

A case of amoebic colitis with Crohn-like endoscopic and histopathological features

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SUMMARY

Amoebic colitis represents a common parasitic infection in developing countries. In western world, it is encountered only sporadically. The clinical presentation is usually non-specific, non-invasive laboratory tests are often false negative and endoscopic and histopathological appearance may mimic other illnesses, especially Crohn's disease. The disease therefore harbours a huge risk of misdiagnosing and a proper diagnosis is usually challenging. We present a case of an amoebic colitis with Crohn-like features and negative parasitological testing in a 53-years-old woman, in which the final diagnosis was established on the basis of its histopathological examination.

Keywords: Colitis – Crohn's disease – Entamoeba histolytica – Histopathology

Případ amébové kolitidy s endoskopickými i histopatologickými rysy Crohnovy choroby

SOUHRN

Amébová kolitida je v rozvojových oblastech běžnou parazitární infekcí. V západních zemích se s ní však setkáváme jen sporadicky. Klinická symptomatologie je obvykle necharakteristická, neinvasivní laboratorní testy bývají často falešně negativní a histopatologický náález může mimikovat řadu jiných onemocnění, zejména Crohnovu chorobu. Diagnostika je tak svízelná a nese s sebou vysoké riziko chybně stanovené diagnózy. Prezentujeme zde případ 53leté ženy, u které byla tato diagnóza stanovena až na základě mikroskopického obrazu.

Klíčová slova: kolitida – Crohnova choroba – Entamoeba histolytica – histopatologie

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Amoebic colitis represents a common parasitic infection in developing countries and one of the main causes of local morbidity and mortality. Contaminated water and food are main sources of such infection (1). In western countries, travellers and immigrants from endemic regions are usually the affected groups (2,3). A worldwide annual incidence is approximately 50 billion of new infections, with mortality reaching up to 10 000 patients, which makes amoebiasis the third most common parasitic cause of death on a global scale (4). The majority of fatal cases are caused by extraintestinal complications, with amoebic liver abscess at first (5). We present a case of an amoebic colitis in a 53-years-old woman with protracted non-specific gastrointestinal symptoms, negative parasitology testing and Crohn-like endoscopic and microscopic morphology, in which the final diagnosis was established on the basis of its histopathological examination.

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CASE REPORT

A 53-years-old Caucasian female was referred to a gastroenterological department for non-specific dyspeptic symptoms. She complained of frequent loose stools and non-specific abdominal pain lasting for 3-4 months. No fever, vomiting, profuse diarrhoea nor blood nor mucus in the stool were noted. The consecutive medical history-taking revealed that she has been suffering similar clinical symptoms intermittently during the last 4 years, which included pain in both upper abdominal quadrants, cramping, flatulence and general malaise. The patient had no other significant medical history and has not taken any regular medication. However, her epidemiological and travel history was remarkable as she reported annual long-term stays lasting 1-2 months in Southeast Asia and Latin America including Thailand, Sri Lanka, Cambodia, Cuba and Brazil during the last 15 years. She travelled as a backpacker staying in non-touristic remote rural areas. She did not attend any pre-travel health consultation nor underwent any vaccination. While abroad, she did not suffer any significant health problems and negated any febrile or diarrhoeal illness. At home in the Czech Republic, she has been working as a housekeeper and sewage cleaner for ten years. She was investigated by a general practitioner and gastroenterologist three years before diagnostic examination. Endoscopic findings revealed a few small isolated ulcerations in

