Amebiasis

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ABSTRACT

Amebiasis is an important cause of death from parasitic disease worldwide. The causative organism is *Entamoeba histolytica*, which has an infective cyst stage and a pathogenic and motile trophozoite stage. The clinical presentation can vary from an asymptomatic carrier state to fulminant colitis and colonic perforation. The majority of patients can be managed medically. However, a small percentage of patients require urgent exploration and resection with an associated high mortality rate. Early recognition and initiation of medical therapy including treatment of asymptomatic carriers are vital to preventing catastrophic outcomes.

KEYWORDS: Ameba, colitis, fulminant, parasite

Objectives: On completion of this article, the reader should be able to summarize the diagnosis and management of intestinal amebiasis.

Intestinal infestation with *Entamoeba histolytica* is common throughout the tropics and subtropics, where it is endemic. It is the second leading cause of death from parasitic disease worldwide. In the United States, amebiasis has become the most frequent parasitic infestation encountered by surgeons. This is largely due to the migratory influx of immigrants from Mexico and Central America, where amebiasis is endemic.¹ Conversely, there is a reported incidence of 20% to 30% in selected populations of homosexual men in North America and Europe.² Despite its growing incidence, there is limited mention of amebiasis and acute fulminant amebic colitis in major surgical textbooks dealing with diseases of the colon and rectum. Amebic colitis can often arise in a similar fashion to other colitides, but failure of the treating physician to consider this in the differential may lead to catastrophic complications. The purpose of this article is to review the pathogenesis, clinical presentation, work-up, and management of amebiasis.

PATHOGENESIS

E. histolytica exists in two forms: a nonmotile cyst, which is infective, and a motile trophozoite stage, which causes the invasive disease. The trophozoite lives in the wall and lumen of the colon.³ Often the cytoplasm of the trophozoites contains ingested red blood cells, which aids in the diagnosis.⁴ Trophozoites, however, do not exist outside the body and therefore do not transmit the disease. The primary mode of transmission is ingestion of cysts from contaminated food or water. Venereal transmission also occurs through the fecal-oral route. Once ingested, the cyst disintegrates in the small bowel and releases the trophozoites in the colon. These organisms live in the colon and feed on the bacteria and superficial mucosal cells, occasionally invading deeper and resulting in distant disease. The parasite creates a mucosal defect and a characteristic flask-shaped ulcer with necrosis in the submucosa and muscularis of the colon.⁵

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Miscellaneous Colitides; Guest Editor, Judith L. Trudel, M.D.

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The inflammatory response can be slight with intervening normal mucosa, or at times the tissue can be indistinguishable from that in ulcerative colitis, even progressing to frank perforation. Transmural necrosis has been shown to be due to amebic invasion of the segmental arteries of the colon, with consequent thrombotic occlusion and necrosis.⁶ The omentum plays a role in sealing the perforations and is believed to aid in revascularization of the colon. Lesions can occur anywhere in the colon but appear more frequently in the cecum and ascending colon and less frequently in the rectum and sigmoid. Occasionally, the trophozoite enters the portal circulation and travels to the liver, creating an amebic liver abscess.^{7,8} Rarely, they travel to the brain, resulting in abscesses,⁹ and to the perineum, genitalia, and skin, creating ulcerations.¹⁰

EPIDEMIOLOGY

E. histolytica is distributed throughout the world and poses a significant health risk in locations where barriers between feces and food and water supplies are limited. *Entamoeba* exists as two genetically distant species—*Entamoeba dispar*, a commensal, and *E. histolytica*, the pathogen. This has changed our understanding of the prevalence and distribution of the parasite worldwide. Indeed, the majority of the asymptomatic individuals infected are actually colonized with *E. dispar*, an organism that is not a pathogen and causes no mucosal disease even in severely immunocompromised individuals.¹¹ *E. histolytica* has also been demonstrated in stool samples of asymptomatic patients, yet it is also the causative agent in amebic colitis and associated extra-intestinal manifestations. Amebiasis can spread within families; therefore, household contacts of patients with the disease should be screened for colonization and treated.

