

Amebic Colitis

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Abstract

Amebic colitis, also known as amebiasis, is a gastrointestinal disorder caused by invasion of the intestine by the protozoan parasite, *Entamoeba histolytica*. Although primarily a disease found in underdeveloped countries, this condition may exist in patients who have recently traveled outside the United States. Obtaining an accurate history and testing are crucial to correctly diagnosing and treating amebic colitis. This paper will examine the epidemiology, clinical presentation, and differential diagnoses of amebic colitis as well as recommend a standardized treatment plan based on current research.

DEFINITION AND EPIDEMIOLOGY

Amebic colitis, also known as amebiasis, is a protozoal disease affecting the large intestine caused by *E. histolytica*. Annually, 40 to 50 million symptomatic cases are reported across the globe (1), with 40,000 to 100,000 deaths each year, making this condition the second leading parasitic cause of death in the world (2). Amebic colitis case fatality ranges from 1.9 - 9.1%; fulminant amebic colitis has a mortality rate of greater than 40% (2,3). A commensal organism to *E. histolytica* is *Entamoeba dispar*, which is similar in morphology to *E. histolytica*, but does not produce signs or symptoms of dysentery (4).

E. histolytica can be found worldwide. Africa, Central and South America, and Asia are areas where the disease is endemic (1). Contamination of water stores in countries with poor sanitation processes can lead to the spread of the protozoan to humans. Water contaminated with feces allows for the fecal-oral transmission of the disease. Consuming food prepared by one who has not washed his or her hands after defecation also can lead to transmission of *E. histolytica* (4). Oral and anal sex, particularly between men, has also been implicated in the spread of the disease (5).

Amebiasis affects both adults and children equally (2). In the U.S., most cases are found in people who have recently traveled to developing countries where food and water sanitation are less sophisticated (2). Once infected, an individual can easily pass the protozoan on to other family members in the household (2).

PATHOPHYSIOLOGY

E. histolytica has a two-part life cycle. The protozoa enter

the gastrointestinal (GI) tract as cysts during the first part of the cycle. These cysts have a cell wall made of chitin, making them resistant to gastric acid in the stomach (6). The cysts are quadrinucleated, and released four ameboid trophozoites once in the small intestine, which travel to and inhabit the colon (6,7).

Trophozoites begin to attach to the epithelial cells of the colon by releasing D-galactose/N-acetyl-D-glucosamine (Gal/GalNAc), which allows adherence to the epithelial surface of the colon (7). Cysteine proteinases from the trophozoite causes the mucus lining of the colon to disperse and the affected epithelial cells quickly begin to lose their structure (7). The trophozoite uses structures called amebapores to puncture the epithelial cell's phospholipid bilayer, causing cytolysis (2). Lysed cells release pre-Interleukin 1 β , which is degraded by amebic cysteine protease to form Interleukin-1 β (IL-1 β), a cytokine (8). IL-1 β then attaches to adjacent epithelial cells, causing them to release the cytokines cyclooxygenase-2 (COX-2) and Interleukin-8 (IL-8) (2). These substances attract neutrophils, which squeeze into the intestinal lumen from the mucosa by creating a passage between the epithelial cells, providing an entryway for the amebae to enter the colonic mucosa. Neutrophils, killed when exposed to *E. histolytica*, release their own destructive contents and cause further injury to nearby epithelial cells (2).

Trophozoites are also able to cause host cell death by causing the cell to enter apoptosis, or programmed cell death. This process adds to the ability of the ameba to invade the mucosa via channels created by macrophages called to destroy the dying epithelial cell (6). Once in the host's

mucosa, the trophozoite is able to continue its tissue destruction in a lateral direction. This destruction results in an ulcer that is characteristically “flask-shaped,” with a wide base and a thin neck that extends to the intestinal lumen (6). This ulcer produces bloody stools that are a hallmark of amebic colitis (2). The host is at risk of developing paralytic ileus, sloughing of colonic mucosa, and perforation of the GI tract, causing fulminant amebic colitis, which has a mortality rate of greater than 40% (2). Toxic megacolon may also develop, particularly if the patient has been treated with corticosteroids, which inhibit the inflammatory process and allow *E. histolytica* to continue attacking the now further compromised host (2). Trophozoites in the mucosa may be able to escape the intestinal mucosa and invade the liver and brain. Entering the liver through the venous portal system, *E. histolytica* attacks hepatocytes and neutrophils, producing liver abscesses and causing further liver damage due to the release of cytokines from the damaged neutrophils (2).

