AMEBIASIS IN CHILDREN

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Amebiasis is a global problem which assumes a greater magnitude in developing countries in the tropics. *Entameba histolytica* infects the gastrointestinal tract of approximately 10% of the world population(1). In India the incidence of the disease in general population varies from 0.7% in parts of Himachal Pradesh to 72% in Urban Calcutta(2). In children the reported incidence of intestinal amebiasis varies from 0.2% to 10.8%(3).

Pathogenesis

Entameba histolytica is a protozoan parasite and exists in two forms, a rigid cyst or an ameboid trophozoite of 15-50 μm in diameter. Infection is usually transmitted by ingestion of cysts in contaminated water and food particularly fresh vegetables. Cysts are killed by hyperchlorination but not by usual municipal chlorination methods(4). In the small intestine the cysts develop into trophozoites which invade the tissues mainly the colon involving the cecum and rectosigmoid area although all portions of the bowel may be involved.

Infection with *Entameba histolytica* does not necessarily lead to disease. In fact, in most cases it remains within the lumen of large intestine as a commensal. The factors that determine tissue invasion are not fully understood. Studies of the epidemiology of infection, isoenzyme analysis and DNA probe hybridization indicate that there are distinct pathogenic and nonpathogenic strains of *Entameba histolytica*(1). *Entameba histolytica* strains have been classified into 22 different zymodemes and of these only 9 are invasive (pathogenic), rest being commensal in nature(5). Trophozoites and cysts of pathogenic and nonpathogenic zymodemes are indistinguishable on morphological grounds. There are suggestions that isolates may change their zymodemes upon exposure to certain bacteria or viruses upon transmission to a different host(6). Even in endemic areas, avirulent zymodemes are far more common than virulent ones, which account only for 10% of infections. All pathogenic strains isolated from India belong to zymodeme XIV(5). A second marker for virulence is susceptibility to lysis by human serum, invasive strains being resistant and avirulent strains susceptible(5).

The pathogenesis of invasive amebiasis follows a specific pattern. Colonization of the bowel lumen with adherence of trophozoites to the colonic mucus blanket, amebic penetration or depletion of protective mucus layer with disruption of epithelial barrier and parasite lysis of responding host inflammatory cells accompanied by deep tissue penetration(1). The ameba proliferate and

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establish contact with the mucosal cells through specific receptors. The trophozoites also secrete numerus proteases active against basement membrane constituents and collagen which undoubtedly facilitate amebic lysis of host cells(1).

Host factors such as stress, malnutrition, alcoholism, steroid therapy and immunodeficiency may influence the outcome of infection. Alteration in the nature of quantity of colonic mucus may influence virulence. Virulence may also be conditioned by the bacterial flora in the colon(5).

Tissue invasion by ameba quickly induces specific antibody formation by the host but the frequency of reinfection suggest that little or no protective immunity develops(4).

Pathology

The motile trophozites invade the large bowel often at cecum, ascending colon and rectosigmoid causing deep seated ulcers which have a broad base and narrow neck and hence are described as flask shaped ulcers. A deep and wide base is because of the digestion of the submucosa by proteolytic eyzymes. In typical cases mucosa between ulcers is grossly normal. With deeper penetration by the trophozoites, the walls of mesenteric venules may be penetrated. Such amebas are swept by the circulation into the portal stream and then to liver, the dynamics of the system favour seeding of the right rather than the left lobe(7). Although host defenses probably eliminate the majority of invading trophozoites one or more tiny colonies may remain which coalesce to form an amebic hepatic abscess. Such abscesses do not contain pus or bacteria but consist of necrotic liver debris accompanied by variable amounts of blood. Invading amebas are characteristically found at the periphery of the lesion. The liver abscess can burst into the pleural cavity and lung, pericardium or may form a subdiaphragmatic abscess. Metastatic amebiasis arises uniformly as a secondary complication to a hepatic abscess and may occur as a rarity in any part of the body.

Clinical Features

The illness may occur within two weeks of infection or may be delayed for months.

(1) *Intestinal amebiasis:* It is markedly protean in its clinical features.

(*a*) *Asymptomatic cyst passers:*

(*b*) *Acute watery diarrhea:* In some patients the diarrhea is not fulminant but of mild intensity. The stools are mushy to watery and are accompanied by flatulence(7).

(*c*) *Non-dysenteric colitis:* This has been reported by several workers from India(3). Recurring diarrhea, abdominal pain and flatulence may be present for months or even years.