Approximately 40,000 to 100,000 people die yearly from amebiasis, making it the second leading cause of death from parasitic diseases.⁵ In the United States, the majority of the reported cases are in immigrants from or travelers to endemic areas such as Mexico, Central America, and South America. A subgroup of the population that needs to be addressed is homosexual men. A prevalence rate of 20% to 30% has been documented in selected populations of homosexuals of North America and Europe.¹² A study of a venereal disease clinic population demonstrated 55% positivity rate for *E. histolytica* from repeated stool specimens, although there was only 56% compliance.¹³ The relationship is thought to be related to a large reservoir of infection and a prevalent mode of transmission, such as oral-anal sex, promiscuity, and anal hygiene. Despite the frequent isolation of *E. histolytica* from homosexuals, the occurrence of amebic colitis or liver abscesses is infrequent.

Amebic colitis affects children and adults of both sexes equally. However, amebic liver abscesses appear more often in men between the ages of 18 and 50, in whom rates are 3 to 20 times higher than in other populations.¹⁴ The reason for this profound difference is unknown. Several studies have suggested that hormonal differences between sexes may play a vital role.⁷

CLINICAL PRESENTATION

Amebic disease has a variety of clinical manifestations. These can be subdivided into intestinal and extraintestinal presentations. Within any one patient there can be considerable overlap in the sites of infection.

Intestinal

The majority of patients are asymptomatic carriers. The organism lives in the bowel lumen and sheds cysts in the stool. The potential for invasion still exists in these patients, and it seems reasonable to begin these patients on treatment. Indeed, 4% to 10% of asymptomatic carriers eventually develop invasive disease.¹⁵

Clinical presentation can vary from fulminant colitis to mild, intermittent episodes of blood-tinged diarrhea. Associated symptoms include fever (< 40% of patients), weight loss, dehydration, and anorexia. Symptoms can persist for months to years with asymptomatic intervals.^{16,17} Others have signs and symptoms similar to those of ulcerative colitis, with a small percentage developing toxic megacolon.¹⁸ The lack of specificity means that amebiasis must be considered in the differential diagnosis for all patients presenting with colonic symptoms.

Physical findings vary from no findings to mild tenderness with an enlarged liver. Occasionally, patients present severely ill with tachycardia, hypotension, and peritonitis.¹⁵ In this group, perforation must be considered and quick action is necessary as mortality is high. Routine blood counts vary from normal to mild anemia. However, severe anemia is rare.¹⁵

Noncolitic diseases, such as amebomas and strictures, are infrequent. Strictures can be long or short, symptomatic or asymptomatic.¹⁷ They can mimic malignancy, mandating biopsy. Amebomas appear as tumors—firm and nodular, with a fibrous outer wall and an inner core of necrotic tissue and trophozoites. They occur most frequently in the cecum and appear as filling defects on barium enema.¹⁷ Amebomas can occur in the presence of active colitis or can be independent of active disease, mimicking malignancy. The differentiation is important as the treatment for an ameboma is medical. They often disappear after initiation of appropriate therapy.¹⁵ On examination, a right lower quadrant mass or a rectal mass may be palpated.

Extraintestinal

LIVER

The most common extraintestinal manifestation of the disease is amebic liver abscess. The disease usually predominates in young adult males. It usually arises from spread by the portal circulation as amebic trophozoites breach the colonic mucosa. In the liver they produce a well-circumscribed area of necrosis surrounded by a halo of hemorrhagic tissue, which eventually progresses to a cavity containing necrotic debris.⁸ Characteristically, the fluid is chocolate brown or resembles ketchup and is usually odorless and sterile. The trophozoites are most often found in the wall of the cavity.¹⁹