Brain abscesses due to amebic invasion are rare, with death occurring in about half of patients developing this complication (2). Trophozoites are able to encase themselves in cysts, which are then excreted in the feces. An individual coming into contact with the infected feces is then at risk for developing amebiasis (4).

SIGNS AND SYMPTOMS OFTEN ENCOUNTERED IN THE EMERGENCY DEPARTMENT

The typical amebic colitis patient presents to the emergency department (ED) with a chief complaint of abdominal cramping. History of the present illness usually presents as a sudden onset of fever, abdominal pain, and diarrhea that may be bloody (3). Social history should include questions about any recent travel outside the U.S., particularly to underdeveloped countries, as well sexual practices, particularly anal-oral intercourse (4,5). Review of systems may reveal a recent bout of nausea and vomiting, fever, weakness, and unintentional weight loss. An accurate past medical should be obtained, as comorbidities such as acquired immune deficiency syndrome (AIDS) can severely impair the patient's ability to fight the infection (3). Physical exam of the patient may reveal a person in mild to severe distress with profuse diarrhea that is guaiac positive and sometimes containing frank blood. Cramping abdominal pain with distension and rebound tenderness may also be present (3). Orthostatic hypotension may also be present due to fluid loss from diarrhea (3).

DIFFERENTIAL DIAGNOSES

Differential diagnoses for this type of patient may include *Escherichia coli* O157:H7 (*E. coli* O157:H7), giardiasis, shigellosis, ulcerative colitis, and Crohn's disease. *E. coli* O157:H7 is a common cause of bloody diarrhea and abdominal pain in the U.S (3). Often the cause can be traced to eating undercooked hamburger or other type of meat, but an outbreak of *E. coli* O157:H7 in the U.S. in 2006, was due to contaminated spinach (5,9). *E. coli* infection can be ruled out if the patient has fever, as *E. coli* O157:H7 does not cause fever (3).

Giardiasis is caused by the protozoan *Giardia lamblia*, and is the most common form of diarrhea contracted from fecal contaminated water. Often called “backpacker's diarrhea,” stools are greasy, foul smelling, and often explosive in nature (10). Giardiasis does not produce bloody stools, which helps to rule out this differential diagnosis (10).

Shigellosis can be found worldwide, particularly in countries with poor water sanitation. Seventy-five percent of U.S. cases are caused by the bacterium *Shigella sonnei*, although other forms of *Shigella* are found worldwide (3). The patient with shigellosis may present with watery, green diarrhea that may be bloody. One can rule out this disease if fecal leukocytes (FLs) are found in the stools. FLs are generally very high in number in shigellosis, but not commonly found in amebic colitis (5,11).

Ulcerative colitis, a type of inflammatory bowel disease (IBD), typically presents with bloody diarrhea. The patient usually does not complain of abdominal pain, but is often anemic, leading to fatigue. The lack of abdominal pain helps to rule out this disease process (12).

Crohn's disease, another form of IBD, usually presents with abdominal pain, bloody diarrhea, anemia, and weight loss. Contrast radiography using barium enemas has been useful in identifying the characteristic “skip lesions” and cobblestone-like appearance found in the colon. Normal findings from the barium enema studies help to rule out both ulcerative colitis and amebiasis (12).

