

# Characteristics of Endoscopic and Pathological Findings of Amebic Colitis

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## Research article

**Keywords:** Inflammatory Bowel Disease (IBD), biopsies and microscopic examinations, trophozoites

**Posted Date:** November 18th, 2020

**DOI:** <https://doi.org/10.21203/rs.3.rs-106377/v1>

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# Abstract

**Background** The clinical features of amoebic colitis resemble those of Inflammatory Bowel Disease (IBD), and therefore the risk of misdiagnosis is very high.

**Methods** We retrospectively reviewed data of all amoebic colitis cases admitted to Beijing Friendship Hospital from January 2015 to January 2020. Cases were diagnosed by clinical presentation, laboratory examinations, and colonoscopy with biopsy and histological examination.

**Results** 16 patients were diagnosed with amoebic colitis by colonoscopies accompanied by biopsies and microscopic examinations. At first, 12 (75%) patients were misdiagnosed with IBD. The cecum was the most common site of amoebic colitis (100%), and the caecum and rectum were also involved in many lesions (68.75%). Multiple lesions of erosion and/or ulcers were recognized in all patients (100%). The features of endoscopic findings included multiple irregularly shaped ulcers and erosions with surrounding erythema, and the ulcers and erosions were covered by the white or yellow exudates. The intervening mucosae between the ulcers or erosions were normal. The features of the rectums can be divided to 2 types: in 6 patients (54.5%), the irregular ulcers or erosions covered with white or yellow exudates were observed in the rectum and the cecum, and the bloody exudates in the rectum were more severe than those in the cecum; in the other 5 patients (45.5%), rectal lesions were much less severe than those in the cecum, and small superficial erosions or reddened mucosa were observed in the rectal ampulla. All patients were diagnosed as detection of amoebic trophozoites from HE-stained biopsy specimens. The number of trophozoites ranged from 1 /HPF to  $\leq 50$ /HPF. Among 16 cases, mild architectural alteration of colon crypt was observed in 10 cases (62.5%), and serious architectural alteration of colon crypt was found which had a crypt branch in 1 case (16.7%). Cryptitis was observed in 12 cases (75%) and its severity was mild or moderate. No crypt abscesses were observed in all cases.

**Conclusions** Colonoscopies with histological examinations are very important to diagnose amoebic colitis. Detecting the amoebic trophozoites in the exudates by histological examination is vital. Sometimes a negative biopsy does not rule out amebiasis, repeated biopsies may be needed to make the diagnosis.

## Background

Amebic colitis, caused by intestinal infection with the parasite, *Entamoeba histolytica*, is a common cause of diarrhea worldwide. The vast majority of amoebic infections are asymptomatic, with approximately 10% of those infected progressing to have symptoms[1]. Amebic colitis is the most common symptomatic manifestation, with variable presentations, including watery diarrhea, dysentery, abdominal pain, tenderness, and, rarely, the formation of a tumor-like granulation mass referred to as an ameboma[2]. Although the complications are unusual, some complications are very serious, such as fulminant necrotizing colitis, toxic megacolon, and fistulizing perianal ulcerations when diagnoses and treatments are not timely. Prevalence is disproportionately higher in developing countries because of poor socioeconomic and sanitation conditions. Areas with the highest rates of amoebic infection include India,

Africa, Mexico, and some parts of Central and South America. In developed countries, therefore, amoebiasis is not common. Inflammatory Bowel Disease (IBD) is common in developed countries and an increasing incidence and prevalence of inflammatory bowel disease have been witnessed in developing countries. The clinical features of amoebic colitis resemble those of IBD, and therefore the risk of misdiagnosis is high[3-6]. The consequences of not recognizing amoebic colitis can be catastrophic[7,8]. It may result in the administration of steroids or major intestinal resections for suspected inflammatory bowel disease, a disease that is relatively simple to treat with metronidazole. Early and accurate diagnosis is extremely important. Some endoscopic and histologic features could be useful for differential diagnosis[9-11]. But in non-endemic countries and areas, amoebic colitis is still often misdiagnosed. Therefore, this study aimed to analyze the characteristics of the endoscopic and pathological findings of amoebic colitis and the lessons from our patients, which were useful for diagnosing amoebic colitis and avoiding serious complications.