(*d*) *Amebic dysentery:* There is considerable range in the severity. Mild disease is associated with abdominal discomfort and increased frequency of bowel action with blood stained mucus or frank blood with stools. At the other extreme there can be severe dysenteric diarrhea. In severe cases it leads to fulminant colitis leading to gangrene of bowel, peritonitis intestinal obstruction and hemorrhage(3,8,9).

Intestinal amebiasis may lead to prolapse of rectum indicating the necessity of careful examination of all such cases for presence of *Entameba histolytica*(3,9).

(2) *Extraintestinal amebiasis:* Extraintestinal spread of the disease may occur

even in the absence of amebic dysentery.

(*a*) *Amebic liver abscess:* Liver is the commonest organ involved. It usually follows after 1-2 months of amebic dysentery. Amebic liver abscess is relatively uncommon in children(7,9). Udani, *et al.*(10), have reported the incidence in children to be 0.002% to 0.009% of all hospital admissions. It often presents as acute process manifesting as fever, tender hepatomegaly, anemia and leucocytosis. To make the diagnosis easier, antecedent or concurrent dysentery is present in more than 50% cases(9). It affects equally both sexes and is more often multiple in children in contrast to single large abscess seen in adults(9). The liver abscess may rupture externally through the parieties or into the pleural cavity, lungs, pericardium, stomach, peritoneum, *etc.*

(*b*) *Pulmunory amebiasis:* It can be primary or secondary due to extension of hepatic abscess.

(*c*) *Cerebral amebiasis:* It is one of the rare varieties of metastatic emebiasis. The abscess is generally single and of small size.

(*d*) *Cutaneous amebiasis:* It is usually found over the region adjoining a visceral lesion such as in the areas of drainage of liver abscess, colostomy wound or infected rectum.

Diagnosis

The various diagnostic modalities which can be useful are:

(1) *Examination of stool:* Stool sample must be examined within one hour of collection for identification of motile trophozoites in saline preparation. Stool sample must be free of contaminants like barium, castor oil, mineral oil *etc.* Pretreatment with tetracycline, sulphonamide, bismuth and kaolin interfere with the diagnosis. Feces can be preserved in polyvinyl alcohol and later stained with iron hematoxylin. Examination of 3-6 stool samples if carried out adequately allows the diagnosis to be made in 80-90% of patients(4). In asymptomatic group of patients, stool must be examined for cysts directly as well as by concentration method. Cysts of *E. histolytica* are present in the stool sample in less than 15% of cases of liver abscess.

(2) *Colonoscopy*: This must be performed cautiously in patients with severe colitis. In patients of amebic dysentery, the typical findings are scattered elliptical ulcers with surrounding normal mucosa. Scrapings or direct aspirate from the ulcerated rectal mucosa must be examined microscopically for motile trophozoites. Biopsy specimen from the rectal mucosa can also be examined for making the diagnosis(8,11).

(3) *Upright X-ray Chest:* The *X*-ray of chest in patients with liver abscess may reveal elevation of right dome of diaphragm and evidence of pleural effusion.

(4) *Ultrasonography:* Localization of liver abscess is best accompalished by ultrasonography as it is safe, non-invasive, economical and a quick method. Early findings may be manifested as focal or diffuse areas of increased or decreased parenchymal echoes. With time a well defined cavity demonstrating irregular thick inner walls and varying degree of echogenecity may develop. Approximately, 20-30% of pyogenic liver abscesses contain gas whereas amebic abscesses do not contain gas unless secondarily infected(12). When amebic liver abscess is suspected, repeated ultrasound examination is required as it not only helps in diagnosis but is an accurate way of follow-

ing the treatment. During the follow-up period, ultrasound examination will show that many abscesses heal without any residual deformity, but this may take many months(7,13).

(5) *Serology:* Various serological tests like indirect hemagglutination, Agar gel immunodiffusion precipitate, latex agglutination CIEP, *etc.* are available for diagnosis. In general these tests are positive in 80-90% of patients with extra-intestinal disease(4,14,15). The performance characteristics of diagnostic methods in amebiasis show serological tests have superior sensitivity and predictive value in recognizing invasive disease(15). Indirect hemagglutination test seems to be most sensitive of serological tests and probably the best for epidemiological studies(15).

(6) *ELISA test:* It has become possible to detect amebic antigen in stool sample by this method. It is a very simple and highly sensitive method but not yet conclusively evaluated(14).