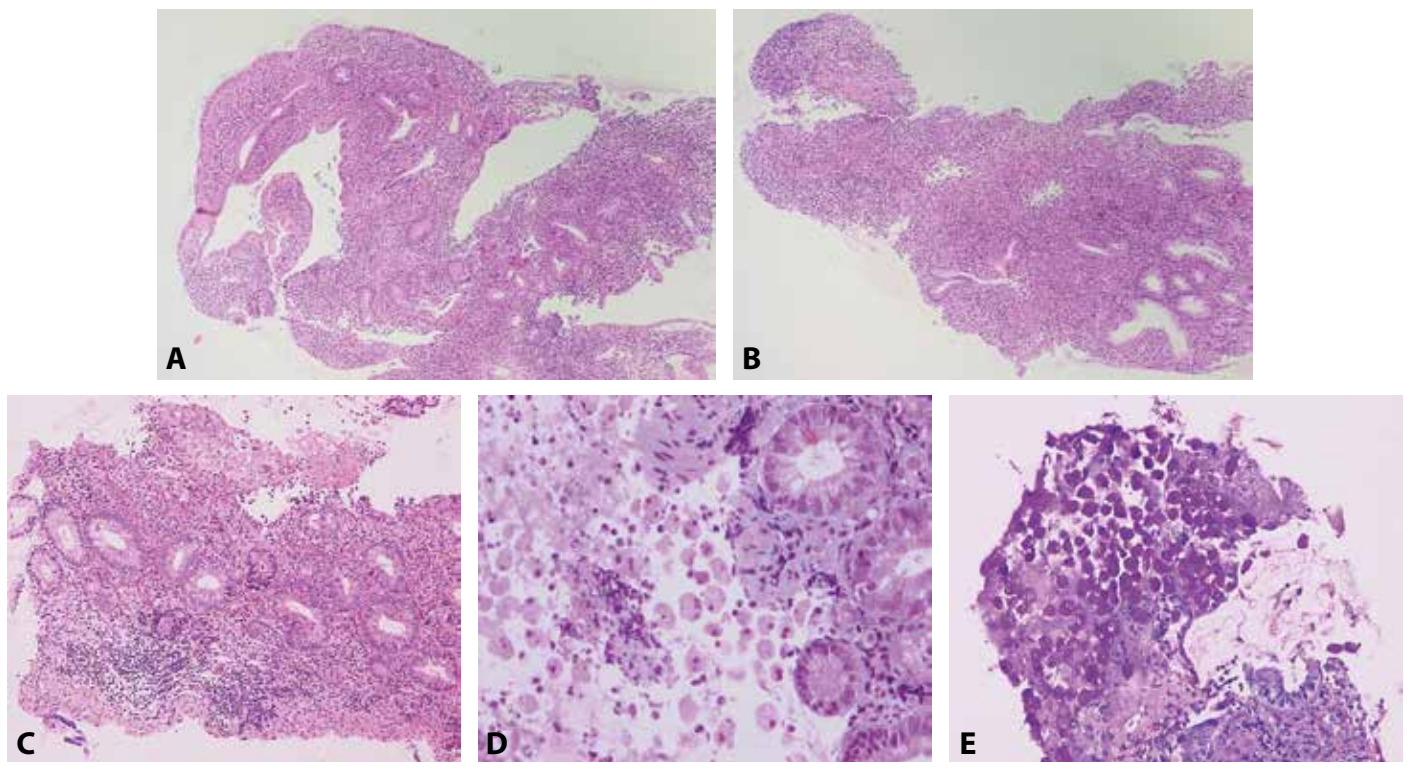


Figure 1. **A:** Colonic mucosa with distortion of the architecture and severe chronic active inflammation in the lamina propria including cryptitis (haematoxylin & eosin, 100x). **B:** Deep mucosal defect with granulation tissue on the bottom (haematoxylin & eosin, 100x). **C:** Colonic mucosa with chronic active inflammation including numerous eosinophils, crypt distortion and basally localised nodular infiltrate. There is a defect on the top with numerous oval elements in the mucus layer (haematoxylin & eosin, 100x). **D:** *Entamoeba histolytica* elements with phagocytized erythrocytes on the surface of the ulceration (trichrome stain, 200x). **E:** Numerous *Entamoeba histolytica* elements with cytoplasm strongly positive in periodic acid Schiff stain (200x).

coecum in otherwise normal bowel mucosa. Since all other investigations including laboratory parameters, stool cultivation and parasitological examinations were inconclusive, the specific diagnosis was not established at that time and the early control colonoscopy was recommended. Her symptoms resolved temporarily and the patient was non-adherent to the follow-up examinations.