Microscopic examination of the stool is often negative for *E. histolytica* trophozoites or cysts.⁷ A careful history is mandatory as individuals can present months to years after travel to endemic regions. The most common presenting symptom is right upper quadrant pain with radiation to the shoulder, right chest, or epigastrium, often accompanied by fever, night sweats, malaise, and anorexia. Additional signs can include a nonproductive cough and anorexia. On physical examination the patient often appears tired, wasted, febrile, and uncomfortable. There may be rales over the right lung base and a tender, enlarged liver. Patients often have a leukocytosis, mild anemia, elevated alkaline phosphatase, and an elevated erythrocyte sedimentation rate. The presentation can often be acute, less than 10 days in duration, or it can be chronic with anorexia and weight loss. The colon is rarely involved, so endoscopic examination is of minimal value. Computed tomography is a helpful adjunct in making the diagnosis. In one series of amebic liver abscesses, 83% of the lesions were located in the right hepatic lobe.²⁰ Finally, indirect hemagglutination assay, which detects antibodies directed against *Entamoeba*, is a critical laboratory test and is positive in 100% of patients with amebic invasion. Early false-negative results do occur, so the test should be repeated if clinical suspicion is high.²¹

Amebic liver abscesses can extend into the thorax, producing an empyema (~7% to 20% of patients),^{22,23} or into the pericardium.²³ They can freely rupture into the peritoneum (2% to 7% of patients)²⁴ and bowel. Overall, mortality rates are low with thoracic involvement—patients present with a productive cough and sputum containing trophozoites—but increase with pericardial (mortality rate of 30%) and peritoneal involvement.^{22–24} This further substantiates the role of an early treatment protocol.

BRAIN

Amebic brain abscesses are rare and arise concurrently with hepatic abscesses (0.1% of hepatic abscess cases), demonstrating the importance of invasion in their

pathogenesis.⁹ Patients present with sudden onset of symptoms—headache, seizures, vomiting, and mental status changes, with a rapid progression to death. Outcomes appear to improve with early initiation of medical therapy.

OTHER

There have been case reports of urinary tract problems, rectovaginal fistulas, perianal disease, and cutaneous abscesses.^{10,25}

DIAGNOSIS

The diagnosis of amebic colitis depends on the demonstration of *Entamoeba* in the stool or the colonic mucosa of patients. A single formed stool will demonstrate one third to half of amebic infections, and examining three successive stools on three separate days improves the yield to 60% to 70% of patients with colitis and 43% of patients with amebic liver abscesses. Furthermore, barium, bismuth enemas and antibiotics can interfere with the study, producing false-negative results.²⁶ However, this method cannot distinguish between *E. histolytica* and its nonpathogenic counterpart *E. dispar*.

With escalating health care costs, it is difficult to justify keeping patients under observation without initiating medical therapy. As a result, serologic testing has become a valuable adjunct in the diagnosis of amebiasis. Numerous tests are available, but the indirect hemagglutination assay (IHA) is highly sensitive with a high negative predictive value. In one study, 91% of patients with amebic colitis and 95% of patients with amebic liver abscesses had a positive IHA. A negative test implies that invasion did not occur.²⁷ IHA remains positive for up to 20 years and does not differentiate a previous infection from an acute one. However, this test is expensive, require experience to perform, and requires time to demonstrate results.

Endoscopy can be a useful adjunct in the diagnosis. Ulcers can grow to approximately an inch and have a flask shape. They are often covered with a yellow exudate. The intervening mucosa is often normal in appearance. Fulminant colitis can have an endoscopic appearance similar to that of diffuse ulcerative colitis, underlining the importance of a thorough clinical history.

TREATMENT

Amebiasis

The cornerstone of treatment for amebiasis remains the nitroimidazole derivatives (metronidazole, tinidazole, ornidazole). Ninety percent of patients are cured with metronidazole at 750 mg three times per day.³ Surprisingly, resistance has not been detected. Following a

10-day course, treatment with a second-line intraluminal agent (paromomycin, iodoquinol, diloxanide furoate) is required to eradicate the colonization. Follow-up stool examination is recommended in all patients to ensure clearance. Asymptomatic carriers with documented *E. histolytica* should be treated with a luminal agent to eradicate the infection.^{28,29} This is based on the known risk of developing invasive disease in these patients. In addition, these individuals shed cysts and are a potential risk to public health. Interestingly, *E. dispar* infection does not require treatment but is a marker for exposure to contaminated food or water, or both.

