


CASE REPORT

Amoebic colitis: A case series of a recurring missed diagnosis

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Key words

amoebic colitis, antibiotics, *Entamoeba histolytica*, travel history.

Accepted for publication 10 December 2020.

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Declaration of conflict of interest: None.

Author contribution: Joshua Haron Abasszade, Robert Little, Fiona Yeaman, Marcus Robertson, and Sally Bell conceived and designed the case study, were primarily responsible for the manuscript preparation, and were part of the treating team.

Introduction

Entamoeba histolytica (*E. histolytica*) is the pathogenic protozoan responsible for amoebic colitis, a common parasitic infection,¹ and the second leading cause of death from parasitic infections worldwide.² The clinical presentation of amoebic colitis is varied and may include cramping abdominal pain, watery and/or bloody diarrhea, weight loss, fever, and anemia. Complications such as toxic megacolon, perianal ulceration, and colonic perforation are described,³ and extraintestinal complications may arise secondary to hematogenous spread to sites such as the liver, brain, and lungs.³

We present a case series of four patients diagnosed with amoebic colitis. These cases highlight the importance of obtaining a thorough travel and exposure history, maintaining a high index of suspicion, and understanding the limitations of available investigations in order to differentiate amoebiasis from common differential diagnoses such as inflammatory bowel disease (IBD), bacterial colitis, and colorectal cancer.³

Case series presentations

Case 1. A 36-year-old Indian woman with a medical history significant for thalassemia minor was diagnosed with ulcerative proctitis in India in May 2019. She was treated with sulfasalazine and corticosteroids. A flare of ulcerative colitis (UC) was documented following medication noncompliance, which settled with

Abstract

Entamoeba histolytica, a pathogenic protozoan that causes amoebiasis, remains the second leading cause of death from parasitic infections worldwide. We present a case series of patients presenting to metropolitan tertiary gastroenterology units in Melbourne, Australia, highlighting the complexities of diagnosing amoebic colitis and the potential for misdiagnosis. These cases illustrate four key lessons in the identification of amoebic colitis: (i) obtaining a thorough travel and exposure history, (ii) having a high index of suspicion, (iii) understanding the limitations of available investigations, and (iv) being aware that amoebic colitis may masquerade as other common conditions.

oral metronidazole prescribed by a local general practitioner. Following travel to Australia, her symptoms recurred and persisted for several months until she presented to hospital with bloody diarrhea, nausea, vomiting, and loss of weight; she was noted to be 24 weeks' pregnant. Treatment with rectal and oral 5-aminosalicylic acid and oral prednisolone was commenced with an initial improvement in symptoms. Given her pregnancy status and improvement with medical management, endoscopy was not performed. She subsequently re-presented with severe bloody diarrhea associated with tachycardia, anemia (hemoglobin 76 g/L), and leukocytosis. Intravenous corticosteroids were commenced, and a sigmoidoscopy demonstrated Mayo 3 proctitis (Fig. 1a). Fecal microscopy and tissue histology both demonstrated *E. histolytica* organisms, consistent with amoebic colitis. Intravenous metronidazole (750 mg three times a day) and metronidazole suppositories were commenced with rapid resolution of rectal bleeding. She was discharged with a seven-day course of oral metronidazole (400 mg three times a day) followed by paromomycin (500 mg three times a day). She remained well and delivered a healthy child at term.

Case 2. A 75-year-old previously well man, on holiday from India, presented to hospital with a two-week history of abdominal pain, fever, watery, nonbloody diarrhea and anorexia. On examination, he was tachycardic (heart rate 115 beats per minute), tachypneic (respiratory rate 28 breaths/min), and febrile

