensive care, and use of effective antibiotic therapy have resulted in a decline in the mortality rates of liver abscess in India from 24% in earlier series to 1% to 3% in more recent studies.[1] The course of ALA is usually benign in the absence of poor prognostic factors. Management involves medical management in all patients along with drainage of abscess in certain patients with high-risk features. Unlike ALA, patients with PLA require an upfront combination of drainage and appropriate antibiotics, along with appropriate treatment of primary infection.

CORRESPONDENCE

Vineet Ahuja, M.D., D.M., Department of Gastroenterology and Human Nutrition, All India Institute of Medical Sciences, New Delhi 110029, India. E-mail: vineet.aiims@gmail.com

REFERENCES

1) Jindal A, Pandey A, Sharma MK, et al. Management practices and predictors of outcome of liver abscess in adults: a series of 1630 patients from a liver unit. J Clin Exp Hepatol 2021;11:312-320.

2) Sharma MP, Dasarathy S. Amoebic liver abscess. Trop Gastroenterol 1993;14:3-9.

3) Sharma MP, Ahuja V. Amebiasis. N Engl J Med 2003;349:307-308; author reply 307-308.

4) Sharma MP, Dasarathy S, Verma N, et al. Prognostic markers in amebic liver abscess: a prospective study. Am J Gastroenterol 1996;91:2584-2588.

5) Haque R, Kabir M, Noor Z, et al. Diagnosis of amebic liver abscess and amebic colitis by detection of Entamoeba histolytica DNA in blood, urine, and saliva by a real-time PCR assay. J Clin Microbiol 2010;48:2798-2801.

6) Noordin R, Yunus MH, Saidin S, et al. Multi-laboratory evaluation of a lateral flow rapid test for detection of amebic liver abscess. Am J Trop Med Hyg 2020;103:2233-2238.

7) Sharma MP, Ahuja V. Management of amebic and pyogenic liver abscess. Indian J Gastroenterol 2001;20(Suppl. 1):C33-C36.

8) Kumar R, Ranjan A, Narayan R, et al. Evidence-based therapeutic dilemma in the management of uncomplicated amebic liver abscess:

a systematic review and meta-analysis. Indian J Gastroenterol 2019;38:498-508.

9) Kumar R, Anand U, Priyadarshi RN, et al. Management of amoebic peritonitis due to ruptured amoebic liver abscess: it's time for a paradigm shift. JGH Open 2019;3:268-269.

10) Ahmed S, Chia CLK, Junnarkar SP, et al. Percutaneous drainage for giant pyogenic liver abscess—is it safe and sufficient? Am J Surg 2016;211:95-101.

11) Haider SJ, Tarulli M, McNulty NJ, et al. Liver abscesses: factors that influence outcome of percutaneous drainage. Am J Roentgenol 2017;209:205-213.

12) Sharma MP, Dasarathy S, Sushma S, et al. Long term follow-up of amebic liver abscess: clinical and ultrasound patterns of resolution. Trop Gastroenterol 1995;16:24-28.

13) Roediger R, Lisker-Melman M. Pyogenic and amebic infections of the liver. Gastroenterol Clin North Am 2020;49:361-377.