The majority of patients respond well to medical management alone. Occasionally, for unknown reasons, the disease progresses to a fulminant necrotizing colitis that may be indistinguishable from other forms of acute colitis. This is a rare but frequently fatal complication. It is vital to recognize the difference early as treatment with steroids can often be fatal. Several studies have advocated urgent exploration in addition to intensive support and medical management when the diagnosis has been made. Aristizabal et al reviewed their experience of 50 adult patients with fulminating amebic colitis over an 18-year period and reported a mortality rate of 60% for the various operative procedures performed.³⁰ Additional studies in the literature support a mortality rate of 50% to 100% (Table 1).^{1,30-38} Finally, fulminating colitis has been observed with increasing frequency in patients suffering from malnutrition, diabetes, and other chronic illnesses.³¹

The classic operative finding in a patient with fulminating colitis is an inflamed, extremely friable colon. It is wrapped with omentum, which conceals the underlying full-thickness necrosis and perforation. The colon is so friable that it can disintegrate with any form of manipulation.³¹ The mucosal lining is often replaced by necrotic debris with the lumen being filled with foul-smelling pus.

Table 1 Mortality Rates of Necrotizing Amoebic Colitis: Review of the Literature

Reference	N	Mortality (%)
Chen et al ³³	8	87.5
Vajrabukka et al ³¹	11	55
Elhence et al ³²	10	70
Wig et al ³⁴	9	67
Giacchino et al ³⁵	5	60
Stein et al ³⁶	7	57
Thuse ³⁷	3	100
Hadley and Mickel ³⁸	29	66
Ellyson et al ¹	6	83
Aristizabal et al ³⁰	50	60

Table adapted from Ellyson et al.¹

Resection of the necrotic colon is the treatment of choice.^{30,32} However, the extent of resection depends on the degree of colonic involvement. If only the right colon is involved, a right colectomy with an ileostomy and mucous fistula is the preferred management strategy. Frequently, the entire colon is involved, and these patients often require a total abdominal colectomy. Primary anastomosis is never an option as these patients are often critically ill and there is a high risk for suture line dehiscence. Other forms of management include diverting the fecal stream with a loop ileostomy and blow-hole colostomy,³⁹ simple suture repair of the perforations and drainage, and exteriorization of the diseased segment. These procedures are fraught with significant complications, perhaps because they leave the diseased colon behind. Luveno reported experience with 45 patients with transmural amebic colitis treated with intraoperative prograde colonic lavage and diverting loop ileostomy.⁴⁰ This is based on the previous observation that the adhesive wraps help seal perforations and have the capacity to revascularize the ischemic colon.⁶ Disturbing these wraps could have a deleterious effect. The reported mortality was 13% after the initial phase of the procedure and 5% after ileostomy closure. Despite the small numbers and lack of randomization, this study represents an attractive alternative to a radical resection with its associated high mortality rate.

Amebic Liver Abscesses

The management of amebic liver abscesses is distinctly different from that of other forms of hepatic abscesses. The majority of patients respond to metronidazole therapy within 72 to 96 hours.^{28,29} These patients should also be treated with a luminal agent to eliminate the intestinal source. Surgical or percutaneous drainage of uncomplicated abscesses is usually not necessary and should generally be avoided. However, aspiration of large abscesses (> 300 cm³) appears to decrease hospital stay and improve overall clinical status.⁴¹ Aspiration should be considered in individuals where the diagnosis is in question (such as pyogenic liver abscesses), there is failure of medical management, or there are large left lobe abscesses (potential for rupture into the pericardium) and in severely ill patients where rupture may be imminent.⁵ Certainly, aspiration or catheter drainage has a role in amebic empyema and has demonstrated improved outcomes. There may also be a role for percutaneous techniques as well as surgical drainage in patients with amebic pericarditis.⁴²

CONCLUSION

Despite its low incidence within the United States, amebiasis can be a source of significant morbidity and mortality if not recognized early. Most forms respond

appropriately to medical therapy. Surgery and other less invasive techniques are reserved for nonresponders and patients presenting in acute distress.

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