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Amoebic Liver Abscess: An Appraisal

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Intestinal protozoa have gained importance in recent years as a result of increasing world travel, economic globalization, and increasing number of immunosuppressed individuals. Acquired immunodeficiency syndrome (AIDS) and an increase in organ transplants have led to a new population at risk for protozoal infection. Protozoa that infect the gastrointestinal tract include *Entamoeba histolytica* and *Giardia lamblia*, the most common causes of waterborne diseases. Of these, *E. histolytica* is the most prevalent protozoa in India and tropical countries that causes amoebiasis.[1] It invades the intestinal mucosa and may spread to other organs, mainly the liver and manifest as amoebic liver abscess (ALA) (synonyms: tropical liver abscess, dysenteric abscess, metastatic abscess of intestinal amoebiasis). Sushruta, who practised in 6th century BC in ancient India, authored the manuscript Sushruta Samhita in which he described ''Atisara'' (amoebic dysentery).[2] In 1848 Charles Morehead, reported the index case[3] and in 1875 Loschs first described *E. histolytica*.[4] In 1887, Robert Koch, while studying cholera, came across 2 cases of dysentery complicated by liver abscess and demonstrated *E. histolytica* in the walls of capillaries near the abscess.[5] In 1919, Sir Leonard Rogers first introduced emetin for the treatment of amoebic liver abscess,[6] whereas in 1951 Debakey showed that antiamoebic drugs with closed aspiration carried good prognosis.[7] In 1966 Powell *et al* reported success of metronidazole in the treatment of amoebiasis.[8] Even after 4 decades metronidazole continues to remain the drug of choice.[9]

ALA is more common in India and other developing countries because of economic drawbacks, improper hygiene and sanitation, as well as deficiency in health education. Water contamination (cystic forms are resistant to chlorination) is the most common cause of infection. Alcoholics, cirrhotics, and those individuals with human immunodeficiency virus (HIV)/AIDS or immunosuppression are more susceptible.[10,11] HIV/AIDS may play a major role in the development of multiple amoebic liver abscesses.

E. histolytica passes its life cycle in a single host, humans, with two phases of development, trophozoite and cyst with a transitory stage of precystic form. The trophozoite invades and proliferates in the submucosa of the large intestinal wall and causes amoebic dysentery. Development of amoebic liver abscess after an attack of dysentery will depend on host resistance, virulence of organism, and early treatment of intestinal amoebiasis. No acquired immunity is achieved by first infection, hence reinfection is common. Healing does not occur with fibrosis and hence cirrhosis is not a sequelae.

With regard to the terminology, ideally it should be termed amoebic liver necrosis as the ''pus'' is not as a result of suppuration but a mixture of sloughed

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Table 1 Age distribution

Age group (y)	No. of patients	Percentage (%)
12–20	4	1
21–30	76	19
31–40	172	43
41–50	128	32
51–60	12	3
61–70	8	2

liver tissue and blood. It is chocolate brown in color and thick in consistency, hence often termed anchovy sauce pus.[12] The smell is rarely offensive, and the pus is sterile. Microscopic examination reveals degenerated liver cells, red blood cells, and an occasional leukocyte. Trophozoites of *E. histolytica* are not generally found in freshly aspirated liver pus but appear in the escaping pus 4 or 5 days after the initial evacuation. Often secondary infection by *Escherichia coli*, staphylococci, and streptococci may occur in about 30% of the patients.

Patients and Methods

This is a prospective analysis of 400 cases of ALA during a 4-year period from June 2006 to May 2010 in a single referral unit. Diagnosis of amoebic liver abscess was based on clinical suspicion, and confirmed by ultrasonographic findings, aspiration of characteristic pus, and therapeutic response to antiamoebic therapy within 48 to 72 hours.

Data collection

Parameters included patient's age, gender, risk factors, clinical features, laboratory tests, imaging studies, drug therapy, need of radiologic intervention or surgery, and mortality.

Table 2 Distribution

	Number affected (%)
Sex	
Male	394 (98.5)
Female	6 (1.5)
Alcohol abuse	
Present	162 (40.5)
Absent	238 (59.5)
Amoebic abscesses	
Solitary	304 (76)
Multiple (HIV +ve)	96 (24)
	52 (54.15)

N = 400.