## Methods

### Patients

This retrospective study was approved by the Ethics Committee of Beijing Friendship Hospital. 16 adult patients with amoebic colitis referred to Beijing Friendship Hospital were included in the study from January 2015 to January 2020.

### Colonoscopy

Colonoscopy was performed for all included patients and the biopsies were done during the colonoscopic procedure. Amoebic colitis was defined as the detection of amoebic trophozoites from HE-stained biopsy specimens.

### Data collection

Clinical features, endoscopic data, pathological findings, and effectiveness of treatment were all analyzed.

## Results

### 1. Clinical features of 16 patients with amoebic colitis

From January 2015 to January 2020, 16 patients were diagnosed with amoebic colitis by colonoscopies accompanied by biopsies and microscopic examinations. Amoebic colitis was defined as the presence of amoebic trophozoites in biopsy specimens. Among the 16 patients, 15 were male and 1 was female. The age range of the patients was from 31 to 67 years (median 42 years). Symptoms among 16 patients were bloody stools (56.3%, 9/16), abdominal pain or discomfort (62.5%, 10/16), and diarrhea (25.0%, 4/16). 1 patient had no symptoms; he underwent a colonoscopy because of a positive fecal occult blood test in

routine physical examination. There were no patients with HIV infections, but 1 patient with syphilis. The time from onset to diagnosis was 1 month to 3 years. At first, 12 (75%, 12/16) patients were misdiagnosed as IBD (8 ulcerative colitis, 2 Crohn's disease, and 2 unclassified IBD). There was no complication such as fulminant necrotizing colitis, toxic megacolon, fistulizing perianal ulceration, and amebic liver abscess in all patients. Among 10 patients with blood routine examination, the level of hemoglobin decreased in 2 patients (67g/l and 108g/l), who had bloody stools with 3-6 times per day for 1-2 years, and others were normal. Unfortunately, the results of stool parasites were negative in all patients.

## 2. Endoscopic findings

All patients underwent colonoscopy before diagnosis. 12 patients underwent multiple colonoscopies before diagnosis: 3 patients 3 times and 9 patients twice. The lesion distribution of colitis was as follows: 9 patients (56.2%, 9/16) in the cecum and the rectum, 2 patients (12.5%, 2/16) in the cecum and the sigmoid colon, 2 patients (12.5%, 2/16) in the cecum and the rectosigmoid colon, 2 patients (12.5%, 2/16) in the cecum, ascending colon and transverse colon, and 1 (6.3%, 1/16) patient in the cecum. Multiple lesions of erosion and/or ulcers were recognized in all patients (100%). The features of endoscopic findings included multiple irregularly shaped ulcers and erosions with surrounding erythema, and the ulcers and erosions were covered by white or yellow exudates. The intervening mucosae between the ulcers or erosions were normal. 11 patients had lesions involving the rectum; the features of the rectums can be divided to 2 types: in 6 patients (54.5%, 6/11), the irregular ulcer or erosions covered with white or yellow exudates were observed in the rectum and cecum, and the bloody exudates in the rectum were more severe than those in the cecum (figure1); in other 5 patients (45.5%, 5/11), rectal lesions were much less severe than those in the cecum, the small superficial erosion or reddened mucosa were observed in the rectal ampulla - however, irregular ulcers or erosions covered with white or yellow exudates were observed in the cecum (figure2). In the other 4 patients with multisegmental lesions, the lesions, such as the size of the ulcer, exudates, and erythema around the ulcers, in the cecum were more serious than those in other segments. The lesions located only in the cecum showed the irregular superficial ulcers covered with the white exudates, and this patient had no apparent symptoms.

