# Chronic Diarrhea Caused by Amebic Colitis and Inflammatory Bowel Disease

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***ABSTRACT***

*The diagnosis of intestinal amebiasis is easily established based on colonoscopy, i.e. there is a specific characteristic of ulcer/lesion "discrete flask-shape ulcer" with normal mucosa among the ulcers. However, most patients with amebic colitis have non-specific clinical manifestations and their colonoscopy findings are hardly distinguished from inflammatory bowel disease.*

*In the present case, the patient had a chief complaint of chronic bleeding diarrhea and abdominal pain. The fecal analysis found trophozoites of Entamoeba histolytica. Serology test (sero-amebic) revealed negative result. The colonoscopy examination reveals hyperemic mucosa, edema, and multiple ulcers with various sizes covered with fragile and easily bleed debris, from the rectum to ascending colon, rigid colon, narrowing lumen and tumor/mass appearance on ascending colon. The differential diagnosis was severe amebic colitis and inflammatory bowel disease. Based on the colonoscopy biopsy, we found an active chronic colitis along with dysplasia. The patient received management and treatment of severe amebic colitis and inflammatory bowel disease.*

***Keywords:*** *amebic colitis, bleeding diarrhea, fecal analysis, colonoscopy, biopsy, inflammatory bowel disease*

## INTRODUCTION

Chronic diarrhea last for more than 4 weeks and it usually needs a diagnostic evaluation. It is estimated that the prevalence of chronic diarrhea in population is 3-5%. There are various etiologies of chronic diarrhea, but a meticulous history taking and physical examination as well as selective laboratory examination usually may discover accurate diagnosis.[1]

There are four mechanisms/types of chronic diarrhea, i.e. osmotic diarrhea, inflammatory diarrhea, and motility disorder.[1] Inflammatory diarrhea is caused by disrupted integrity of intestinal mucosa, inflammation, and ulceration that precede the development of mucus, serum protein and blood in intestinal lumen. Infection colitis and inflammatory bowel disease are common etiologies of such diarrhea.[1]

Infection of amebic colitis is caused by *Entamoeba histolytica,* a protozoa parasite that is able to invade the intestinal mucosa and spread to the other organ, especially the liver.[2] The prevalence of amebiasis is highly varied. It is estimated that there is 10% of infected citizen/population and the highest prevalence are tropical countries, i.e. 50-80%.[3] According to UNESCO, the world's burden caused by amebiasis nowadays includes 50 million symptomatic infected people and more than 100,000 people died annually.[4] In Indonesia, a developing country, amebic colitis is still an important community health problem. The diagnosis and management are still problematic.

Clinical manifestations of intestinal amebiasis vary, starting from mild diarrhea up to classic dysentery.[2,3,4] Patients with amebic colitis usually complain about abdominal pain for several weeks, weight loss, mucinous/bleeding diarrhea.[3,5,6] Other manifestations

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include severe amebiasis and the following manifestations that rarely occur, i.e. acute necroticans, toxic megacolon, ameboma, perineal ulcer which lead to fistula. Necroticans colitis rarely occurs (0.5%) but the mortality rate is more than 40%.[7]

The diagnosis of amebic colitis is still primarily established based on microscopic examination, i.e. positive findings of cyst or trophozoites in feces or specimens of colon biopsy through sigmoidoscopy/ colonoscopy.[7] Similar clinical manifestation between amebiasis and inflammatory bowel disease should encourage doctor to exclude the amebiasis through fecal examination or amebic serology test in all patients before establishing the diagnosis of inflammatory bowel disease, particularly before giving corticosteroid treatment.[7]

## CASE REPORT

A 54 years old woman was admitted to private hospital with a chief complaint of diarrhea that had been last for 2 weeks. She had diarrhea 8 times daily, bleeding and mucinous stool, abdominal pain, bloating and tenesmus. She had a fever, loss of appetite, weight loss, and fatigue. The diarrhea was not affected by previous food or drugs consumption. She never had any other serious disease. There was no history of diabetes, other chronic or autoimmune disease. She also had no history of hypertension and prior surgery.

The physical examination when she was admitted revealed that the patient seemed weak, fully alert, body weight 54 kg, body height 60 cm, BMI 19.7 kg/m$^2$ (normal weight), blood pressure 110/70 mmHg, temperature 38.6° C, pulse rate 112 x/minute, reduced turgor of the skin. The heart and lungs were normal. There were distended abdomen, pain in all abdominal regions particularly on the right upper quadrant and a mass was palpable in that region. The mass/tumor had no distinct edge, elastic consistency, smooth surface. The abdomen was distended and digital rectal examination revealed mucus, tenderness, and smooth surface without hemorrhoid and fissure. There was no organomegaly or lymph nodes enlargement. Other physical examination revealed normal result.