At the time of her last examination, the laboratory findings were still unremarkable and stool cultivation was negative. Thus, a control endoscopy was performed. The colonoscopy revealed small pseudopolyps and flat ulcerations in the coecum, slightly larger than those described during her previous examination, whilst the residual mucosa in the large bowel and terminal ileum was intact. The differential diagnosis remained wide after this examination, but the gastroenterologist suspected an inflammatory bowel disease (IBD), specifically Crohn's disease (CD).

The histopathologic examination (Figures 1A-E) of the tissue sample revealed a colonic mucosa with features supporting the suspected diagnosis of CD at the first glance, especially due to mucosal crypt distortion and the presence of deep chronic ulcerations with granulation tissue at the bottom. There was an intense florid inflammation found in the surrounding lamina propria, with cryptitis and abundant admixture of eosinophils. Focally, an infiltration of smooth muscle bundles of muscularis mucosae by inflammatory cells was evident. However, cellular elements resembling macrophages were observed in the debris and mucus on the bottom of the ulcerations. These were larger oval cells with finely granular cytoplasm and dark round nuclei. Cytoplasm was strongly positive in periodic acid Schiff staining (PAS) and contained phagocytized erythrocytes. A histiocytic origin of the cells was excluded by the negative

anti-CD68 antibody immunohistochemistry. Based on these findings, the diagnosis of amoebic colitis was established. *Entamoeba histolytica* was proposed as a probable etiological agent, which was subsequently confirmed by two expert parasitologists.

The patient was then referred to the Department of Infectious, Parasitic and Tropical diseases for further examination and initiation of therapy. Based on this information, full diagnostic work-up has been performed.

Laboratory findings including blood count, inflammatory and renal parameters, iron metabolism and liver function tests were unremarkable. Screening for celiac disease, anti-Saccharomyces cerevisiae and anti-neutrophil cytoplasmic antibodies (ASCA and ANCA) were negative. Faecal calprotectin was slightly increased (209 ug/g). Stool specimens were repeatedly examined by a parasitologist (a total of 9 samples) including microscopy and multiplex real-time polymerase chain reaction (PCR) for stool parasites, each with negative results. Serology of *Entamoeba histolytica* was negative as well.

The diagnosis of amoebic colitis was confirmed by the real-time PCR of the amoebic DNA, isolated from the paraffin block slices by standard organic extraction method. Subsequent abdominal ultrasonography excluded the presence of liver abscess.

Treatment was initiated with high dose of metronidazole (750 mg three times a day for 14 days), followed by luminal amoebicide. Since paromycin was not available, chloroxine was used. The treatment was well tolerated and led to complete remission of abdominal symptoms. Six months after the treatment, the control endoscopy and biopsy confirmed normal bowel mucosa and faecal calprotectin and parasitological examinations were all negative.

DISCUSSION

Our case illustrates a variable clinical presentation of amoebic colitis. A traditional image of dysentery with bloody diarrhoea, fever, weight loss and tenesmus is not the rule, the manifestation of the disease is highly variable and may be presented with non-specific symptoms or as an asymptomatic carrier only (1,6). In attenuated persons, it can manifest as a fulminant colitis with almost 50% mortality. However, these cases are rare and amoebic aetiology isn't always considered, even in endemic regions (4,7).

Clinical complains often lead to an endoscopic examination. Not only clinical, but even a morphological appearance of amoebic colitis is variable, from endoscopically normal bowel mucosa to an extensive inflammatory involvement (8). Flask type ulcers with narrow neck and widening base in otherwise intact mucosa, as described in older literature, are only one out of many morphological appearances that the disease can present itself (8). Multiple small round shallow and prominently tumid ulcerations of size 2-10 mm (so called "dirty ulcers"), covered by a thick layer of fibrin and blood clots are more usual. A mucosa between the defects is often markedly oedematous, focally forming small gelatinous polyps (9,10). Defects occur particularly in cecum, appendix and following parts of the ascending colon. This localisation in particular, together with negative findings in terminal ileum, is an important discriminating criterion of diseases that stands in the first line in differential diagnosis, which is mainly CD and IBD generally (9,11).