## 3. Pathological Findings

All patients were diagnosed as detection of amebic trophozoites from HE-stained biopsy specimens. However, there were 12 patients (75%, 12/16) were not diagnosed timely, so these patients underwent multiple colonoscopies. In this study, all the biopsy specimens were examined again. The amebic trophozoites were observed in necrotic material admixed with mucin, proteinaceous exudate covering the ulcerated mucosa in all patients on every colonoscopic biopsies examination.

Among the 16 cases, superficial ulcers which are all located in the lamina propria of mucosa were observed by microscopy examination in 8 cases (50%, 8/16). In all cases, various inflammatory exudates were observed on the surface of the mucosa, and the exudates consisted of fibrin, necrotic material, and inflammatory cells. Amoebic trophozoites were observed mainly in inflammatory exudates or on the

surface of the mucosa. The number of trophozoites ranged from 1 /HPF to  $\leq$ 50/HPF. Tissue invasion was not observed in all cases. Among the 16 cases, mild architectural alteration of colon crypt was observed in 10 cases (62.5%, 10/16), and serious architectural alteration of colon crypt which had a crypt branch in 1 case. Cryptitis was observed in 12 cases (75%, 12/16) and mainly located in the superficial layer of mucosa, whose severity was mild or moderate. No crypt abscess was observed in all cases. There were lymphocytes, neutrophils, and eosinophils in the lamina propria of the mucosa. The number of eosinophils in the lamina propria was 5-80 /HPF, and the number of eosinophils was more than 50 /HPF in 10 cases (62.5%, 10/16). (figure 3, figure 4)

#### 4. Treatment

All patients misdiagnosed IBD were treated by mesalazine at first, and this treatment was not effective for all patients. There was no administration of steroids for all patients. When the patients were diagnosed with amebic colitis, they were treated with metronidazole 400mg, three times per day for 14 days. Among 16 patients, 10 patients followed up. The symptoms disappeared after the treatment of metronidazole. 2 patients underwent a colonoscopy 1 month after the metronidazole treatment; the results showed the ulcers and erosions disappeared and the mucosa of the colon was normal. 8 patients underwent colonoscopies 6-12 months after the metronidazole treatment; the results also showed normal appearances.

## Discussions

Currently, amebic colitis is not very common in many areas and counties. A total of 4,366 amoebic dysentery cases were reported without death in China during 2015-2018 and the reported average annual incidence was 0.08/100,000, and the patients were mainly children aged under 5 years (42.28%)[12]. A systematic review of patients with amoebic colitis who received steroids for initially misdiagnosed colitis noted that rapid progression of disease following steroid therapy was common. Nearly half of all cases underwent surgical intervention, and 25% of cases died, despite all patients eventually receiving treatment with metronidazole[13]. So amoebic colitis is often misdiagnosed in adults at first, and the timely diagnosis of amebic colitis is very important.

Various diagnostic tools exist for the diagnosis of *Entamoeba histolytica* including microscopy, serology, antigen detection, molecular techniques, and colonoscopy with histological examination[14]. Amebic colitis is not common, therefore the kits for serology assays or antigen detection are not available in many hospitals. Examination of stool is a simple and inexpensive investigation in a patient with diarrhea and may reveal trophozoites of *E. histolytica*[15]. However, the results of the stool parasite were negative in all patients in our study which is similar to the previous studies[16]. Therefore, the diagnostic sensitivity and specificity of microscopic examination to detect *E. histolytica* in the stool is considered low. A majority of the time, amebic colitis appears to be one of the differential diagnoses of colonic ulcers. In many non-endemic countries and areas, a colonoscopy with a histological examination is available and effective[17,18] for diagnosing the amebic colitis. Some studies suggest that on an