Table 3 Frequency of clinical features

Symptoms	No. of patients
Pain	384 (96%)
Fever	354 (86%)
Nausea and vomiting	240 (60%)
Anorexia	224 (56%)
Weight loss	104 (26%)
Malaise	100 (25%)
Diarrhea	40 (10%)
Cough	32 (8%)
Signs	
RHC tenderness	354 (86%)
Hepatomegaly	340 (85%)
Anemia	104 (26%)
Pleural effusion	48 (12%)
Jaundice	20 (5%)
Ascites	2 (0.5%)

RHC, right hypochondrium.

Results

The commonly affected age group was 31 to 40 years (43%); the youngest patient was 16 years, the oldest, 70 years (Table 1). There was a distinct male preponderance and alcohol abuse was a major factor. Of the study population, 24% had multiple amoebic abscesses and among these, 54% were HIV +ve (Table 2). Pain (96%) and fever (86%) were the commonest symptoms, compelling admission, whereas right hypochondrium (RHC) tenderness (86%) and tender hepatomegaly (85%) were the commonest clinical findings (Table 3). On ultrasound assessment, solitary liver abscess was seen in 76% of patients, of which 95% were right sided and 5% left sided.

Solitary liver abscesses were differentiated on ultrasonography into three types depending on their liquefaction status as nonliquefied, partially liquefied, and liquefied (Table 4). Computed tomography (CT) scan was done in all 96 cases with multiple abscesses and in 8 patients with complications. When there was diagnostic doubt, CT was found to be helpful. All patients were treated by a combined pharmacologic and radiologic approach. Metronidazole (750 mg thrice daily) was given to all patients for 10 days, followed by chloroquine (600 mg/d for 2 days followed by 300 mg/day for

Table 4 Differentiation of solitary abscess on USG

Forming liver abscess	42 (14%)
Partially liquefied liver abscess	196 (64%)
Liquefied liver abscess	66 (22%)

USG, ultrasonography.

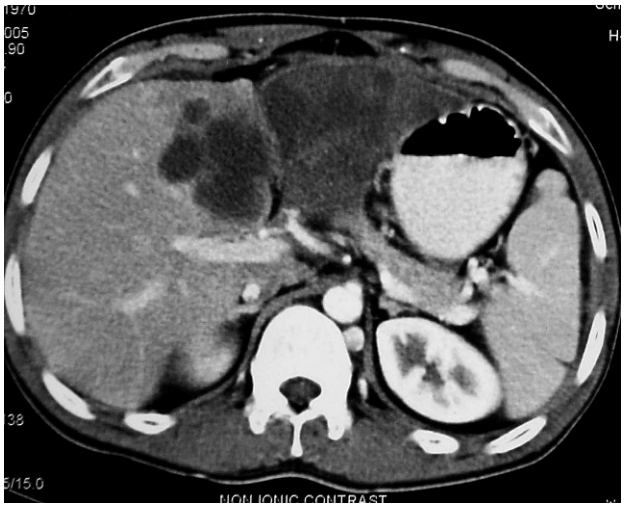

Fig. 1 Cholangicarcinoma masquerading as amoebic liver access.

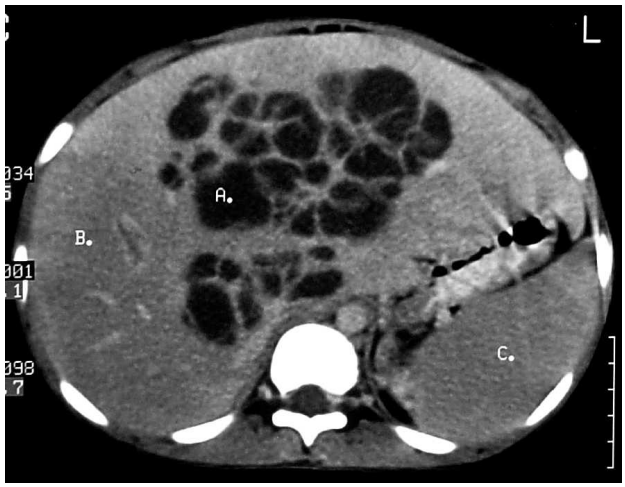

Fig. 2 Atypical amoebic liver access.

