

# THE ASSOCIATION OF AMOEBIC COLITIS AND CHRONIC ULCERATIVE COLITIS

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## ABSTRACT

Three patients with idiopathic ulcerative colitis and infection of *Entamoeba histolytica* were reviewed. They represented three different relationships between the two conditions, viz asymptomatic carrier, coexisting infection and superinfection causing exacerbation of colitis. A two-way relationship between amoebic colitis and ulcerative colitis has been discussed and the possible mechanisms in the literature have been reviewed. In patients with a short history of diarrhoea and in tropical countries where amoebic infection is endemic, it is important to rule out amoebic colitis before commencing steroid therapy for inflammatory disease.

**Keywords:** amoebiasis, ulcerative colitis

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## INTRODUCTION

As the prevalence of amoebic infection was as high as 50% in some tropical countries and about 5% in the United States<sup>(1)</sup>, amoebiasis was not infrequently misdiagnosed as ulcerative colitis<sup>(2-4)</sup>. Differentiation between idiopathic ulcerative colitis and colonic amoebiasis by clinical and histological features can be difficult in some patients. Failure to differentiate between the two conditions or to recognise their association could cause delay in implementation of appropriate treatment and even disastrous consequences. Few studies had looked into the possible relationship between amoebic and ulcerative colitis<sup>(5)</sup>. We report three Chinese patients suffering from both idiopathic ulcerative colitis and intestinal amoebiasis which illustrated different possible relationships between the two conditions.

## CASE REPORTS

### Case 1

A 28-year-old man with a known history of ankylosing spondylitis presented with bloody diarrhoea and weight loss for 2 months. Cysts of *Entamoeba histolytica* were identified in stool on three separate occasions. Colonoscopy showed granular mucosa in rectosigmoid colon and biopsy revealed inflammatory infiltrates, cryptitis and crypt abscesses compatible with ulcerative colitis. Amoebic trophozoite was not found. In view of the high prevalence of amoebic infection in Asia, metronidazole was given which eradicated the amoeba but failed to relieve his symptoms. He was then

given steroid and sulphasalazine and the diarrhoea finally responded to the therapy. The patient remained symptom-free in subsequent follow-up.

### Case 2

A 37-year-old lady who frequently travelled in China presented with weight loss and chronic diarrhoea for 1 year. Her stool was mixed with blood and mucus. Colonoscopy showed granular mucosa in the rectosigmoid colon and histology revealed features consistent of ulcerative colitis. However, trophozoites of *Entamoeba histolytica* were also detected on stool microscopy. The patient was treated with metronidazole. Her symptoms responded initially but deteriorated again after 6 weeks. Both cysts and trophozoites of *Entamoeba histolytica* were found again in the stool. Metronidazole, tetracycline and chloroquine were given sequentially but failed to eradicate the parasites. Her condition continued to deteriorate and at one time, parenteral nutrition therapy was required. A second colonoscopy showed diffuse mucosal hyperaemia, fissures and punched-out ulcers in the rectum. *Entamoeba histolytica* was finally eradicated with diloxanide furoate but the diarrhoea persisted. Her symptom was eventually brought under control by using steroid and sulphasalazine.

### Case 3

A 27-year-old man presented with intermittent rectal bleeding for 2 years. Colonoscopy showed rectosigmoid inflammation and histology was compatible with the diagnosis of ulcerative colitis. The patient was treated with prednisolone enema and sulphasalazine. Two years later, his rectal bleeding recurred. Rectal biopsies showed trophozoites of *Entamoeba histolytica* (Fig 1 and 2). Metronidazole was used which eradicated the amoeba but his symptom persisted and the patient developed peripheral neuropathy due to the treatment. A second colonoscopy revealed multiple aphthous ulcers involving the whole colon. Heavy inflammatory infiltration, goblet cell depletion, cryptitis and crypt abscesses were seen. His symptoms finally responded to steroid.

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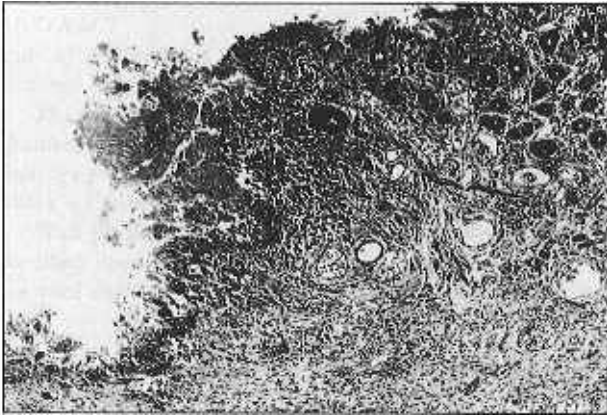
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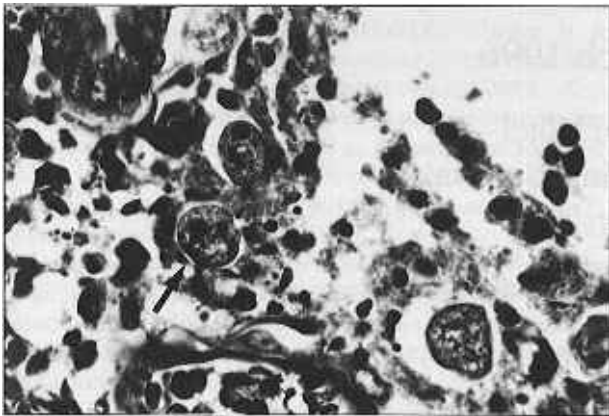
## DISCUSSION