endoscopy, it is difficult to distinguish amebic colitis from IBD, CMV colitis, intestinal tuberculosis, and pseudomembranous colitis due to *C. difficile* infection[19,20]. Other studies reported the endoscopic procedure may contribute to early diagnosis of the disease and the prevention of serious complications. Nagata et al. investigated the sensitivity and specificity of endoscopic findings that were significantly associated with amebic colitis were: cecal lesions, multiple numbers of lesions, presence of aphthae or erosions, and the presence of exudate. Multivariate analysis revealed that the best combination of findings to predict amebic colitis was the presence of cecal lesions, multiple lesions, and exudates[9]. Lee KC et al. observed distinct differences in findings based on right-side amebic colitis vs. proctosigmoiditis, the colonoscopic findings of right-sided colitis included aphthae or erosions, ulcers, exudates, or edematous swollen mucosa in the cecum, and findings for proctosigmoiditis were edematous swollen mucosa with bloody exudate[21]. In our study, the cecum was the most common site of amebic colitis, and the caecum and rectum were also involved in many lesions (11/16, 68.75%). The features of the lesions in rectums had 2 types: in some patients, the irregular ulcer or erosions covered with white or yellow exudates were observed in the rectum and cecum, and the bloody exudates in the rectum were more severe than those in the cecum; in other patients, rectal lesions were much less severe than those in the cecum, the small superficial erosion or reddened mucosa were observed in the rectal ampulla. However, the irregular ulcer or erosions covered with white or yellow exudates were observed in the cecum, which was different from the report of Lee KC[21]. The features of the typical lesions in our study were similar to the previous reports[10,22], which included multiple irregularly shaped ulcers and erosions with surrounding erythema, and the ulcers and erosions were covered by the white or yellow exudates which were named "dirty ulcers".

The diagnostic value of the colonoscopy lies in the ability to take biopsies and microscopically identify intestinal amoebiasis. The pathological findings are vital in diagnosing amebic colitis[22]. In our studies, the amebic trophozoites were observed in the HE-stained biopsy specimens in all patients, although the biopsy specimens were misdiagnosed at first in 12 patients. The reasons for the misdiagnosis are: 1) In some specimens, the number of the trophozoites were less and the pathologist did not observe carefully, which led to misdiagnosis. 2) Some pathologists had no experience in diagnosing amoebic enteritis. Therefore, they often spent time observing the structure of the colonic mucosa and changes of the epithelium, while ignoring the exudates, which were the most common type of trophozoites. In one case of our study, the active inflammation in colonic mucosa and the disordered structure of crypts were significant, which was similar to IBD, and the trophozoites were very less in the exudates, so the pathologist made a misdiagnosis at first. In our study, in addition to the observation of amoebic trophozoites, there were some characteristics of pathologic findings in amebic colitis: 1) The ulcer was generally superficial. 2) The surface of the ulcer was often covered with inflammatory exudates. 3) The degree of the structure disorder was relatively mild, and generally, there was no branch. (In our study, there was only one case which had a crypt branch). 4) Cryptitis was mild and generally located in the superficial layer of mucosa. 5) Crypt abscess was not common. Prathap and Gilman reported that crypt abscesses were not found in any of the 53 rectal biopsies in acute amebic colitis[23]. 6) There were a lot

of eosinophils in the mucosa lamina propria, but it was not specific. All of the histologic features could be useful in differentiating amebiasis from IBD and other colitis.

This study had some limitations. First, Beijing is a no-epidemic area of amebiasis, so the number of patients with amebic colitis in our study was small. Second, the selection bias was present because there were no patients with fulminant amebic colitis or amebic abscess in our study, which meant there were no acute serious cases in our study.

## **Conclusions**

Colonoscopies with histological examinations are very important to diagnose amebic colitis. When the characteristic of the colonoscopy is similar to that of the amebic colitis. Biopsies with pathological examinations are necessary. Detecting the amoebic trophozoites in the exudates is vital. Sometimes a negative biopsy does not rule out amebiasis; repeated biopsies may be needed to make the diagnosis.

