The Flourishing Parasite- Amoebic Colitis

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Preface

A protozoan parasite cogitated as Entamoeba histolytica was initially scripted by Losch in 1875. Parasites appear localized within post-mortem colonic ulcers and amoebic colitis can be induced in vivo due to faecal inoculation of the rectum. An estimated 10% of world population is infected with Entamoeba histolytica, a parasite which is endemic in tropical and subtropical region. Amoebic colitis, additionally nomenclated as amoebiasis, is engendered by infective infiltration of the colonic mucosa with a pathogenic species of amoebae, particularly Entamoeba histolytica. Apart from Entamoeba histolytica, individuals can carry non-pathogenic parasites such as Entamoeba dispar or Entamoeba moshkovskii which are morphologically identical to Entamoeba histolytica [1,2].

Disease characteristics

Entamoeba histolytica demonstrates a geographically universal distribution. Parasitic protozoon Entamoeba histolytica engendering amoebiasis commonly accumulates within the intestinal tract in a majority (90%) of susceptible subjects. Asymptomatic infestation emerges in around 10% individuals where the parasite invades colonic mucosal barrier in order to infiltrate the lamina propria. Infestation with Entamoeba moshkovskii, majority of Entamoeba dispar and roughly 80% of infections with Entamoeba histolytica can be asymptomatic or individuals can demonstrate intraluminal amoebiasis. Entamoeba dispar is usually non pathogenic although it can occasionally delineate symptomatic disease [1,2].

Entamoeba histolytica implicates an estimated 10% of comprehensive global population and is responsible for mortality exceeding > 100000 deaths/year on account of amoebic dysentery or a hepatic abscess. An estimated fifty million instances of amoebic diarrhoea arise annually. Although amoebiasis is observed in developing countries, specific population groups especially recently immigrated population, travellers within endemic zones, homosexuals, institutional residents and immunocompromised individuals as enunciated with autoimmune deficiency syndrome (AIDS) can demonstrate cogent parasitic infestation within the western world [1,2].

Entamoeba histolytica can disseminate on account of ingestion of amoebic cyst which concurs within faeces contaminated food and water especially within regions and countries demonstrating inferior levels of sanitation or suboptimal personal hygiene. Besides, parasitic transmission is engendered with oro-faecal route and oral-anal sexual contact. Asymptomatic infestation with Entamoeba histolytica necessitates treatment on account of enhanced probability of invasive infection and dissemination to accompanying family members. Complications of infective intestinal infiltration with Entamoeba histolytica are comprised of perforation or fistula of the colon or a hepatic abscess [2,3].

Disease pathogenesis

Protective barrier of gastric acid and intestinal mucosa restricts the cyst of Entamoeba histolytica from adhering to intestinal epithelium. Parasitic encystation emerges within the terminal ileum or colon with a subsequent release of parasitic trophozoites within the
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intestinal lumen. Excystation to eight motile trophozoites occurs within the small intestine. Trophozoites demonstrate a potential for tissue infiltration and multiply by binary fission. Cogent interaction betwixt host’s defensive factors and parasitic features of virulence are responsible for the occurrence of intestinal amoebic invasion [2,3].

Three significant factors of parasitic virulence engender pathogenic manifestations such as:

a) N acetylgalactosamine- inhabitable lectin initiates parasitic adherence to the colonic mucin and impaction of host cellular surface.

b) Amoebapores are accumulated which are essentially miniature peptides facilitating decimation of host cells.

c) Cystine proteases are proteins which augment the lysis of host extracellular matrix.

With disease evolution, colonic mucosa is diffusely inflamed, oedematous and necrotic and occasionally demonstrates perforation of the intestinal wall.

Cysts of *Entamoeba histolytica* are resistant to gastric acid and chlorinated water. An estimated 20% parasitic infections are associated with invasion into the colonic wall with consequent tissue destruction [2,3]. Following parasitic adherence to colonic mucosa, mediated by a specific lectin upon the surface of *Entamoeba histolytica*, apoptosis of intestinal epithelial cells is induced through configuration of a channel via a pore-forming protein. *Entamoeba histolytica* can ingest cellular remnants. Certain trophozoites can undergo encystation via signalling pathways which essentially completes the parasitic life cycle.

*Entamoeba histolytica* is cytotoxic to specific cellular subtypes such as neutrophils, T lymphocytes and macrophages. The parasite adheres to underlying intestinal mucosa, invades and disorganizes the protective mucosal barrier with consequent contact- induced parasitic decimation [3,4]. Aforesaid mucosal decimation and apoptosis of intestinal epithelial cells is accompanied by lysis and phagocytosis of intestinal epithelial cells by the parasite. Cysteine proteases are enzymes which eradicate collagen and fibronectin, thereby mobilizing parasitic infiltration of deep-seated intestinal layers [3,4].