Laboratory examination revealed hemoglobin 12.1 g%, leukocytosis with leukocytes of 20,500/ì L, erythrocyte sedimentation rate of 66/114, hyperglycemia with blood glucose level of 366 mg/dL, mild increase of ureum and creatinine level (74.1 mg/dL and 1.78 mg/dL respectively, hyperuricemia 8.6 mg/dL, mild hypoalbuminemia (albumin 3.21 g/dL), hyponatremia (sodium 127.6 mmol/L). Serologic diagnosis for amebiasis infection and tuberculosis were negative. CEA tumor marker revealed negative result. On fecal analysis, there were trophozoites of *Entamoeba histolytica*, full of leukocytes, erythrocytes 0-2/HPF. The ECG examination revealed sinus tachycardia. Chest X-ray of the heart and lungs was within normal limit. USG examination revealed fatty liver and a sausage-like mass with hypo echoic wall at right lower quadrant of the liver lobe. Impression: fatty liver and suspect colitis.

Colonoscopy was performed and we found results as follows: decreased motility of colon lumen/wall, narrowing lumen of ascending colon, hyperemia on the mucosa, multiple ulcers with varied size, covered with fragile and easily bleed debris that almost occur in all of colon segments (starting from rectum to ascending colon), there was intra luminal mass/tumor in ascending colon. Impression: severe inflammatory bowel disease with differential diagnosis of infection of amebic colitis and ameboma (figure 1).

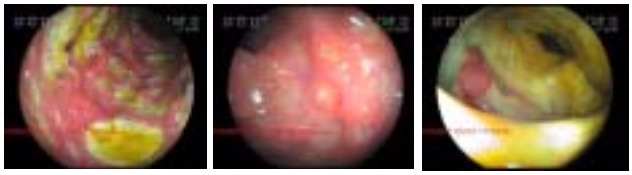

Figure 1. Colonoscopy: Edematous mucosa, hyperemia with multiple ulcers. Varied sized ulcers covered with fragile and easily bleed debris starting from rectum to ascending colon, lumen narrowing, and intraluminal tumor mass (ameboma?)

On the biopsy of rectum and all colon segments, we found erosive mucosa, edematous lamina propria, inflammatory cells (neutrophils, eosinophils, lymphocytes, histiocytes, plasma cells and bleeding sites. There was no decreased amount of goblet cells. We found sites of glands with mild epithelial dysplasia. There was no specific sign of malignancy. *Entamoeba histolytica* in either cyst or trophozoites forms were not found. Based on biopsy examination, it was concluded that there was chronic colitis with mild dysplasia (figure 2).

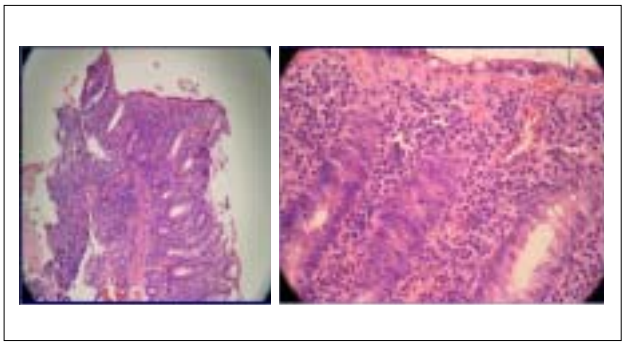

Figure 2. Colon biopsy: there is erosive mucosa, edematous lamina propria with inflammatory cells of neutrophils, eosinophils, lymphocytes, histiocytes, plasma cells and bleeding sites. There are sites of glands' epithelial with mild dysplasia