## **Abbreviations**

Not applicable

## **Declarations**

### **Ethical Approval and Consent to participate**

Beijing Friendship Hospital Research Ethics Committee has approved this research. And all patients signed a consent form giving permission to use their anonymous data for research.

### **Consent for publication**

All patients signed a consent form giving permission for publication.

### **Availability of supporting data**

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

### **Competing interests**

The authors have no conflicts of interest. The authors are responsible for the content of the paper

### **Funding**

High-level health personnel training program of Beijing Health System. The role of the funding body supported us in writing the manuscript .

## Authors' contributions

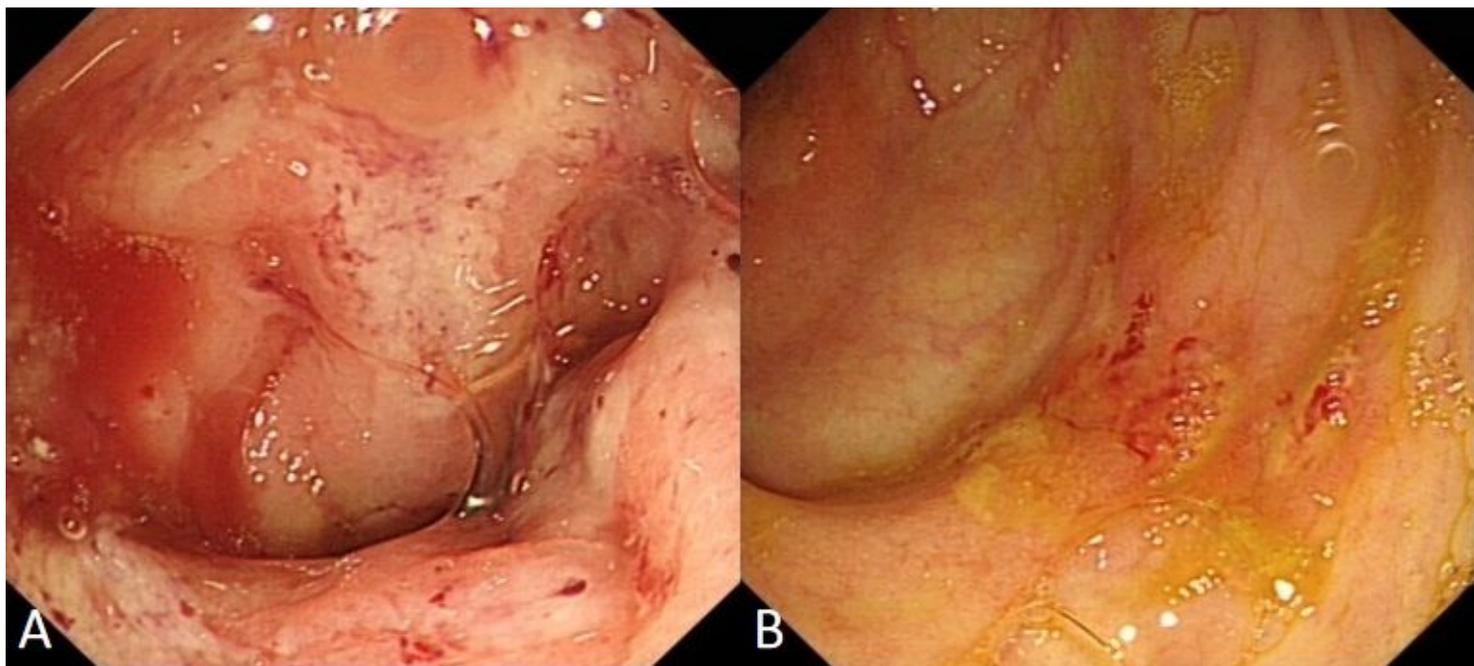
ZY, YB, and MY participated in the idea, protocol design, and data collection. ZY and YB wrote the first version and edited the final version. YH Z and NN D participated in the idea, and data collection and approved the final version. HY Z participated in the idea, edited the first version, and approved the final version. YD W participated in the idea and approved the final version. All authors have read and approved the manuscript in its current state.