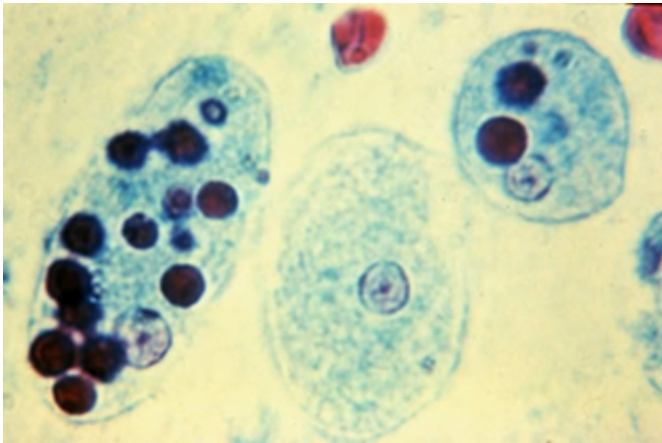
DIAGNOSTIC TEST FOR AMEBIASIS

Historically, testing for amebiasis was done using visualization with the presence of the characteristic ameboid protozoan in the patient's stool confirming the diagnosis. This method has since become non-diagnostic in the U.S. with the discovery of *E. dispar* and its similar morphology to *E. histolytica* (2). On careful microscopic exam, one may be

able to observe the presence of ingested red blood cells inside *E. histolytica* amebas (13). However if *E. dispar* is observed and mistaken for *E. histolytica*, the clinician may conclude amebiasis, when in fact shigellosis may be the cause (2).

Figure 1

Figure 1: Trophozoites of with ingested erythrocytes stained with trichrome.



Picture used with permission from DPDx: CDC's Web site for parasite identification <http://www.dpd.cdc.gov/dpdx>

Link to DPDx Amebiasis webpages:

http://www.dpd.cdc.gov/dpdx/HTML/ImageLibrary/Amebiasis_il.htm

Conclusive diagnosis of *E. histolytica* is now obtained by using ELISA antigen tests, which are almost 100% sensitive for *E. histolytica* (2,13). The *E. histolytica* II antigen detection kit is currently the only test that conforms to the World Health Organization's recommendation for diagnosis of *E. histolytica* (1). Complete blood counts will help to determine if the patient has become anemic from bloody diarrhea. A basic metabolic profile is helpful to determine electrolyte status of the patient, particularly whether the patient has developed hypokalemia from excessive fluid loss.

Colonoscopy may be helpful if stool tests for *E. histolytica* are negative or unavailable (2). Visualizing the colon may reveal small ulcerations, covered with yellow exudates. Tissue samples from the affected colon may reveal trophozoites, as well as the flask-shaped ulcerations characteristic of the disease (3,11).

Many areas where amebic colitis is endemic do not have the resources to afford the ELISA test, and may not have access to equipment needed for a colonoscopy. In these situations,

accurate microscopy coupled with the clinical presentation for acute amebic colitis may provide enough evidence to treat the patient for the disease. If microscopy were not available, the clinical signs and symptoms of amebic colitis may be the only information available to diagnose the patient, and treatment for amebic colitis should be initiated.

STANDARDIZED TREATMENT PLAN FOR AMEBIC COLITIS

Maintenance of the airway, breathing, and circulation must be monitored at all times while in the ED. Treatment of amebic colitis involves the prescription or administration of several drugs. Patients with mild colitis (not needing intravenous [IV] fluid therapy) may be treated on an outpatient basis with metronidazole (Flagyl) 750 mg orally three times daily for 10 days (3). This treatment should be followed by luminal agent such as the aminoglycoside paromomycin (Humatin) to destroy the cysts in the intraluminal. Dosing of paromomycin is 25-35 mg/kg orally three times daily for seven days (3). Taking these two medicines at the same time is not recommended, as paromomycin may cause diarrhea and may become difficult to distinguish from the signs of amebic colitis (11).

The use of loperamide (Imodium) is discouraged. Loperamide slows the ability of the intestinal smooth muscles to move, allowing increased water uptake in the colon for the typical diarrhea case (14). However, decreased smooth muscle activity increases the time the luminal wall is exposed to *E. histolytica*, increasing the chance of further amebic invasion (15). The use of corticosteroids is discouraged as well, as these agents may result in toxic megacolon (1).

Patients with severe colitis should be admitted to the hospital and given intravenous (IV) hydration (3). Normal saline with 5% dextrose may be useful for severe volume depletion as well as providing glucose lost to diarrhea. Potassium should be replaced if the patient is found to be hypokalemic because of the diarrhea. Admitted patients should receive metronidazole 500 mg IV every six hours for ten days (11). In the case of fulminant amebic colitis, broad-spectrum antibiotics should be given in addition to metronidazole, particularly if intestinal perforation is suspected (16). Ciprofloxacin (Cipro) may be given IV at 400 mg every eight hours (17).