The patient was managed and the problems were severe chronic diarrhea caused by amebic colitis (+ suspicion of ameboma) with differential diagnosis

of coincidence illness with inflammatory bowel disease, renal insufficiency, hyponatremia, hypoalbuminemia, hyperuricemia, and diabetes type 2 with normal weight. The management included rehydration for electrolyte imbalance, intravenous insulin to regulate the blood glucose level, antibiotics: metronidazole 3 x 500 mg and ceftriaxone 1 x 1 gram intravenous, anti-inflammatory drug: mesalazine enema 4 g for 3 days, continued with oral administration 3 x 500 mg. There was clinical improvement after 7 day treatment and the patient continued the treatment as outpatient care, i.e. metronidazole treatment of 4 x 500 mg oral and chloroquine 2 x 250 mg as well as mesalazine 3 x 500 mg oral, which was continued for 3 weeks. After 1 month treatment, colonoscopy was conducted for evaluation. The colonoscopy result revealed that most of colon segment has obvious improvement starting from rectum, sigmoid colon, descending colon totransversal colon with multiple small-sized polyps. Erosion, ulcer and lumen narrowing occurred only in ascending colon and caecum therefore the colonoscope was not able to reach caecum (figure 3).

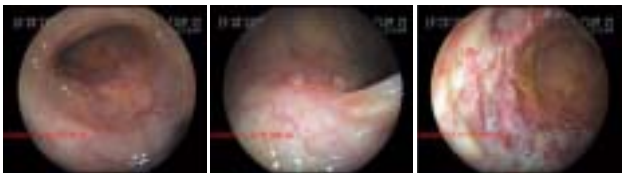

Figure 3. Colonoscopy result after one month therapy. Nearly all colon segments show lesion improvement, starting from the rectum, sigmoid colon, descending colon up to transversal colon with multiple polyps. Erosion, ulcer and lumen narrowing are found only on ascending colon and caecum

## DISCUSSION

A 54 years old woman was admitted to the hospital with chief complaints of chronic bleeding diarrhea, generalized abdominal pain, palpable mass at right hypochondria region, and there was positive result of *Entamoeba histolytica* on fecal examination. The colonoscopy found signs of severe colitis infection + ameboma with differential diagnosis of inflammatory bowel disease. The histopathology biopsy of colonoscopy specimens found that there was active chronic colitis with mild dysplasia. Serology-antibody test revealed negative result. What is the final diagnosis of this case? Is it a colitis infection due to amoeba or inflammatory bowel disease that coincidences with amebic colitis?

Missed diagnosis of amebic colitis which is diagnosed as inflammatory bowel disease followed by corticosteroid therapy may be fatal. Diagnosis techniques to establish diagnosis of amebiasis infection include fecal examination, endoscopic biopsy and serology. Positive result of motile trophozoites in feces or biopsy tissue is a definite diagnosis method. However, both examinations have some drawbacks.[8] The drawbacks of trophozoites assessment in fecal analysis include low sensitivity and high false positive results for *E. dispar* or *moshkowskii.* At least 3 fecal specimens should be taken by 3 different periods for the assessment because such bacteria are secreted into feces intermittently and they are not well distributed in feces.[7]

In the present case, there was positive result of trophozoites amoeba in fecal analysis although it was not supported by serologic examination of antibody *E. histolytica*. This condition may be caused by energy or may be affected by underlying or concomitant disease, i.e. diabetes mellitus, which will cause low level of antibody response. Theoretically, anti-amebic antibody will remain for months to years after eradication of infection.[7]

Amebic serologic test revealed negative result. There are some problems in interpreting the result of serologic test for amebiasis intestinal, i.e. low antibody blood level even in a case with definite diagnosis of intestinal amebiasis. In addition, the remained antibody in blood is cause by previous infection that can reduce the benefit of serologic test, particularly in acute cases of intestinal amebiasis.[9] Ideally, a diagnosis should be based on serologic test with a specific antigen or DNA of *E. histolytica* and positive result of amebic antibody in the blood.[7]

Diagnosis of amebic colitis by endoscopic examination should be conduction without any intestinal preparation in order to increase the possibility of amebic parasites in intestinal mucosa "Discrete shallow-based ulcers" covered by white or yellowish exudates together with edematous mucosa is frequently found in invasive amebic colitis. The mucosa surrounding ulcers is usually normal. Parasites in trophozoites form can be found in specimens taken from the lesion base by scrapping or aspiration technique.

The diagnostic value of endoscopic biopsy or scrapping is high.[7] Usually, trophozoites are easily identified in specimens by routine examination using light microscope. However, immunohistochemical staining for *E. histolytica* can be performed for further examination in order to increase diagnostic value.[10]

In the present case, we cannot found amebic trophozoites form by colonoscopy examination. It may be caused by the effect of amebicides drug, which had been given since 2 days prior to colonoscopy procedures, and by the effect of intestinal preparation for colonoscopy procedures.