19 days) for 21 days and luminal amoebicide diloxanide furoate (500 mg thrice daily) for 10 days. Therapeutic intervention was performed in the form of a single aspiration in 104 patients, more than 1 aspiration in 189, and percutaneous catheter drainage in the remaining 104 patients. We used a 14 Fr pigtail catheter for percutaneous drainage. We had to use two catheters in patients with multiple abscesses involving both lobes of the liver. Surgery, open drainage, or laparoscopic drainage was not required in any patient, except for a diagnostic laparoscopy in 1 patient in whom diagnosis was uncertain. He was 54 years old, habitual alcoholic, who was admitted with complaints of upper abdominal pain, fever, dysentery, and on examination, was found to have tender hepatomegaly. Clinical diagnosis of ALA was made and ultrasonography (USG) confirmed the same. The indirect hemagglutination (IHA) test was strongly positive, antiamoebic therapy was initiated, but only partial clinical response was seen. USG reassessment showed no liquefaction and hence a CT scan was done, which was indicative of either hepatic cholangiocarcinoma or ALA (Fig. 1). Diagnostic laparoscopy confirmed the diagnosis of hepatic cholangiocarcinoma. Another patient, in whom there was diagnostic uncertainty, was a 32-year-old woman, who presented with complains of upper abdominal pain, fever, and on examination, was found to have hepatomegaly. IHA test was positive and USG showed multiple cystic lesions in the liver. CT scan was indicative of angiosarcoma (Fig. 2). Antiamoebic therapy was initiated based on the clinical picture and excellent response was seen. USG-guided aspiration was confirmatory of ALA. No case of resistant liver abscess was encountered, but 2 patients died as a result of rupture of amoebic liver abscess in the peritoneal and pericardial cavity, as seen on autopsy. One patient, who was a cirrhotic, had multiple abscesses and autopsy showed rupture into the pericardial cavity and the other patient, a drug and alcohol abuser, HIV positive, had a solitary large abscess with intraperitoneal rupture.

Discussion

The present study highlighted a few points not supported by literature, especially the duration of drug therapy and efficacious role of therapeutic intervention when combined with pharmacotherapy. In the case of poor responders it is imperative to revise the diagnosis. Abscesses in patients who also have hepatic malignancy or chronic granulomatous disease (tuberculosis, sarcoidosis) are poor responders and treatment in these cases is hepatic resection. Conversely, therapeutic response to antiamoebic therapy is often diagnostic of ALA and it may be helpful in patients with an atypical presentation.

Early diagnosis, based on the common clinical presentation of right upper abdominal pain, fever, and tender hepatomegaly,[13,14] and treatment prevents the onset of complications, which can be general or local. General complications include metastatic abscesses in other organs, skin involvement leading to amoebiasis cutis, and hepatic coma, whereas local complications as a result of extension, rupture, or perforation into an adjacent organ are subphrenic and lung abscess, intraperitoneal rup-

ture, rupture into surrounding organs, mediastinitis, pericardial rupture, myocardial abscess, secondary infection and inferior vena cava (IVC), or biliary tree or portal vein compression.[15]

Hematologic and biochemical investigations are not diagnostic but have a prognostic significance. Stool examination is not useful in endemic areas due to high prevalence of carriers. Serologic investigations include IHA, enzyme immunoassay, and enzyme-linked immunosorbent assay (ELISA).[16] The IHA test has sensitivity of 90%. It is more significant if negative, especially in endemic areas. After cure, the IHA test may remain positive for more than 3 years. IHA as a diagnostic test was not used in our study because India is an endemic area and high titers are present in other forms of invasive amoebiasis. Enzyme immunoassay is a simple, rapidly performed, and inexpensive test. It has a sensitivity of 99% and a specificity of more than 90% in patients with amoebic liver abscess. Unfortunately, the presence of antibodies may reflect an old infection and interpretation can be difficult in endemic areas. For ELISA, demonstration of antiamoebic antibody in titers more than 1:400 is considered strong evidence of ALA. Serum antibodies to *E. histolytica* become positive after 1 week of onset of symptoms and may remain positive for up to 6 months. Up to 10% of patients with acute amoebic liver abscess may have negative serologic findings.[17] Multiple ALA is an established entity in patients infected with HIV and hence ELISA for HIV is mandatory.[11] Ultrasonography is the investigation of choice for ALA. Based on echogenecity, ALA are classified as nonliquefied or forming liver abscess, partially liquefied, or liquefied liver abscess. Sensitivity of ultrasound is 85% to 90% and increases with experience of the sonologist. CT scan is more sensitive than ultrasound and is helpful in differentiating amoebic from pyogenic liver abscess with rim enhancement noted in the later. CT scan can also be helpful in diagnosing simple cyst, necrotic tumors, multiple liver abscess, and complicated abscess. Magnetic resonance imaging (MRI) has no distinct advantage over CT scan or ultrasound in typical cases, but it may be helpful in differentiating atypical lesions.