Pro-inflammatory cytokines are secreted by the host with the enunciation of an acute inflammatory exudate accompanied by migration of neutrophils and macrophages into the surrounding tissue. The parasite also configures chemo-attractants for neutrophils, eradicates cells with contact- dependent lysis with subsequent release of lysozymes, superoxide and collagenases from neutrophilic granules, a feature which enhances degradation of the intestinal mucosa [4,5].

Clinical elucidation

Diverse clinical symptoms are comprised of dysentery with diarrhoea, rectal haemorrhage simulating inflammatory bowel disease, hepatic abscess and granulomatous inflammation of the colon akin to colonic carcinoma. Infiltrative amoebiasis in the absence of cogent therapy can result in severe colitis along with fulminant infection with consequently enhanced mortality.

Majority (90%) of infections are asymptomatic. Parasitic cysts colonize asymptomatic individuals, a manoeuvre which enhances possible infectivity in associated subjects as infectious, asymptomatic individuals excrete cysts [5,6].

Amoebiasis commonly implicates the colon, cecum, right colon, rectum, sigmoid colon, appendix and terminal ileum. Parasitic infestation frequently metastasizes to the liver; apart from thoracic or infrequent brain dissemination. Recto-vesical fistula and cutaneous fistulous tracts are observed.

Symptomatic parasitic infection with *Entamoeba histolytica* emerges as an acute phase within the colon and is cogitated as amoebic colitis. Typically, diarrhoea or blood in stools are exemplified although the clinical symptoms can be non specific. Amoebic colitis is a gradually progressive disorder, in contrast to bacterial colitis. Amoebic colitis can clinically simulate ulcerative colitis or Crohn’s disease. On palpation, diffuse or localized tenderness of the implicated gut is noted. Infrequently, a mass may be palpable [5,6].

Clinical symptoms ensue gradually during a period of three weeks to a month along with enhancing intensity of diarrhoea and abdominal pain. A frequent symptom of amoebiasis is diarrhoea in the absence of faecal blood or mucus or symptoms of dysentery. An estimated 15% to 33% instances demonstrate diarrhoea. Amoebic dysentery or colitis is accompanied by grossly visible or microscopic presence of faecal mucus or blood [5,6].

With acute onset of clinical symptoms, instances may recapitulate acute abdomen. Alternatively, a gradual onset with emergence of clinical symptoms over several months can ensue.

Implicated children can depict intussusception or necrotizing colitis with emerging intestinal perforation. Infrequently, colonic amebomas can be articulated.

An estimated beneath < 1% subjects with amoebic colitis demonstrate concurrent extra-intestinal infections, frequently a hepatic abscess.

Amebic liver abscess demonstrates a solitary focus and is frequent in males with a male to female ratio of 10:1. Symptoms appear within two to four weeks. Emergence of a hepatic abscess can be asymptomatic or delineates symptoms such as pyrexia with chills, upper right quadrant pain and an enlarged, tender liver although jaundice is absent [5,6]. Declining body weight, enhanced white blood cell counts or elevated levels of hepatic enzymes can be discerned.

Toxic megacolon, representing an acute dilatation of the colon, can arise in untreated or undetected subjects of amoebic colitis. Toxic megacolon enunciates an enhanced mortality on account of accompanying intestinal necrosis and perforation.

Pulmonary abscess ensues due to penetration of diaphragm with infiltrative amoeba arising from a hepatic abscess or due to hematogenous dissemination. Pulmonary invasion manifests with chest pain, dyspnoea and productive cough [5,6].

Histological elucidation

Characteristically, endoscopy demonstrates discrete foci of mucosal ulceration with superimposed fibrinous exudate interspersed with uninvolved intestinal mucosa.

Additionally, foci of non-specific colitis or inflammatory polyps can be discerned [2,3].

Amoebiasis can incriminate the bowel in its entirety although a predilection for caecum and ascending colon is exemplified along with occasional disease extension into terminal ileum. Intestinal perforation is engendered in roughly 5% to 10% instances.

Microscopic assessment of a rectal biopsy is preponderantly non specific. Parasitic amoeba generally burrow within the lamina propria to engender tissue necrosis accompanied by minimal inflammation. Preliminary lesions depict disseminated neutrophils. Delayed phase of parasitic infestation demonstrates broad-based, flask shaped ulcers varying from one to two millimetre in magnitude. Paucity of inflammatory infiltrate beneath the classical flask shaped ulcer is indicative of infection with Entamoeba histolytica [2,4].

