INTRODUCTION
Liver is an important and vital organ of the body. This organ is subjected to numerous systemic infections viral, bacterial and parasitic and lies at the distal end of the portal circulation; it is therefore bathed with portal blood containing viruses, bacteria parasites, ova, products of digestion and other antigens.\textsuperscript{1}

Hepatic or liver abscesses are infectious, space-occupying lesions in the liver; the two most common abscesses being pyogenic and amoebic. Pyogenic liver abscess (PLA) is a rare but potentially lethal condition, with a reported incidence of 20 per 1,00,000 hospital admissions in a western population.\textsuperscript{2} Its severity depends on the source of the infection and the underlying condition of the patient. Amoebic liver abscesses (ALA) are common in tropical regions mainly where ‘\textit{Entamoeba histolytica}’ is endemic and is more prevalent in individuals (mostly young males) with suppressed cell mediated immunity.\textsuperscript{3}

In both the types of hepatic abscesses, right lobe of the liver is the most likely site of infection. The clinical presentation of both the types may be elusive with combination of fever, right upper quadrant pain and hepatomegaly with or without jaundice.

PYOGENIC LIVER ABSCESS (PLA)

\textbf{Etiology}

Over the past 50 years, there has been a major shift in the etiology of PLA. PLA may be of biliary, portal, arterial, or traumatic origin (Table 1). Ascending infection of the biliary tree secondary to obstruction is now the most identifiable cause of PLA. The etiology of biliary obstruction has some geographic differences: in Western countries this scenario is common in patients with malignant disease,\textsuperscript{4} while in Asia, gall stone disease and hepatolithiasis are more common.\textsuperscript{5} Between 15 to 55\% patients in different series, no identifiable cause or source for PLA was found (hence called cryptogenic).\textsuperscript{4-6} There is an increase in the median age of patients with PLA in recent years, that is mostly responsible for increased severity and mortality in spite of advancement in antibiotic therapy.\textsuperscript{6,7}

\textbf{Clinical presentation:}

- Early symptoms during the onset of a PLA are non-specific and include malaise, nausea, anorexia and weight loss, headaches, myalgia, and arthralgia in most of the cases.
- These prodromal symptoms may be present for many weeks before the appearance of more specific symptoms, such as fever, chills and abdominal pain, although the pain is not always localized to the right upper quadrant.
- An abscess adjacent to the diaphragm may cause pleuritic type pain, cough and dyspnea, and when this presentation is associated with the above-mentioned non-specific symptoms, it can cause diagnostic difficulty.
- Septic shock may occur in a few patients, especially in the setting of an obstructed biliary tree.
Plain abdominal and chest radiographs are usually too non-specific to be diagnostic.

Ultrasound (USG) is the imaging modality used in the initial evaluation. The appearance on USG varies according to the stage of evolution of the abscess. Initially the abscess is hyperechoic and indistinct, but with maturation and pus formation, it becomes hypoechoic with a distinct margin. When the pus is very thick, a fluid-containing lesion may be confused with a solid lesion on USG. USG has a sensitivity of 75% to 95%, but has difficulty in detecting an abscess high in the dome of the right hemiliver and especially multiple small PLAs. By showing gallstones, dilated bile ducts, and hepatolithiasis, USG has the advantage of imaging underlying biliary tract pathology.

A computed tomography (CT) scan is more accurate than USG in the differentiation of PLA from other liver lesions and is reported to have a sensitivity of approximately 95%. The portal venous phase using intravenous contrast material gives the best differentiation between the liver and the abscess, with the periphery of the PLA having contrast enhancement as opposed to non-enhancement of the central portion (Figure 1).

Magnetic resonance imaging (MRI) does not seem to have any advantage over CT or USG.

The spectrum of organisms that may be cultured in PLA is listed in Table 2. E. coli is cultured most frequently in Western series and Klebsiella in Asian series.