Large intestines react in relatively monomorphic form against various stimuli. Therefore, it may bring similar differential diagnosis as occurred in the present

case. The result of colonoscopy showed that general manifestation of amebic colitis may have a wide variation/spectrum, starting from a relatively normal mucosa to multiple ulcers, a big single ulcer, edematous mucosa which is diffuse and fragile or it may mimic malignancy if there is concomitant ameboma.[9]

The result of colonoscopy in the present case indicated similar manifestation with inflammatory bowel disease such as multiple ulcers on all over intestinal segments with normal mucosa among them and multiple polyps that are frequently found in Crohn's disease.

Accurate diagnosis of amebic colitis which only relies on histopathology examination will meet various difficulties/problems because of the common manifestations as follows: a diffuse non-specific inflammatory process, and low detection level of amebic trophozoites in biopsy specimens.[11] For example, in the present case, the histopathology examination did not found any amebic trophozoites although the colonoscopy revealed the signs of severe intestinal inflammation. Amebic colitis occurs when the trophozoites penetrate into intestinal mucosa, which functions as a barrier against invasion. Such invasion is mediated through epithelial, neutrophils and lymphocytes cell damage by the trophozoites when the lectin of parasites is bound to N-acetyl-D-galactosamine on the O-linked sites on the surface of host cells. Lectin is secreted through amebic pore, i.e. pores that consist of 5 kD sized protein which contribute to cell damage.[6,7,12,13,14,15]

Invasive disease is characterized by release of toxic substance that cause inflammation and mucosa damage.[2,11,13] If the process continues, there will be flask-shaped ulceration, which will extent to sub mucosa or muscular layer. In several cases, amebic invasion may extent up to portal circulation in the liver, causing liver abscess. The edge of ulcer is covered by mild inflammation. Mucosa among the ulcers seems normal. Ulcers may be found on all parts of colon, but they are frequently found in caecum, ascending colon, sigmoid, appendix, and terminal ileum.[2,6]

Diagnosis of amebiasis intestinal will be more easily established if we found ulcers with a specific characteristic, i.e. discrete flask shape ulcers with normal mucosa among them. However, in most patients with amebic colitis there are non-specific clinical manifestation and the endoscopic findings almost indistinguishable to inflammatory bowel disease. Moreover, the diagnosis will be more difficult due to failure to obtain amoeba in feces or biopsy specimen as well as low sensitivity of serologic test for amebiasis intestinal.[9] As in the present case, amebic trophozoites were only found in fecal analysis but they were not found in colonoscopy biopsy examination and the antibody of serologic test also revealed negative result.

Colonoscopy examination for amebic colitis may reveal various results, i.e. indistinct boundary, irregular form, geographic ulcer with edematous and hyperemic mucosa, partial lumen obstruction, easily bleed and similar to the manifestation of ulcerative colitis or ischemic colitis.[9] Ameboma on colon or rectum is one of amebiasis manifestations, but it is rarely found. In amebic colitis, apart from tissue necrotic (histolysis), there is a strong inflammation reaction in ameboma and a pseudo-tumor which is formed by granulation tissues that may be induced by secondary infection.[16]

In the present case, ameboma was only found in colonoscopy but there was no evidence of ameboma in histopathology examination. This may be caused by a relatively small amount of specimens for colonoscopy biopsy. Biopsy through surgical techniques will increase the quality of examination.

The management for patients with *E. histolytica* infection should include parasites eradication treatment. The aim of such management is to cure invasive disease and to eradicate the intestinal carrier. Based on their sites of action, the amebicides agents are categorized into 3 groups: (1) Tissue amebicides; dehydroemetine; dehydroemetine, emetin, and chloroquine; (2) Lumen amebicides:diodohydroxyquine, iodochlorhydroxyquine, chiniophone, glycobiarsol, carbarsone, emetin, clefamide, diloxanid furoat, tetracycline and paromomyscine; (3) Tissue and intestinal lumen amebicides; metronidazole.[17]

The patient had amebiasis treatment, i.e. 3 x 500 mg intravenous metronidazole for 5 days, followed by oral chloroquine 2 x 250 mg daily for 1 month. Because we could not exclude the symptoms of inflammatory bowel disease syndromes (positive symptom of axial arthritis, increased ESR, other results of colonoscopy and biopsy) so we also provided treatment regimen for inflammatory bowel disease such as 5-ASA enemas for 5 days followed by oral 5-ASA 3 x 500 mg for 1 month. Cefotaxime was used to control secondary infection because of severe clinical condition and pathological problem of colon based on the colonoscopy result.

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