Disease confirmation is contingent to identification of trophozoites of Entamoeba histolytica upon examination of paraffin embedded, haematoxylin and eosin stained sections. Typically, the parasite is spherical or ovoid with a circumscribing halo, magnitude varying from 6 nanometres to 40 nanometres, simulates macrophages, are impacted with abundant, vacuolated cytoplasm along with miniature, centric nuclei, prominent nuclear membrane and a centroidal karyosome (chromocenter). Trichrome stains depicts the clean, non-vacuolated parasitic cytoplasm to be devoid of ingested bacteria [2,4].

Nuclear chromatin is finely granular; evenly disseminated upon the nuclear membrane and demonstrates a dark-purple, miniature, centric karyosome. Trophozoites are frequently clustered upon the luminal surface or within the cellular debris.
Ingestion of red blood cells as a characteristic of trophozoites of *Entamoeba histolytica* may not be consistently discerned.

Parasitic organisms can be distinguished with Periodic acid Schiff and immune-peroxidase stain whereas immune staining with CD68 fails to demonstrate the cysts [2,4].

**Disease complications**

Parasitic infestation with *Entamoeba histolytica* induces complications such as fulminant or necrotizing colitis, toxic megacolon, intestinal perforation, bacterial peritonitis, gastrointestinal haemorrhage, intestinal strictures and intestinal obstruction. Fulminant colitis emerges in around 0.5% subjects with the occurrence of copious dysentery, pyrexia, peripheral blood leukocytosis and vague abdominal pain. Intestinal mucosa can undergo necrosis with subsequent transmural intestinal perforation and emerging bacterial peritonitis [7,8].

Toxic megacolon appears in 0.5% subjects and is indicated by total or segmental non-obstructive colonic dilatation in combination with systemic toxicity. Amoebic liver abscess appears in an estimated 3% to 9% of comprehensive instances of amoebiasis.

Pleuro-pulmonary amoebiasis is an extra-intestinal form of amoebiasis, sequential to amoebic liver abscess in frequency [7,8].

**Differential diagnosis**

Amoebic colitis requires a segregation from conditions such as appendicitis, infestation with Balantidium coli, aggregates of histiocytes or non-pathogenic amoeba, inflammatory bowel disease, pseudomembranous colitis, pyogenic liver abscess and tuberculosis. *Entamoeba histolytica* infrequently implicates the appendix, a feature which manifests as an extension from infected right colon [2,3].

Classical inflammatory bowel disease lacks superimposed fibrinous material impacted with parasitic organisms. Typically, ulcerative colitis demonstrates a diffuse colonic incrimination with mucosal derangement and a basal plasma cell infiltrate within the lamina propria. Crohn’s disease exhibits a patchy, mucosal ulceration which appears as a distinctive fissure-like ulcer instead of a classic flask shaped ulcer of amoebic colitis. Mucosal ulcers of Crohn’s disease are predominantly horizontal whereas an amoebic ulcer extends perpendicularly to long axis of the intestine [2,4].

Tuberculosis of the colon demonstrates gross mucosal ulceration with diffuse fibrosis extending throughout the intestinal wall, thereby engendering intestinal stenosis and obstruction. Tubercular peritonitis can co-exist in exceptional instances. On microscopic examination, typical epithelioid cell granulomas are exhibited [2,4].

**Investigative assay**

A routine stool examination for discerning ova and parasitic cysts of *Entamoeba histolytica* is required. Assays employing polymerase chain reaction (PCR) or antigen detection can be adopted to segregate *Entamoeba histolytica* from non-pathogenic amoeba.

Amoebic colitis is thus categorized through detection of trophozoites of *Entamoeba histolytica* within the colonic ulcers, assayed with microscopic evaluation of tissue specimens obtained with colonoscopy or exceptionally with examination of fresh faeces. Subjects with diarrhoea can definitely depict trophozoites within the faecal specimens, discernible in direct wet mounts or trichrome stained smears [7,8].

Characteristically, cecum and ascending colon delineate multiple, punctate ulcers interposed with uninvolved, healthy intestinal mucosa. On cogent histology, ulcers typically appear as flask shaped. Severe instances of amoebic colitis can depict coalesced ulcers, identical to ulcers visualized with ulcerative colitis [7,8].

