

AMEBIC LIVER ABSCESS IN IRANIAN CHILDREN

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Abstract- Although amebic liver abscess can be a cause of significant morbidity and mortality in all ages, there are few reports dealing with this entity in children.

Twenty-four children with amebic liver abscess, ages ranging between 8 weeks and 14.5 years were managed at the Tehran University Hospital of Children, Iran, between November 1987, and October 2001. The most frequent presentation was high grade fever and right upper quadrant pain, associated with tender hepatomegaly, leukocytosis and an elevated erythrocyte sedimentation rate. The diagnosis was confirmed by elevated indirect hemagglutination titers and ultrasonography of the liver. Unlike the experience in adult patients, none of the patients had concomitant jaundice and significant derangement of liver enzymes.

The abscesses were likely to be solitary (22 of 24 patients). There were 17 males and 7 females. Most patients (80%) were between 8 weeks to 14.5 years of age. In five patients possible predisposing factors were tuberculosis, chickenpox, tetralogy of fallot and thalassemia major. All patients received metronidazole (50 mg/kg/day), followed by a therapeutic course of a luminal amebicide. There were no deaths despite a mean delay of 15 days before presentation to our hospital.

In conclusion a high index of suspicion, early institution of metronidazole therapy and aspiration of abscesses with potential to rupture are believed to have contributed to the better outcome in these children when compared with results in previous reports.

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INTRODUCTION

Amebiasis is endemic in the tropical and subtropical regions of the world and contributes to public health problems in industrialized countries (1,2). Amebic liver abscess (ALA) occurs in approximately 5-7% of patients who develop amebic infestation of the intestinal tract (3,4,5). ALA is more common in adults and is a cause of significant morbidity and mortality particularly when rupture of the abscess occurs into the peritoneal, pericardial or pleural cavities. Despite a worldwide prevalence of amebiasis, reports describing experience with ALA in the pediatric age group are sporadic (6,7).

After amebic dysentery, amebic liver abscess is the second most common form of invasive amebiasis caused by *E. histolytica*. It occurs in 1-5% of children and 10-50% of adults with invasive intestinal amebiasis. In the USA, persons with amebic abscesses often have migrated from or travelled to Mexico or to Central or South America. Often they are typically, young adult male, during the second and fourth decades of life, but

ALA in children is variable for age (8,9,10).

The clinical features of ALA are usually non-specific, with onset that is insidious for several days or weeks. Although right upper quadrant abdominal pain, less commonly, epigastric pain is associated with ALA, this type of pain is more common in adults than in children, who complain mostly of diffuse abdominal pain (11,12). A low-grade fever, malaise and anorexia are the most typical symptoms but are not always considered in children. So hepatic abscesses should be thought in the evaluation of children with obscure abdominal pain, or prolonged fever of unknown origin (13,14). The purpose of this study was to review the presentation and management of children with ALA from one center in Iran and to compare the outcome with the experience reported by others.

MATERIALS AND METHODS

Medical records of all patients younger than 15 years of age managed at one of Tehran University Hospitals of children, in Iran, with a diagnosis of ALA were retrospectively reviewed. The study period was between November, 1987 and October, 2001. The diagnosis was established via elevated indirect

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hemagglutination (IHA) test, titers ($>1:250$) and ultrasonography of the liver. The patients' characteristics noted included age, sex, height, weight, potential risk factors, duration of symptoms and any treatment preceding admission to hospital. For this study anemia and leukocytosis were defined as a hematocrit less than 30% and a white blood cell count more than 11000/mm³, respectively. Elevation of alanine aminotransferase and serum alkaline phosphatase to twice the normal values was regarded as significant. Criteria for aspiration of ALA included lack of clinical improvement within 96 hours of medical treatment, abscesses larger than 7 to 10 cm in diameter and those located in the left lobe of the liver with a potential for rupture. All aspirations were performed with ultrasound guidance in the radiology department under sedation or ketamine anesthesia. The pus was examined microscopically for *Entamoeba histolytica* and cultured for aerobic and anaerobic organisms.

RESULTS

Twenty-four children with ALA were identified during the 14 years period. They constituted 0.16% of the annual pediatric admission to hospital. In contrast during a 7 year period, 0.5% of adult admissions to the other institution were ALA-related (there were 17 males and 7 females). The ages ranged from 8 weeks to 14.5 years (mean 6.3 years) with most patients (80%) presenting at between 2 and 10 years of age. Eighteen patients were below the standard 5th percentile in height and weight. Possible predisposing factors were present in five patients, including pulmonary tuberculosis (1) chickenpox (2), tetralogy of Fallot (1) and thalassemia major (1,4). The mean duration of symptoms before presentation to hospital was 15 days (range 3-45 days). Fifteen patients had previously received broad spectrum antibiotics including ampicillin and gentamycin. Of the 9 patients who presented first to hospital, 8 of them were suspected to have ALA at the time of admission. In one, ALA was diagnosed after abdominal pain and fever persisted after a negative abdominal exploration for appendicitis.

A combination of high grade fever and tender hepatomegaly was the most consistent clinical presentation (Table 1). None of the children had elevated serum bilirubin concentrations and the hepatic enzymes (alanine aminotransferase and serum alkaline phosphatase) were significantly raised in only 16.6% of the patients. The IHA titers were elevated in all patients, ranging between 1:256 and 1:4600. The stool was

examined microscopically in all patients but cysts of *E. histolytica* were detected in only 2 patients. Roentgenograms of the chest available in 23 patients revealed an elevated right diaphragm and atelectasis in 8 and a sympathetic pleural effusion in 6 patients. On ultrasonography 22 abscesses were solitary and, in 17 patients, localized to the right hepatic lobe. In 2 patients the abscesses were bilateral, in one giving a "Swiss cheese" appearance on ultrasonography (Fig. 1). The size of the abscesses varied from 3.5 by 3.0 cm to 12 by 10 cm. One patient with a large abscess (12 by 10 cm) presented with perforation into the peritoneal and pericardial cavity but recovered with surgical intervention.