PHARMACOTHERAPEUTIC AGENTS

METRONIDAZOLE

Metronidazole is the most effective medication for treating amebic colitis. This agent is effective only against obligate anaerobic organisms. The trophozoite phase absorbs the inactive form of the drug, transforming this agent to the active form. The active form then causes degradation of the anaerobe's DNA, eventually causing death of the organism. Death of

E. histolytica prevents further reproduction of the organism, thereby slowing the progression of the disease (18).

Side effects of metronidazole include nausea, headache, and dry mouth. Consumption of alcoholic beverages can cause severe and intractable vomiting (16). Use of cimetidine (Tagamet) may increase plasma levels of metronidazole due to cimetidine's ability to inhibit enzyme activity (3).

Metronidazole may also synergistically act on warfarin, resulting in prolonged bleeding times (11).

PAROMOMYCIN

Paromomycin is an aminoglycoside antibiotic. Aminoglycosides disrupt protein synthesis in aerobic bacteria, causing cell death. Although *E. histolytica* is an anaerobic protozoan, paromomycin has been shown to help eradicate the protozoa found in the lumen of the colon, but not in the tissue of the colon (19). By killing amebae in the lumen, transmission of cysts in the feces is decreased, limiting the spread of the disease via the oral-fecal route.

Paromomycin's primary side effect is diarrhea, but this drug may also cause nausea and abdominal pain (20).

Nephrotoxicity may result if paromomycin is used with other aminoglycosides, penicillins, or loop diuretics (11). Paromomycin may decrease plasma levels of digoxin (3).

CIPROFLOXACIN

Ciprofloxacin is a fluoroquinolone, a class of broad-spectrum antibiotics. This class inhibits bacterial DNA gyrase, preventing DNA from uncoiling from its normal supercoiled state. Unable to uncoil, DNA is incapable of replicating and producing new strands for daughter cells (18).

The side effects of ciprofloxacin side effects include nausea, vomiting, and diarrhea (18). *Candida* yeast infections have been known to occur with ciprofloxacin use (18). Blood plasma levels of theophylline and warfarin have been noted to increase when used concurrently with ciprofloxacin (18).

NON-MEDICAL TREATMENT METHODS

An herbal remedy used in Mexico for amebiasis is chaparro amargo, scientific name *Castela texana* (21,22). Thirty drops of this tincture is consumed with water in the morning, and repeated in the evening before dinner (21). This dosage is taken for one week, halted for one week, and then taken again for another week. This regimen is conducted three times a year (21). The exact mechanism of action for this substance is unknown, but the protective effect of *C. texana* is thought to involve antioxidant properties of the shrub (22).

HEALTH PROMOTION AND LIFESTYLE CONSIDERATIONS

Patients with amebic colitis must take care to prevent passing the *E. histolytica* cysts to family members and significant others. Family members living with the patient should be screened for *E. histolytica*, even in the absence of symptoms (3). Sexual practices involving oral/anal contact should be stopped until post-treatment stool samples have shown eradication of the disease (3).

Any person traveling to a developing foreign country should be counseled about prevention of amebic colitis. All unbottled water should be boiled prior to consumption or other use (3). Typical chlorine treatment alone is ineffective at destroying amebic cysts (11). Eating raw vegetables should be discouraged (11). Vegetable preparation includes washing with soap and water, then placing them in vinegar for 10-15 minutes prior to cooking (3).

CONCLUSION

Amebic colitis can present a true medical emergency for the advanced practice nurse (APN). Accurate history taking, including questions of recent travel to underdeveloped countries, is essential (4). Microscopy of stool samples for evidence of *E. histolytica* is no longer considered diagnostic (2), however if ELISA testing is unavailable, the APN may be able to make a diagnosis of amebic colitis based on clinical presentation and presence of amebas with ingested red blood cells (13). Treatment includes maintenance of the airway, breathing, and circulation, as well as antibiotics such as metronidazole and paromomycin (3,11). Broad-spectrum antibiotics should be included for fulminant amebic colitis (16). The use of loperamide to control diarrhea is discouraged (15). Clients planning to travel to underdeveloped countries should be educated about food and water preparation (3,11).

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