**MANAGEMENT OF PYOGENIC LIVER ABSCESS (PLA)**

The principles of treatment are to

**Table 1: Common causes of pyogenic liver abscess**

**Hepatobiliary**

Benign
- Lithiasis
- Cholecystitis
- Biliary enteric anastomosis
- Endoscopic biliary procedures
- Percutaneous biliary procedures

Malignant
- Common bile duct
- Gall bladder
- Ampulla
- Head of pancreas

**Portal**

Benign
- Diverticulitis
- Anorectal suppuration
- Pelvic suppuration
- Postoperative sepsis
- Intestinal perforation
- Pancreatic abscess
- Appendicitis
- Inflammatory bowel disease

Malignant
- Colonic cancer
- Gastric cancer

**Arterial**

Endocarditis
- Vascular sepsis
- ENT infection
- Dental infection

**Traumatic**

Benign
- Open or closed abdominal trauma

Malignant
- Chemoembolization
- Percutaneous ethanol injection or radiofrequency

**Cryptogenic**

- Although uncommon, some patients present with peritonitis after free rupture of an abscess into the peritoneal cavity.

**Diagnosis:**

- Laboratory investigations show an elevated white cell count, anaemia, hypoalbuminemia, elevated transaminases and alkaline phosphatase. Hyperglycemia may be the first indication that the patient is diabetic or there is loss of control because of septic process.
Management of Liver Abscess

Drain the pus, Institute appropriate antibiotics, and Deal with any underlying source of infection, if present.

The advances in USG and CT that provide earlier and more accurate diagnosis also have enabled these modalities to facilitate treatment through guided aspiration and drainage, shifting management away from open surgery to minimally invasive techniques. Percutaneous drainage combined with antibiotics has become the first line and mainstay of treatment for most PLAs.\(^1\)

**Antibiotics:** Before obtaining positive cultures from blood or pus, broad-spectrum antibiotics should be started to cover Gram-negative and Gram-positive aerobes and anaerobes. Initial therapy with amoxicillin, an aminoglycoside, and metronidazole or a third generation cephalosporin and metronidazole generally covers the causative organisms most commonly found, although this regimen may be varied according to geographic differences and antimicrobial treatment policies.

Initially, antibiotics should be administered parenterally, and after 2 weeks of systemic therapy, appropriate oral agents may be used for a further 4 weeks.\(^1\) In patients with multiple PLAs that are too small to drain, antibiotics may be the only treatment possible. In addition, efforts must be made to identify any underlying biliary obstruction, which needs to be overcome for the antibiotic therapy to succeed.

**Percutaneous procedures:** Percutaneous drainage is performed under USG or CT guidance. Aspiration of PLAs to confirm the diagnosis and obtain pus for culture should be accompanied by complete aspiration of the pus or insertion of a drain at the same time.

Clinicians have questioned when should the primary treatment be aspiration alone and when should a percutaneous catheter drain be inserted. Percutaneous needle aspiration (PNA) group has a high success rate and a shorter hospital stay, but a large percentage requires second or third aspirations to achieve success.\(^1\) When PNA fails, catheter drainage should be performed.

Primary treatment by percutaneous catheter drainage (PCD) is performed when:

- The pus is too thick to be aspirated
- The abscess is greater than 5 cm in diameter
- The wall is thick and non-collapsible
- The PLA is multi-loculated

The use of PCD is not precluded by the presence of multiple abscess cavities, but this does necessitate the placement of several catheters.\(^1\)

Although highly successful, PNA/PCD fail in approximately 10% cases. Incomplete or unsuccessful drainage may result from:

- Catheter too small to drain the thick pus,
- Position of catheter not conducive to adequate drainage,
- Catheter removed prematurely
- Thick fibrous encasing wall of PLA that is unable to collapse.