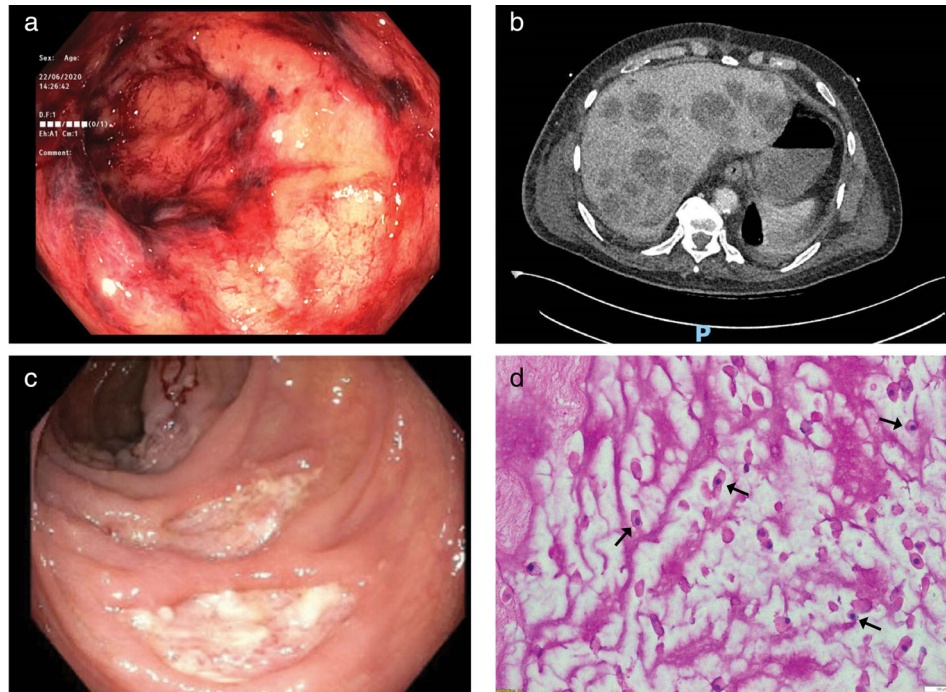


Figure 1 (a) Severe proctitis in the rectum. (b) CT angiography (portal-venous phase) demonstrating hypodense lesions scattered throughout the liver. (c) Inflammation and ulceration of the colon. (d) Histology of the sigmoid colon demonstrating *Entamoeba histolytica* organisms with ingested red cells (arrows). Credit: David Hugo Romero.

(38.1°C). Abdominal examination revealed a soft abdomen with right iliac fossa tenderness. Initial laboratory findings demonstrated an elevated white cell count ($39.2 \times 10^9/L$) and C-reactive protein (CRP) (379 mg/L). A CT abdomen revealed a phlegmonous mass adjacent to the caecum, raising the possibility of appendicitis along with multiple ill-defined hepatic lesions.

The patient underwent a laparotomy where a perforated caecal mass with peritonitis was found. Intraoperative colonoscopy demonstrated ulceration of the rectum and transverse colon, and a subtotal-colectomy with end-ileostomy was performed. Postoperatively, worsening transaminitis was noted, and a CT liver demonstrated innumerable hypodense hepatic lesions consistent with liver abscesses (Fig. 1b), which were subsequently biopsied. Human immunodeficiency virus (HIV), amoebic, and *Echinococcus* serology and *Mycobacterial* microscopy and culture were all negative.

Histology of the resected bowel demonstrated numerous *E. histolytica* organisms with ulceration and caecal perforation; cultures from other sites were negative for amoebiasis. The patient required serial drainage of hepatic abscesses and ultimately recovered following intravenous metronidazole and prolonged oral paromomycin.

Case 3. A 45-year-old healthy man presented with four weeks of worsening nonbloody diarrhea, 11 kg of weight loss, and a perianal abscess with a communicating anal fistula. Prior to admission, his general practitioner had treated him for suspected food poisoning and commenced oral metronidazole following a positive stool culture for *Blastocystis hominis*. The patient denied

recent travel or receptive anal intercourse. In hospital, a fistulotomy was performed, and intravenous hydrocortisone and antibiotics were commenced for ongoing diarrhea. A sigmoidoscopy demonstrated an anal fistula and deep ulceration with rectal sparing. A presumptive diagnosis of Crohn's disease was made. Subsequent magnetic resonance enterography showed no small bowel involvement. The patient was transferred to a tertiary center following large-volume rectal bleeding.

On arrival, the patient was anemic (hemoglobin 70 g/L) with an elevated CRP of 172 mg/L. Three fecal specimens were obtained and tested, and ova-cyst-parasite (OCP) analysis and amoebiasis, schistosomiasis, strongyloides, and syphilis serology were negative. A colonoscopy revealed moderate ileitis and multiple pancolonic serpiginous ulcers (Fig. 1c), further supporting a diagnosis of atypical ileocolonic and perianal Crohn's disease, and infliximab 10 mg/kg was commenced. Three days later, the patient deteriorated with fever and left iliac fossa pain. A CT abdomen demonstrated spontaneous sigmoid colon perforation with intraperitoneal free gas. He underwent an emergency laparotomy and Hartmann's procedure; histopathology demonstrated acute colitis and copious *E. histolytica* organisms (Fig. 1d). Intravenous metronidazole (750 mg tds) was commenced, and the patient made a full recovery.

Case 4. A 24-year-old Indian woman presented to hospital with a 10-day history of abdominal pain, weight loss, and severe bloody diarrhea on a background of known UC. Her UC was diagnosed in India in 2018 and managed with mesalazine monotherapy.

On examination, vital signs were within normal limits, and abdominal examination revealed right-sided involuntary guarding and tenderness. The patient was anemic (hemoglobin 93 g/L) with normal inflammatory markers. A CT abdomen showed rectal mucosal hyperenhancement. Intravenous hydrocortisone was commenced for a suspected UC flare, and a flexible sigmoidoscopy demonstrated Mayo 2 proctitis. HIV, hepatitis, and mycobacterium serology were negative. Stool microscopy was positive for *E. histolytica* organisms. Oral metronidazole followed by paromomycin were commenced, corticosteroids were weaned, and mesalazine was ceased. Bowel histology did not demonstrate amoebiasis.