Amoebic liver abscess is frequently diagnosed with a competent ultrasonography or specific radiographic investigations. Aspiration of amoebic liver abscess demonstrates motile, parasitic trophozoites and necrotic tissue comprised of degenerated cellular material.
Subjects delineating amoebic liver abscess usually depict anti-amoebic antibodies and amoebic antigens within the serum. Aspiration of hepatic cyst can be occasionally performed although parasites are infrequently discerned. Also, absence of accompanying microorganisms is indicative of amoebic liver abscess [7,8].

Serologic methodologies of detecting antibodies to *Entamoeba histolytica* can be adopted. Majority (90%) of subjects with extra-intestinal amoebiasis demonstrate reactivity to essentially non-protective parasitic antibodies. Antibody levels may amplify following parasitic tissue invasion [8,9].

Antibody based assays are not beneficial in distinguishing preceding or recent parasitic infection as antibodies persist for an extended duration following resolution of infection. Additionally, antibody based assessment may not be comprehensively informative for evaluating implicated individuals residing in endemic zones [7,8].

Serological tests that discern *Entamoeba histolytica* antigen within a faecal sample can procure pertinent evidence of recent infection. Application of immune-chromatographic techniques for rapid evaluation of infection with *Entamoeba histolytica* are contemporary manoeuvers. Specific assays are designed to detect cognate antigens within a faecal sample whereas adjunctive assays detect serum antibodies. However, fresh, unpreserved faecal samples are a pre-requisite for appropriate assessment [8,9].

**Prognostic outcomes**

Therapy with efficacious agents and drugs can alleviate amoebiasis within a period of weeks. Intestinal amoebiasis can be contemplated as a fatal disorder, particularly in developing countries, especially in children or subjects beneath < 5 years. Amoebiasis is considered as a third frequent cause of mortality due to parasitic infestation on a global scale, following malaria and schistosomiasis [2,3].

**Therapeutic options**

Amoebic colitis necessitates a combination therapy constituted by adoption of luminal agents in association with tissue amebicides. Luminal amebicides comprise of iodoquinol, diloxanide furoate and paromomycin. Tissue amebicides are constituted by nitro-imidazole (metronidazole), nitazoxanide, erythromycin and chloroquine [8,9].

Infestation with *Entamoeba histolytica* can be appropriately treated with metronidazole. *Entamoeba histolytica* lacks mitochondria and functions as an obligate fermenter of glucose. Metronidazole targets ferrioxidin-dependent pyruvate oxidoreductase enzyme which is critical for fermentation of glucose [8,9].

Surgical intervention is a cogent therapeutic option for amoebic liver abscess requiring drainage. A surgical emergency is manifested with the occurrence of toxic megacolon with impeding or free intestinal perforation.

Invasive forms of amoebic colitis can be administered metronidazole or tinidazole or nitazoxanide followed by administration of a luminal agent such as paromomycin or diiodohydroxyquin, a combination efficacious in decimating intraluminal cysts [8,9].

Complications emerging from amoebic colitis mandate cogent therapy. Definitive or suspected bacterial peritonitis can be managed with administration of broad spectrum antibacterial therapy, nitro-imidazole and preliminary therapeutic interventions [8,9].

Intestinal perforation is preferably managed with the administration of broad spectrum antibiotics. Surgical intervention is necessitated in instances of significant intestinal perforation or intestinal abscesses unresponsive to pertinent antibiotic therapy. Toxic megacolon is accompanied by an enhanced mortality and frequently mandates pertinent colonic resection [8,9].
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Figure 1: Amoebic colitis with perpendicular mucosal ulceration and superimposed fibrinous exudate [10].

Figure 2: Amoebic colitis with trophozoites entangled within the fibrinous exudate and a paucity of inflammatory infiltrate [11].

Figure 3: Amoebic colitis with parasitic cysts and trophozoites superimposed upon the luminal surface, mucosal ulceration and minimal inflammation [12].

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Figure 4: Amoebic colitis with flask shaped mucosal ulcers and a scant inflammatory exudate [12].

Figure 5: Amoebic colitis with superimposed aggregates of parasitic cysts, trophozoites and minimal inflammatory exudate [13].

Figure 6: Amoebic colitis demonstrating trophozoites with abundant, vacuolated cytoplasm, centric nuclei and a prominent karyosome [14].

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Figure 7: Amoebic colitis with a scant, patchy inflammation and a luminal fibrinous exudate with entangled trophozoites [15].

Figure 8: Amoebic colitis demonstrating trophozoites appearing magenta-purple on a Periodic acid Schiff’s stain [16].

Bibliography


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10. Image 1 Courtesy: Deposit photos.

11. Image 2 Courtesy: UPM.

12. Image 3 and 4 Courtesy: Science photo library.


15. Image 7 Courtesy: Pathology outlines.