An abscess with biliary communication has been reported to be treated as effectively by PCD as a non-communicating abscess, although the continuous output of bile leads to a prolonged period of abscess drainage.\(^1\)

**Surgical treatment:** The only indication of primary surgical treatment of PLAs is in patients with an initial presentation with intraperitoneal rupture or in patients with multiple abscesses above an obstructed system that cannot be negotiated by non-operative means.\(^1\) Open operation is also indicated when there is failure of non-operative treatment and for complications of percutaneous drainage, such as bleeding or intraperitoneal leakage of pus. Surgery is required to treat any underlying causative disease if necessitated, particularly those pertaining to hepatobiliary area.

The traditional principles of surgery are: to perform needle aspiration before blunt puncture, finger explorations to break down loculations, insertion of a large bore drainage tube for adequate drainage and to maximize dependent drainage. Postoperative irrigation and suction of the cavity via the drainage tube is usually advantageous.

There have been isolated references to the use of hepatic

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**Table 2: Spectrum of microorganisms causing pyogenic liver abscess**

<table>
<thead>
<tr>
<th>Gram-negative aerobes</th>
<th>Gram-positive aerobes</th>
<th>Gram negative anaerobes</th>
<th>Gram positive anaerobes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia Coli</td>
<td>Streptococcus milleri</td>
<td>Bacteroides spp.</td>
<td>Clostridium spp.</td>
</tr>
<tr>
<td>Klebsiella pneumiae</td>
<td>Staphylococcus aureus</td>
<td>Fusobacterium spp.</td>
<td>Peptostreptococcus spp.</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>Enterococcus spp.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proteus spp.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citrobacter freundii</td>
<td></td>
<td></td>
<td></td>
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resection in the treatment of PLAs.\textsuperscript{4,6,15} There is no single therapy that cures all cases. Antibiotics combined with percutaneous aspiration (which may need to be repeated) or PCD is successful in 90\% of patients.\textsuperscript{1}

**Prognosis:** With modern treatments, the prognosis depends more on the underlying etiology and co-morbid factors than the PLA itself, although delay in presentation and diagnosis contributes to a poor outcome.

The risk factors most commonly associated with mortality include:\textsuperscript{6,9,16}

- Septic shock,
- Clinical jaundice
- Coagulopathy
- Leukocytosis
- Hypoalbuminemia
- Multiple abscesses
- Intraperitoneal rupture
- Malignancy (more in hepatopancreatobiliary malignancy than other malignant diseases)

**AMOEBC LIVER ABSCESS (ALA)**

**Epidemiology:**

ALA is the most common extra intestinal site of infection but occurs in only less than 1\% of *E. histolytica* infections.\textsuperscript{17} ALAs are 3 to 10 times more common in men.\textsuperscript{18} Patients commonly affected are between 20 to 40 years of age with residence in, recent travel to or emigration from an endemic region.

ALA lesions are usually single and mostly found in the right lobe of the liver. The incidence of ALA of the left lobe ranges from 5\% to 21\%. The liver abscess has a thin capsular wall with a necrotic centre composed of a thick fluid. Typically, abscess fluid is odourless, resembling ‘chocolate syrup’ or anchovy paste’ in half, and bacteriologically sterile, although secondary bacterial invasion may occur (in 15 to 20\%). The mortality rate has been estimated to be around 0.2-2.0\% in adults and up to 26\% in children.\textsuperscript{1}

Risk Factors for ALA are:\textsuperscript{19}

- Alcoholism
- Malignancy
- HIV infection
- Malnutrition
- Corticosteroid use
- Disorders of cell mediated immunity
- Homosexual activity
- Recent travel to a tropical region

**Clinical features:**

Approximately 20\% have a past history of dysentery and another 10\% history of diarrhoea or dysentery at the time of diagnosis.\textsuperscript{20}

- Onset is usually abrupt with fever. Fever varies between 38\° and 40\°C, frequently in spikes but sometimes persists for several days, with rigors and profuse sweating.
- Pain in the upper abdomen, usually intense and constant, radiating to the scapular region and right shoulder, increases with deep breathing or coughing, or when the patient rests on the right side. In ALAs localized on the left lobe, pain occurs on the left side and may radiate to the left shoulder.
- Diarrhoea and/or dysentery
- Nausea, vomiting and fatigue
- Anorexia, weight loss
- Cough & dyspnoea

On examination:

- Mild jaundice is quite common, but severe jaundice is rare.
- The cardinal sign of amoebic liver abscess is painful hepatomegaly. On palpation the liver is soft and smooth. 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.