Table 1. Clinical features in pediatric ALA (n= 24)

Symptoms	Frequency (%)	Signs	Frequency (%)
Fever	100		100
Right upper quadrant abdominal pain	91.2	Tender hepatomegaly	
Abdominal distension	83.3	Edema of Abdominal chest wall	2
Anorexia/ vomiting	29.0	Epigastric mass	16.6
History of dysentery	16.6		

Fig. 1. Liver showing multiple amebic abscesses on ultrasonography IHA titers. 1: 4600

All patients received oral metronidazole (50 mg/kg/day) as well as an aminoglycoside and penicillin initially. The latter antibiotics were discontinued after 96 hours once the diagnosis of ALA was established. The duration of metronidazole therapy was ten days, followed by a course of iodoquinol or diloxanide (for 20 days). The duration of hospitalization ranged from 5 to

21 days (mean 10 days) with no difference between medically treated and needle aspirated patients. Thirteen patients underwent needle aspiration of the abscess, but *E. histolytica* was not seen on smears in any of the specimens. Facilities for culture of *E. histolytica* are not available in our institution. Positive cultures for *Staphylococcus aureus* from the pus in two patients were considered to be secondary infections because previous aspirates in both patients were sterile. All patients recovered with resolution of the hepatic lesions documented by ultrasound or computed tomography. There was no mortality or any long term complications during follow-up ranging from 2 to 18 months.

DISCUSSION

Amebic liver abscess, the most common extraintestinal form of invasive amebiasis, has been recognized as a distinct entity since the time of Hippocrates. It occurs more commonly in adults, and few reports describe experience with ALA in children (1,2,3). However, ALA can cause considerable morbidity among children in endemic areas. It can be responsible for 0.03 to 0.6% of annual pediatric admissions, an experience similar to that in the present report. The prevalence of amebic infection varies with the level of sanitation and is generally higher in the tropics and subtropics than in the temperate climates (4,5). Our patients were from various areas of Iran more in rural and lower socioeconomic groups. Although more frequent in children less than 6 years of age, ALA has been reported in all pediatric ages. The present series includes a 8-week-old infant, but one of the youngest patients reported in the English literature was a 3-week-old neonate. The usual presentation in childhood is one of an acute illness with high grade fever, abdominal pain and tender hepatomegaly. The diagnosis is often delayed in cases of unusual presentation which include pyrexia of unknown origin, an epigastric mass, paralytic ileus with toxemia suggestive of typhoid fever and abdominal findings mimicking acute appendicitis (6,7). A past history of dysentery is not frequent and was present in only 16% of the children in the present series.

Nonspecific laboratory findings in children with ALA are similar to those in adults and include anemia, leukocytosis and a raised erythrocyte sedimentation rate. In contrast to an 18% to 31% incidence of jaundice reported in adults with ALA, none of the children in the present series had clinical or laboratory evidence of jaundice. The liver enzymes were significantly raised in

only 16.6% of these children, unlike the significant derangement reported in adult patients (6-8). Only 8% of our patients had multiple abscesses compared with the 25 to 50% incidence reported in adults. Rupture of the ALA into the peritoneal right pleural or pericardial cavity is the most complication of ALA which occurs frequently in adults but was seen in only 1 of the 24 children in this group. The patient recovered with surgical intervention and resolution of the abscess documented by ultrasonography, about 2 weeks later (9,10).

E. histolytica was not identified in the pus aspirated from any of the abscesses in the present series, an experience similar to that of others. This could be a result of indiscriminate use of antibiotics including metronidazole, in the treatment of diarrhea in developing countries. Other factors cited were improper sampling of pus, inexperienced laboratory personnel and nonavailability of the more accurate immunocytochemical methods for detection of *E. histolytica* in pus. The diagnosis of ALA is usually established, therefore, by elevated IHA titers in the presence of characteristic hepatic lesions detected on ultrasonography and/or computed tomography (11). An elevated IHA titer, although a sensitive indicator, should be interpreted in the light of the clinical picture, because it may not distinguish between recent and old infections. Titers ranging above 1:128 and 1:250, however, are considered indicative of invasive amoebiasis. In the present study titers greater than 1:250 were used as diagnostic for ALA in the presence of ultrasound evidence of hepatic abscess (12,13). Sensitivity of ultrasonography and computed tomography is reported to be comparable for the diagnosis of ALA. Sonography is the preferred modality because it is highly accurate, relatively inexpensive, widely available and can be repeated safely on multiple occasions to guide aspiration of the ALA and for assessing success of management. In the present series 13 patients underwent aspiration when the condition was considered nonresponsive to medical treatment with oral or parenteral metronidazole (50 mg/kg/day) when potential for rupture of the abscess was considered significant as a result of its size (more than 5-7 cm) and location. We believe judicious use of aspiration in these children was responsible in preventing the frequent rupture of the ALA reported in previous studies (12-14).

In earlier reports from South Africa and the United States the mortality rate in children with ALA was significant, ranging as high as 45%. Contributing factors were delay in the diagnosis and possibly the relatively immature immune system in the very young child (15).

In contrast, there were no deaths in the present series despite an average delay of 15 days before presentation. Our experience appears to indicate a less fulminant nature of ALA in these children when compared with reports, including one from the hospital dealing with adult patients. We believe that a high index of suspicion, use of metronidazole for treatment and a policy of aggressive aspiration of the ALA could have contributed to the better outcome in these children.

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