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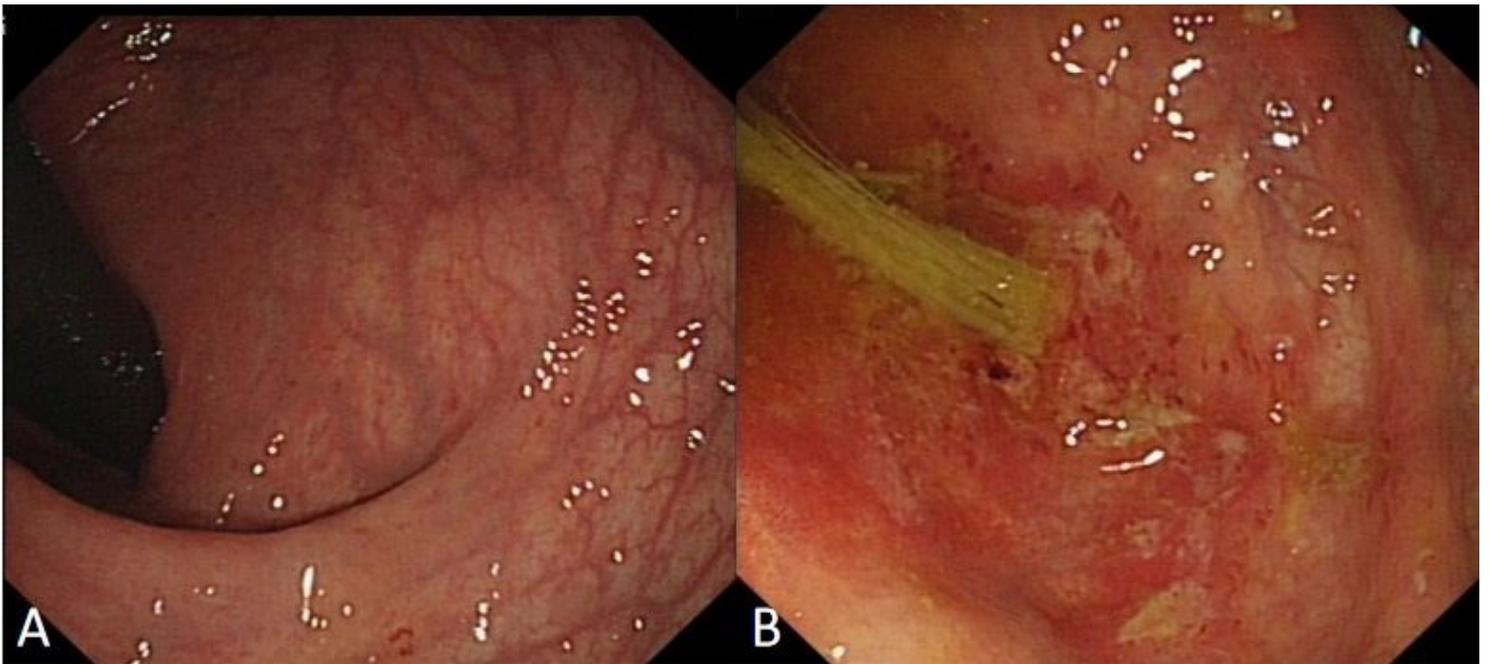
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## Figures