**Investigations:**

- Raised bilirubin, leukocytosis (75\% cases) raised transaminases and alkaline phosphatase (non-specific) and raised markers of acute inflammation are usually found in varying combination.
- Fresh fecal sample may detect trophozoites containing erythrocytes, preferably within 30 minutes of the passage of stool. Wet mount preparation should be made in saline solution, in saline plus iodine, and in saline plus methylene blue. Presence of erythrophagocytic trophozoites is strongly suggestive of invasive disease.
- On aspiration, the amoebae are sparse in necrotic material from the centre of the abscess, but are more abundant on the marginal walls and are therefore more commonly found in the last portion of aspirated material.
- Serology can be useful in the diagnosis of amoebiasis,
particularly in non-endemic areas (incidence of high false positivity in endemic regions). Antibody response is present in 85-95% of patients with invasive disease. Indirect Haemagglutinin assays (IHA) is the most sensitive test (90%). Antibody may be negative in early infection and should be repeated 7 days later. IHA may remain positive for up to 20 yrs and represent a previous infection. EIA (Enzyme-linked immunosorbent assays) is the most commonly employed test and it usually become negative within 6-12 months. A negative serology, however, does not exclude the diagnosis.

- Straight X-ray of abdomen and thorax: May reveal elevation of the right hemidiaphragm, pleural reaction obscuring the right costophrenic angle.
- USG: Typically reveals a round or oval hypoechoic area which is contiguous to the liver capsule and without significant wall echoes (Figure 2). It may also show associated right pleural effusion or evidence of rupture.
- CT scan of abdomen and MRI are sensitive studies for demonstrating an abscess.
- Polymerase chain reaction: also included in molecular diagnosis of amebiasis.

**MANAGEMENT OF AMOEBCIC LIVER ABSCESS (ALA)**

Four groups of treatment modalities are effective:

1. Drug therapy only
2. USG guided aspiration and drug
3. Percutaneous catheter drainage and drug
4. Laparatomy, drainage and drug

**Medical therapy:**

Medical therapy may be instituted using either a single agent or a combination of drugs for the extraluminal parasite (Table 3).

**Table 3: Pharmacotherapy of *E. histolytica* infection in adults and children**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Adult dosage</th>
<th>Pediatric dosage</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Amoebicidal agents</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Metronidazole</td>
<td>750 mg orally three times a day for 5–10 days; 500 mg IV every 6 hours for 5–10 days</td>
<td>30–50 mg/kg/d for 5–10 days orally in three divided doses; 15 mg/kg IV load followed by 7.5 mg/ kg every 6 hours (maximum, 2250 mg/d)</td>
<td>Psychosis, seizures, Peripheral neuropathy and a metallic test</td>
</tr>
<tr>
<td>2. Chloroquine (base) (used as an alternative or adjuvant)</td>
<td>600 mg/d orally for 2 days, then 300 mg/d orally for 14 days</td>
<td>10 mg/kg of chloroquine base 2 gm/ day for 3-5 days</td>
<td>Diarrhoea, abdominal cramps, cardio-toxicity, seizures and hypotension</td>
</tr>
<tr>
<td>3. Tinidazole (Preferable to Chloroquine)</td>
<td>500 mg orally three times a day for 3 days</td>
<td>20 mg/kg/d in three divided doses</td>
<td></td>
</tr>
</tbody>
</table>