*Entamoeba histolytica* infection causing invasive colitis in atypical cases may be difficult, if not impossible, to be distinguished histologically from idiopathic ulcerative colitis. In endemic area such as South-East Asia, infective colitis must always be excluded before considering the diagnosis of ulcerative colitis. Disastrous result might occur if patients

**Fig 1 - Section of rectal biopsy with a typical flask-shaped ulcer, extensive mucosa necrosis and a few organisms are present in the necrotic tissue on the luminal surface. (magnification 40X)**



**Fig 2 - Higher magnification shows the presence of trophozoites in the surface exudate. The trophozoites have typical round nucleus, one with central karyosome and ingested red cells. (magnification 400X)**



suffering from amoebiasis are treated inadvertently with steroid. The identification of amoebic trophozoites in fresh stool microscopy is the gold standard of diagnosis but the yield is generally low. Indirect haemagglutination test (IHA) for *E. histolytica* has claimed to be able to differentiate invasive disease from innocent carrier of the parasite<sup>(6)</sup>, yet IHA anti-amoebic antibody titers could remain elevated for years after invasive disease<sup>(6)</sup>. Endoscopically, colonic amoebic infection typically shows discrete ulcers with normal mucosa in between and histologically quite different from features of ulcerative colitis. Amoebic trophozoites can also be demonstrated usually in colonic biopsy specimens.

These 3 patients represented different relationships between ulcerative colitis and amoebiasis. In the first case, the patient had ulcerative colitis at the outset and he was also an asymptomatic carrier of *Entamoeba histolytica*; based on typical clinical setting, the absence of trophozoites in stool, consistent histological features of ulcerative colitis, and his rapid response to steroid therapy. In the second case, the finding of trophozoites in stool, the initial response to metronidazole and subsequently to steroid confirmed a coexisting amoebic and ulcerative colitis. The third patient who was a known case of ulcerative colitis had an exacerbation of symptoms secondary to amoebic infection.

The relationship between ulcerative colitis and amoebic

colitis is probably bidirectional. On one hand, patients with ulcerative colitis may be more prone to the invasion of *Entamoeba histolytica* and, on the other hand, *Entamoeba histolytica* infection could lead to exacerbation of symptoms in clinically inactive inflammatory bowel disease. Colonic mucus is the most important host defence against invasive amoebiasis. In animal models, mucus trapping of *Entamoeba histolytica* has been observed<sup>(7)</sup> and depletion of the colonic mucus blanket is always observed with parasitic invasion<sup>(8)</sup>. It has been shown that *Entamoeba histolytica* possess N-acetyl-D-galactosamine (GalNAc) inhibitable surface lectin for their adherence to the colonic mucosa<sup>(9)</sup>. Colonic mucus, rich in Gal/GalNAc residue, thus inhibits amoebic adherence to and lysis of colonic epithelial cells by trapping these microorganisms in the mucus layer. In ulcerative colitis, several alterations of colonic mucus have been observed. Depletion of goblet cells result in reduced thickness of the mucus layer<sup>(10)</sup>. It is also known that the sialic acid in mucus is also more susceptible to cleavage by sialidase due to reduction in O-acetylation at the C4 position in both active and inactive ulcerative colitis<sup>(11)</sup>. Finally, the synthesis of mucins with shorter oligosaccharide side chains in ulcerative colitis are relatively ineffective in protecting the mucosa against parasitic invasion<sup>(12)</sup>. Although the relative importance of these changes of the colonic mucus in facilitating the invasion of *Entamoeba histolytica* is not sure, the occurrence of amoebic infection in some pathogens such as *Clostridium difficile*<sup>(13)</sup>, *Campylobacter jejuni*<sup>(14)</sup>, *cytomegalovirus*<sup>(15)</sup>, *salmonellae* and *shigellae*<sup>(16)</sup> have been implicated in causing relapses of ulcerative colitis. Bacterial/parasitic products and cytokines released in infection activate the cascade reaction of intestinal inflammation and hence exacerbate the symptoms.

In summary, it is important to rule out amoebic colitis before commencing steroid therapy for inflammatory bowel diseases, especially in patients with short history of diarrhoea and in tropical countries where amoebic infection is endemic. Asymptomatic carriers of the amoebic cysts should be treated considering that amoebic infection may be activated with steroid therapy. The coexistence of ulcerative colitis and colonic amoebiasis may not be just coincidental. The pathophysiological mechanism between the two conditions await further investigations.

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