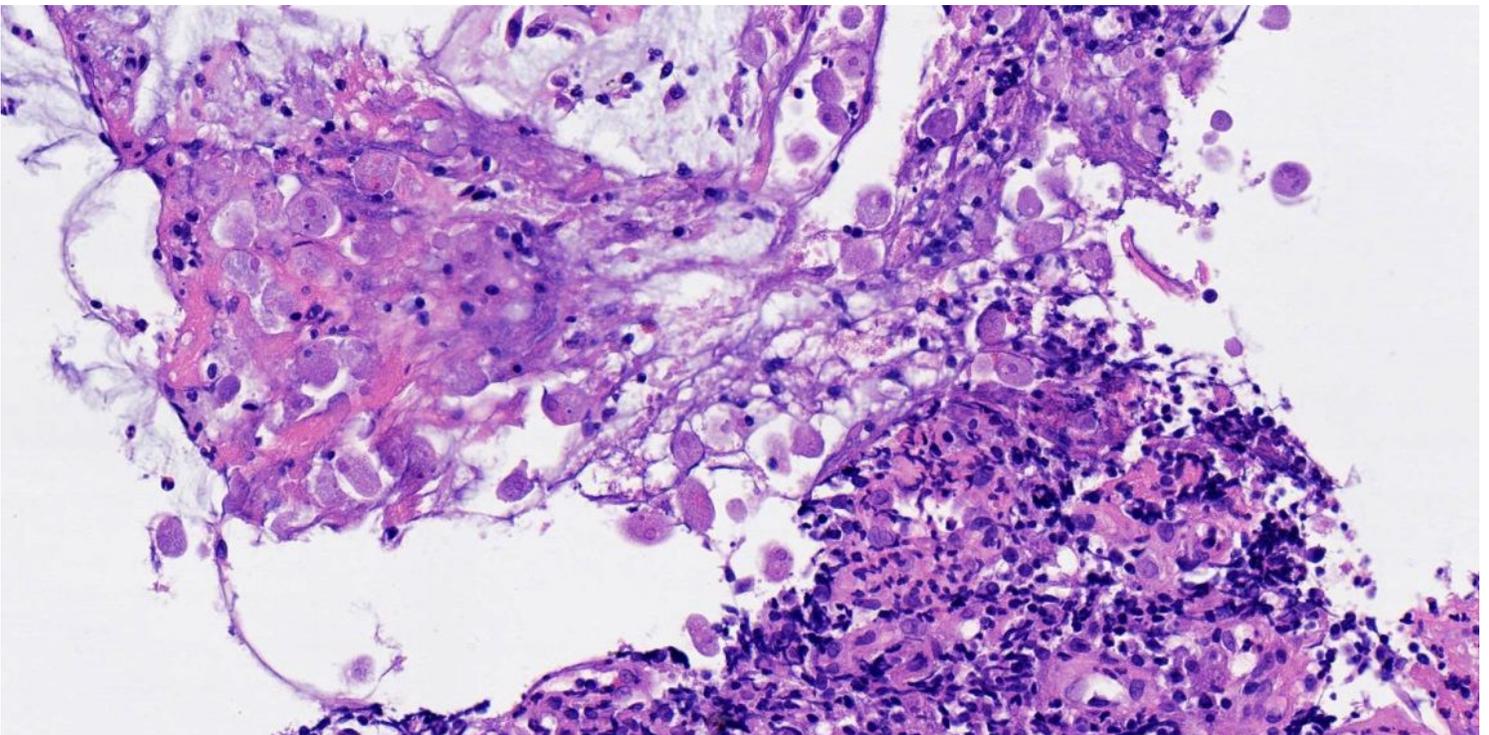
**Figure 1**

The irregular erosions covered with white exudates were observed in rectum (A) and cecum (B), and the bloody exudates in rectum were more severe than those in cecum.