An appearance of ulcers itself can represent a helpful diagnostic clue as well. The aforementioned "dirty" appearance with thick layer of cellular debris, fibrin, mucus and blood clots is not typical for IBD (2). It is important to consider also an ulcerative colitis in some cases, as the disease may present as diffusely inflamed, friable, oedematous and haemorrhagic mucosa without presence of deep ulcers (11). In a minority of cases, an endoscopic appearance can impose as a pseudomembranous colitis. In these cases, it is important to rule out a *Clostridium difficile* infection or ischaemic colitis (8,12).

Considering the endoscopic variability, the diagnosis often relies on the detection of the amoebas or their antigen in the stool or the amoebic DNA from a tissue sample by real-time PCR (6,13). However, a negative result doesn't exclude the presence of amoebas. A blindfold antibiotic therapy, enterography with barium contrast or even a preparation before colonoscopy itself can cause a false negative result (4,11). Therefore, a serological detection of specific antibodies still remains one of the most widely used methods of detection with 82-98% sensitivity in symptomatic patients (4,11). However, the detectability may vary, and in case of asymptomatic carriers the literature denotes only 8-66% sensitivity, since the positivity depends on the invasion of the pathogens into the bowel wall (4,11).

A long-known fact complicating the diagnostic process is the tendency of amoebas to affect patients with IBD as a superinfection, especially in ulcerative colitis (3,11). A direct detection of pathogen is often negative because of a previous antibiotic therapy (14) and a false negative result with consecutive immunosuppressive therapy can be fatal for the patient. A serological

detection of antibodies is particularly beneficial in these cases. In endemic regions, some authors even recommend a routine screening for amoebiasis before initiation of corticotherapy, and for patients with refractory IBD recommend an empirical cure with metronidazole even in cases of negative microbiological examination (14). Moreover, metronidazole is known for its direct therapeutic effect even for some subtypes of IBD, specifically colonic form of CD (15).

In many cases, ours included, a diagnosis of amoebic aetiology is established only by histopathological examination. But even there the approach is not straightforward. The infection can induce changes closely mimicking IBD, including mucosa architecture distortion, cryptitis, crypt pseudoabscesses, inflammatory infiltration of the submucosa or deep ulcerations (2,13). A correct diagnosis relies on direct detection of pathogens. *Entamoeba histolytica* is a medium sized, oval or round microorganism, 25-40 um in diameter, with greyish, finely granular cytoplasm, resembling a histiocyte. However, its nucleus is small and dark, contrasting with larger and paler histiocytic nucleus with apparent nucleolus. A cytoplasm is strongly PAS positive and contains phagocytized erythrocytes (13,16), which is a crucial morphological criterion, that differentiate *E. histolytica* from much more frequent non-invasive *Entamoeba dispar* (6,13) or common non-pathogenic intestinal commensals *Entamoeba coli*, *Entamoeba polecki* or *Endolimax nana* (4).

CONCLUSION

The presented case illustrates a wide range of challenges in properly diagnosed amoebic colitis. Especially in non-endemic countries, the clinical complains are usually non-specific and amoebic colitis is not considered in the differential diagnosis. Since non-invasive parasitological tests are often false negative, the importance of the endoscopy with segmental colonic biopsy is unequivocal. However, the macroscopic and histopathological appearance of the amoebic colitis can be misleading, given the fact that amoebas may easily mimic other non-infectious diseases, especially IBD. Therefore, the close cooperation of the gastroenterologist, microbiologist and pathologist is crucial for correct diagnosis and subsequent proper treatment.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this paper.

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