Amoebicidal therapy is directed to act within the intestinal lumen and wall, as well as systemically, particularly in the liver. Systemic amoebicidal drugs, like metronidazole, tinidazole, and chloroquine diphosphate, are used. The luminal amoebicidial drug, diloxanide furoate, which directly kills trophozoites, is mandatory after initial treatment with the systemic amoebicidal drugs.

Radiologic intervention includes needle aspiration or percutaneous catheter drainage. Routine aspiration of amoebic liver abscess is not generally indicated either for diagnostic or therapeutic purposes,[18] but the philosophy differs in the Indian context where studies have proved that intervention when combined with antiamoebic therapy expedites recovery.[19–23] In our study, patients on a combined approach had a rapid early clinical response and even when large, it did not cause any complications. Although the literature often stresses that medical therapy suffices, our study indicates that a combined approach of medical therapy and radiologic intervention is more effective, as most of the patients in our population had large or multiple abscesses. Needle aspiration leads to a significant decrease in subjective symptoms such as pain and early decrease in the size of cavity even in uncomplicated abscesses of >4 and <6 cm. However, no change was observed in the long-term resolution of the abscess cavity (6 weeks). Radiologic intervention was not associated with any complication and there was no morbidity or mortality.

Prerequisites for intervention are normal coagulation profile and absence of ascites. Indications for aspiration are abscesses of >6 cm or volume >300 mL,[18,24] impending rupture, multiple liver abscess, left-sided abscess, lack of response to medical therapy, secondary infection, compression symptoms like IVC obstruction, obstruction at porta hepatis, and pregnancy. Surgery is rarely required, and it has to be immediate in the case of ruptured abscess with generalized peritonitis and septicaemia, wherein adequate peritoneal toilet with drain placement is the mainstay. Open surgical drainage carries a significant mortality, hence it should only be use when the abscess has ruptured into the adjacent viscera, particularly in pericardium or peritoneal cavity. Adequate peritoneal toilet with drain placement is the mainstay. In cases of diagnostic doubt, laparoscopy is a useful tool.

However, in case of localized rupture USG-guided pigtail drainage is equally effective along with medical therapy. Predictors of adverse outcome or recurrence are gross hepatic dysfunction, cirrhosis, multiple or complicated abscess, HIV/AIDS, immunosuppression, and alcohol abuse.[25]

Newer diagnostic strategies involve detection of protein antigens in feces or serum by monoclonal antibodies and detection of protozoal DNA by use of nucleotide probes and polymerase chain reaction (PCR) amplification.[26] These are more helpful in epidemiologic studies and are not cost effective.

Lectin (surface antigen) vaccine to prevent amoebiasis has been tried but is of doubtful efficacy as no acquired immunity is achieved by first infection and reinfection is common.

ALA has evoked considerable concern and continuous research because of its frequency and complications, particularly in tropical countries. USG is the mainstay of diagnosis, although CT scan may have a role. Serologic tests, although highly sensitive and specific, are not useful in the Indian scenario due to endemicity of amoebiasis. With regard to drug therapy, the duration must be guided by individual experience and institutional protocol as the literature is divided on this issue. Radiologic intervention, along with pharmacotherapy, when routinely used in the Indian scenario helps in expediting recovery and this is an important message not highlighted in the Western literature. Early treatment of intestinal amoebiasis and the basic issues of hygiene, public health, and education need to be reemphasized.

In conclusion, novel information includes the incidence of multiple abscesses, especially in HIV-positive patients, the limited role of serologic tests in areas endemic for *E. histolytica*, and early initiation of a combined therapeutic approach.

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