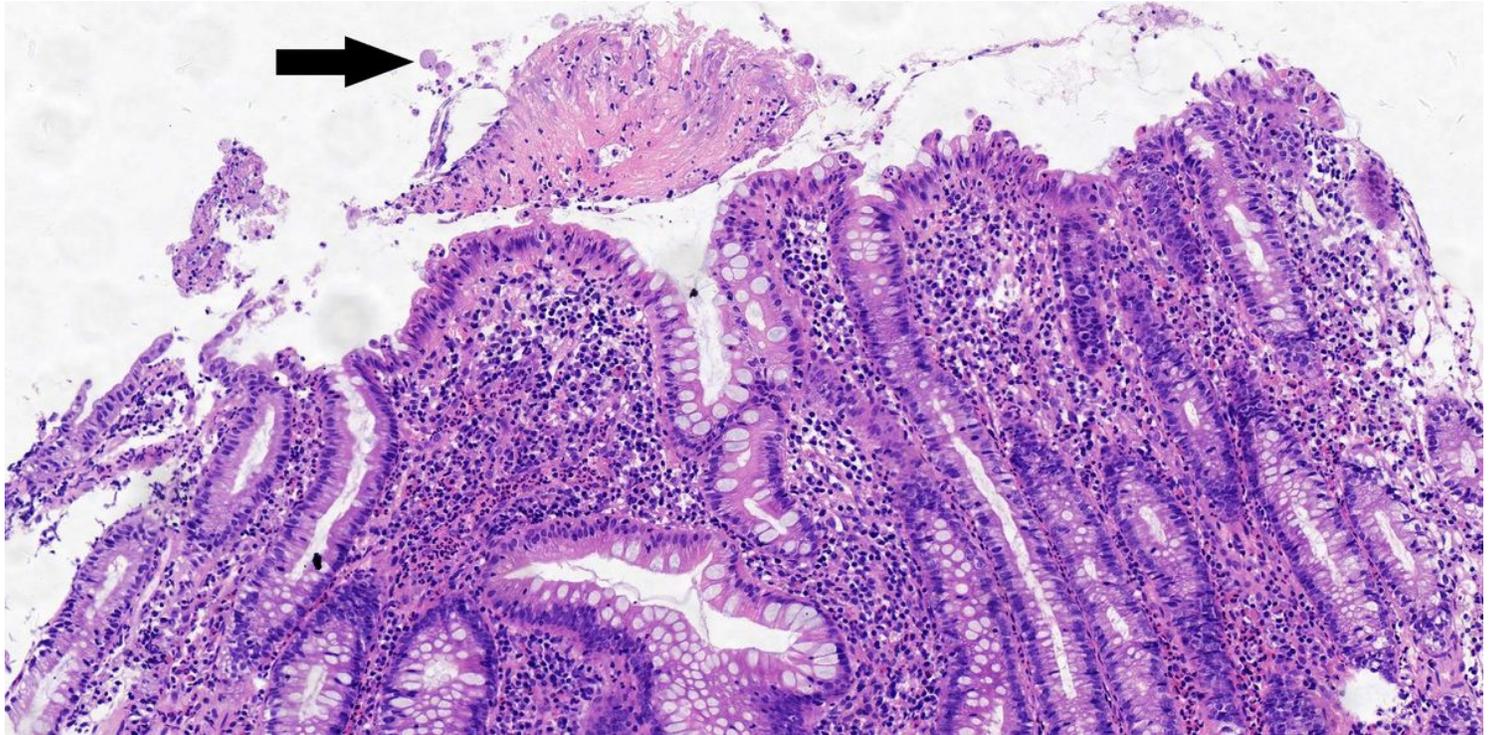
**Figure 2**

The rectal lesions (A) were much less severe than those in cecum (B), the small superficial erosion or reddened mucosa were observed in the rectal ampulla(A) , and the irregular erosions covered with white or yellow exudates were observed in the cecum(B).



**Figure 3**

Typical Pathological Findings of amebic colitis: superficial ulcer was located in the lamina propria of mucosa , inflammatory exudates were on the surface of mucosa, and the exudates consisted of fibrin, necrotic material and inflammatory cells. Amoebic trophozoites were observed in inflammatory exudates.



**Figure 4**

Atypical pathological Findings of amebic colitis which was misdiagnosed at first: acute moderate cryptitis with architectural alteration of colon crypt, few inflammatory exudates, and only 3 amoebic trophozoites in the exudates