**Luminal agents**

(Used to eradicate intestinal colonization after Amoebicidal treatment)

1. 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 g/d) | Diarrhoea, |

2. 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 g/d) | Contra indicated in patients with Hepatic insufficiency or hypersensitivity to Iodine |

3. 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 |                                                  |
Criteria for medical management

- All non-complicated abscess
- No features of rupture / impending rupture
- No compression effect

Nitroimidazoles including metronidazole are effective in over 90%.23 Therapy should continue for at least 10 days. Relapses have been reported with this duration and the drug may be administered for up to 3 weeks. Single agent therapy with metronidazole yields excellent results and the alternative toxic drugs are indicated rarely and used probably in seriously ill patients where the risk of failure of therapy is unacceptable. The response to anti-amoebic drug is usually evident within 48 to 72 hours with the subsidence of toxemia.24

Aspiration or drainage of the abscess:

Routine aspiration of liver abscess is not indicated for diagnostic or therapeutic purposes.25 A combination of USG findings with a positive serology in the appropriate clinical setting is adequate to start drug therapy.

Aspiration has been indicated in the following circumstances:26
- Lack of clinical improvement in 48 to 72 hours
- Left lobe abscess
- Large abscess having impending rupture / compression sign
- Thin rim of liver tissue around the abscess (<10 mm)
- Seronegative abscesses
- Failure in the improvement following non-invasive treatment after 4 to 5 days

Like PLA, percutaneous drainage is indicated when thick collection is not getting aspirated by needle or there is failure of USG-guided aspiration.

Antiamoebic therapy alone is as effective as routine needle aspiration combined with antiamoebic therapy in the treatment of patients with uncomplicated liver abscess.27

Surgical intervention:

Open surgical drainage is rarely indicated and may be required in the setting of:28
- large abscess with a poor yield on needle aspiration or percutaneous drainage
- clinical deterioration despite attempted needle aspiration
- complicated ALA (like ruptured abscess in peritoneal cavity with features of peritonitis)
- complicated ALA (ruptured in the pleural cavity / pericardial cavity/ adjacent viscera)

Surgical mortality is, however, very high. Hence, in clinical practice, it is only used when the cavity has ruptured into adjacent viscera or body cavities.

Long term follow up of ALA patients:

After clinical cure, patients show few symptoms and sonographic follow up demonstrates evidence of persistent hypoechoic lesion. The mean time for the disappearance of the sonographic abnormality is 6-9 months.29 Relapses are very uncommon and the sonographic abnormality does not warrant continued therapy.

The patterns of resolution seen on sonographic follow up include:29 Type I: where 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%).

Factors influencing healing time include: the size of abscess cavity at admission, hypoalbuminaemia and anaemia. The type of clinical presentation, nature of therapy, number of location of abscesses and time for clinical resolution pattern of multiple liver abscesses is similar to solitary abscess. 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 ultrasonographic resolution it is suggested that the results of the therapy should be monitored by clinical criteria rather than USG.

Prognostic markers: Independent risk factors for mortality in ALA are:30
- bilirubin level > 3.5 mg/dl
- encephalopathy,
- volume of abscess cavity
- hypoalbuminaemia (serum albumin <2.0 g/dl)

The duration of symptom and the type of treatment does not influence mortality.

CONCLUSION

PLA and ALA have many features in common and diagnosis is often delayed due to vague clinical symptoms resulting in adverse outcomes. Because of the difficulty in differentiating between these two types of abscesses initially, antiamoebic therapy is usually recommended in addition to broad-spectrum antibiotics.

Medical therapy alone is effective in most cases of ALA while some form of intervention is usually needed or PLA. Mortality is low with ALA compared with PLA. Abscesses are slow to resolve. A multidisciplinary approach, including a gastroenterologist, radiologist, surgeon, and laboratory, is crucial for successful treatment of these curable infections.
REFERENCES