Discussion

These cases highlight the challenges and pitfalls of diagnosing amoebic colitis in developed countries where the incidence is low. Significant variation in presenting symptoms, previous misdiagnosis, and amoebiasis masquerading as other common conditions all contribute to missed or late diagnoses, which can result in development of life-threatening complications. In addition, these cases highlight the importance of a comprehensive travel history and maintaining an index of suspicion, even in patients with diagnosed IBD. We recommend that clinicians consider invasive amoebiasis in their list of differentials and be aware that it is both a local and imported disease.¹

E. histolytica infection begins with ingestion of cysts, typically through fecally contaminated water or food. In the small bowel, excystation occurs with the formation of mobile and invasive trophozoites, which aggregate in the mucin layer of the intestines, forming cysts and destroying colonic epithelium.³ Approximately 90% of cases are self-limiting and asymptomatic,⁴ with spontaneous clearance of infection.¹ Symptoms of abdominal pain, watery and/or bloody diarrhea, weight loss, and fevers occur in 10% cases, and extraintestinal spread is noted in <1%.⁴

E. histolytica is endemic to India, Southeast Asia, Egypt, and Mexico.^{1,2} van Hal *et al.* reported that invasive amoebiasis has been prevalent in northern Australia, leading to locally acquired cases.¹ High-risk populations in Australia include indigenous Australians, immigrants, residents returning from endemic countries, and men who have sex with men.¹ In this series, three of four patients had recently traveled to India; however, one case acquired *E. histolytica* despite no domestic or international travel. This has not previously been reported and illustrates the potential for local transmission.

Diagnostic tools for intestinal amoebiasis include: fecal microscopy, fecal polymerase chain reaction (PCR), fecal and/or serum antigen detection, serology, and histologic examination of colonic biopsy specimens.⁵ Fecal microscopy is the most common first-line investigation, particularly in developing countries; however, the sensitivity to identify cysts and/or trophozoites is suboptimal at 25–60%.⁴ Given that organism excretion can vary, three specimens taken on separate days are recommended to increase the diagnostic yield.⁵ Fecal PCR has a sensitivity >70% and a specificity >90%.⁶ The sensitivity of antigen detection in feces is 90%, and in serum is 65% in the acute setting.^{3,4} Detection of *Entamoeba* antibodies in serum is possible in 70–90% of individuals within 5–7 days of acute infection; however, this is not helpful in differentiating acute from previous infections.^{3–5} Finally, colonic biopsy specimens are not considered a routine diagnostic tool, and visualization of amoeba is rare.

Nonspecific histopathological findings such as hemorrhagic regions of the colon, flask-shaped ulcerations, necrosis of intestinal wall, and focal perforation may be associated with amoebic colitis, and the diagnostic yield may be increased with specialized stains such as the periodic acid-Schiff stain.⁴

Despite these tools, diagnosis of amoebic colitis remains challenging. This is highlighted in Case 3, where serology and serial fecal cultures were negative, possibly as a result of a prior course of metronidazole. In two cases, diagnosis was made on bowel histology, which is not common, and only one case was diagnosed by noninvasive means. Other published series have documented the diagnostic challenges associated with amoebic colitis; however, the majority are from developing countries where the incidence is higher. Gupta *et al.* demonstrated a fatal case of amoebic colitis in India, in which a patient was misdiagnosed and treated for IBD before developing fulminant necrotizing amoebic colitis, leading to multiorgan failure and death.⁷ Cases 2 and 3 in our cohort also demonstrate the dangers of delayed diagnosis as these patients required emergency laparotomy following colonic perforation. Den *et al.* also reported the difficulties of diagnosing amoebic colitis whereby repeated colonic biopsies and stool cultures were negative for *E. histolytica*; diagnosis was ultimately confirmed serologically with resolution of symptoms following appropriate antimicrobial therapy.⁸ Finally, Tufail *et al.* described a case series of amoebic colitis in the United Kingdom masquerading as IBD.⁹ Guidelines were suggested by the authors to screen for *E. histolytica* in all patients presenting with colitis, with amoebic antimicrobial cover to be empirically commenced in patients receiving immunosuppression until results are available.⁹

The Australian Therapeutic Guidelines recommend treatment of acute amoebic colitis (dysentery) using metronidazole 600 mg orally every eight hours for seven days.¹⁰ However, if severe (i.e. blood in the stools, perforation, peritonitis), then escalated doses of metronidazole of either 750 mg intravenously or 800 mg orally every eight hours for seven days are required.¹⁰ Once treatment is completed, an intraluminal cyst eradication agent, paromomycin 500 mg orally, every eight hours for seven days, should be used.¹⁰ Paromomycin prevents relapse given that treatment failure may occur in up to 40–60% of patients treated with metronidazole alone.⁴

In conclusion, this case series highlights the challenges in diagnosing amoebic colitis and the potentially life-threatening consequences of misdiagnosis, inappropriate immunosuppression, and delayed antimicrobial therapy.

Acknowledgements

We acknowledge David Hugo Romero for his contributions to the graphic design.

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