(7) *Diagnostic aspiration of liver abscess:* The diagnosis of liver abscess can be made in majority of cases on the basis of clinician's suspicion and recognition of a well described clinical syndrome. Although with present available therapy, aspiration of abscess is rarely required, the abscess material either aspirated or when the abscess bursts can be examined for confirming the diagnosis. The abscess material is most often odorless and bacteriologically sterile. On exposure to air, the material rapidly darkens to assume a dark brownish color, classically described as "anchovy sauce". The aspirate samples should be obtained in small containers at frequent intervals. Thus, the last fraction, undiluted by the main mass of aspirate is most likely to contain amebae. Secondary infection of amebic abscess has been reported from 10-30% of patients(7). Predominant organisms have been *Staphylococci, Streptococci* and *E. coli*. With specific techniques, a significant number of anaerobes are recovered(7). Hence, the abscess contents should be cultured aerobically and anaerobically as well as being examined for *E. histolytica.*

Treatment

Table I summarizes the most useful drugs and their dosage for the management of intestinal and extra-intestinal infection.

Asymptomatic Carriers

Treatment of asymptomatic carriers living in endemic areas is a debatable issue. It is generally agreed that they must be treated because(16): (*a*) There is no ready means of determining whether encysted amebae belong to pathogenic or non-pathogenic zymodèmes; (*b*) The carrier is a source of infection for himself and the others; and (*c*) Although rare, amebic abscess of liver, brain or lungs may develop in carriers who had few or no previous symptoms of intestinal amebiasis. A reasonable course of action is to treat them with Diloxanide furoate for 10 days(6,16). Alternatively, one can use paromomycin sulfate.

Mild Intestinal Infection

Metronidazole or tinidazole can be used.

Amebic Dysentery

The mainstay of treatment is metronidazole. If patient is very sick and cannot accept the drug orally it can be given intravenously for 7 - 10 days. Recent studies have shown that tinidazole orally is highly effective in the treatment of intestinal as well as amebic liver abscess, the cure rate being 92%(9). In patients where use of nitromidazole group of drugs is contraindicated or

TABLE I—*Choice, Route, Dose and Duration of Administration of Amebicidal Drugs*

Form of infection	Drug	Dose (mg/kg/day)	Route	Duration of therapy (days)
1. *Intestinal*				
(*a*) Trophozoite in stool	(1) Metronidazole	35-50	Orally	10
	(2) Tinidazole	60	Orally	3
	(3) Dehydroemetine	1-1.5	IM or S/C	5-10
	(4) Tetracycline	25	Orally	5-10
	(5) Paromomycin sulfate	25-35	Orally	5
(*b*) Cyst in stool	(1) Diloxanide fuorate	20	Orally	10
	(2) Paromomycin sulfate	25-35	Orally	5-10
	(3) Metronidazole	35-50	Orally	7-10
2. *Extraintestinal*	(1) Metronidazole	35-50	Orally	10
	(2) Dehydroemetine	1-1.5	IM	10
	(3) Chloroquinine	10-20	Orally	14

ineffective, dehydroemetine can be used. Antibiotics such as tetracycline or paromomycin sulfate can be used in conjunction with metronidazole to treat severe form of intestinal amebiasis. The tissue amebicides may not eradicate all luminal organisms, therefore, a luminal amebicide (diloxanide furoate) is usually given after the dysentery resolves.

Cure in cases of intestinal amebiasis is accomplished if no ameba are found in multiple stool specimens properly examined at intervals for 6 months(16).

Amebic liver Abscess

These cases should be hospitalized immediately and treated with metronidazole. Alternative tissue amebicides include emetine or dehydroemetine. An additional drug that is effective against hepatic amebiasis is chloroquinine. It should be used only in combination with tissue amebicides. Secondary bacterial infection of amebic liver abscesses, reported in 10-30% of patients, is suspected when patient is unusually toxic and when liver aspirate is malodorous(7). These cases require antibiotics in addition to anti-amebic therapy and surgical drainage may be needed.

The indications for aspiration of liver abscess are(4,8): (*i*) Imminent rupture; (*ii*) Located in left lobe because of risk of spread to pericardium; (*iii*) Large size (>10 cm); (*iv*) No response to medical therapy in 48-72 h; and (*v*) Uncertainty of diagnosis.

Extension of liver abscess into pleural cavity or pericardium is a serious complication and requires specialized care. Needle aspiration under ultrasonographic guidance is indicated in addition to specific therapy. However, chest tube drainage should never be attempted.

The prognosis in uncomplicated cases of liver abscess is excellent as complete functional and anatomical restoration of liver

can be expected with medical treatment. Overall mortality varies from 10-20%.

Prevention of Amebiasis

The high prevalence of disease in population living in unhygienic areas than in improved urban areas indicate that infection can be prevented. Prevention depends upon significant control of contamination of soil, water and food as well as on improvement in education, personal hygiene and living conditions(17).

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