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Citation	Clinical Journal of Gastroenterology. 2023, 348, p. 1565
Version Type	AM
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A case of fulminant amoebic colitis during systemic chemotherapy for gastric cancer

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Abstract

Amoebiasis is a parasitic infection caused by the protozoan, *Entamoeba histolytica*. At times, amoebiasis is activated under immunosuppressive conditions such as chemotherapy. We report a case of fulminant amoebic colitis resulting from an asymptomatic *Entamoeba histolytica* infection, which was activated by chemotherapy for gastric cancer. The patient developed diarrhea and fever after three courses of chemotherapy for gastric cancer and was diagnosed with acute enteritis. A colonoscopy and biopsy were performed because of the bloody stool. Histopathological findings revealed amoebic invasion of the rectum. Therefore, the patient was diagnosed with amoebic colitis and was treated with metronidazole. Emergency surgery was performed because intestinal perforation was suspected after which his general condition improved and was discharged. Subsequently, gastric cancer surgery was performed and the patient was discharged without postoperative complications. Hence, amoebic colitis should be listed as a differential diagnosis, and a colonoscopic biopsy should be performed when colitis occurs during chemotherapy for cancer.

Keywords

amoebic colitis, chemotherapy, gastric cancer, colonoscopy

Background

Amoebiasis is a parasitic infection caused by the protozoan, *Entamoeba histolytica*. A majority of infected patients remain asymptomatic, however, amoebiasis is activated under immunosuppressive conditions [1]. In such cases, infected patients develop amoebic colitis, defined as amoebic diarrhea with the discharge of mucus or blood, which occurs when the amoeba breaches the mucosal barrier and travels through the portal circulation to the liver, where they may cause liver abscesses. Fulminant amoebic colitis (FAC) is defined as a condition in which ulceration, necrosis, perforation of the intestinal tract, and peritonitis result from amoebic invasion. FAC is found in less than 0.5% of cases, however, it has a mortality rate of 50–100% [2]. Metronidazole is used for treatment; but it is difficult to diagnose amoebic colitis, [3]. Therefore, early treatment is not easy to achieve. Here, we report a successful case of FAC resulting from an asymptomatic *Entamoeba histolytica* infection, which was activated by chemotherapy for gastric cancer.

Case presentation

A 65-year-old man presented with mild anemia. Upper gastrointestinal endoscopy revealed advanced gastric cancer and an abdominal computed tomography (CT) scan indicated intra-abdominal lymph node metastasis. The patient was diagnosed with advanced gastric cancer (cT4aN1M0 cStage III in UICC 8th). Preoperative chemotherapy with docetaxel (50 mg/m² on day1), oxaliplatin (100 mg/m² on day1), and S-1 (80 mg/m²/day on day1–14) for 2 weeks with 1 week of rest was started [4]. After 3 courses of treatment, the patient developed diarrhea and fever. CT scan revealed wall thickening in ~~all colons~~ the whole colon and rectum and a small amount of ascites in the douglas fossa on the same day. The patient was diagnosed with acute colitis. We thought the cause of the acute colitis was a side effect of drugs of chemotherapy. Laboratory results showed significant leukocytosis, renal failure, and electrolyte abnormalities with a white blood cell count $13.9 \times 10^3/\mu\text{L}$ (85.1% neutrophils), blood urea nitrogen level 39.0 mg/dL, serum creatinine level 1.51 mg/dL, serum sodium concentration 125.0 mEq/L, serum potassium concentration 3.2 mEq/L and serum chloride concentration 88 mEq/L. The HIV antibody test results were negative. Following admission, the patient was treated with fasting, fluid replenishment via intravenous drip injection, and broad-spectrum antibiotic therapy. Stool tests and blood cultures were performed, but no apparent cause was identified. On the 21st day after admission, diarrhea and fever persisted, and bloody stools developed for which colonoscopy and biopsy were performed. Biopsy were taken from the bottom of the ulcer and the margins of the ulcer. It revealed hyperemic mucosa, edema, and multiple ulcers of various sizes covered with fragile and easily bleeding debris from the rectum to the caecum (Fig. 1). On the 22nd day after

admission, histopathological findings after HE staining revealed amoebic invasion of the rectum, and on later PAS staining or Grocott staining as additional diagnoses was made (Fig. 2). Thus, the patient was diagnosed with amoebic colitis and was treated with metronidazole. On the 26th day of admission, the patient developed severe abdominal pain. Urgent abdominal CT scan revealed a large amount of ascites, wall thickening in the entire colon and rectum, a small amount of free air around the colon, and a 49 mm × 47 mm liver abscess. (Fig. 3). Emergency surgery was performed because of suspected the colon and rectum perforation. Intraoperative findings revealed extensive necrosis and partial perforation of the colon and rectum. A total colectomy and ileostomy were performed. Postoperatively, septic shock occurred, and intensive care management was initiated. Macroscopic pathological examination revealed frequent ischemic changes and necrosis with ulceration in the dark red segments of the resected specimens (Fig. 4). Pathological examination revealed severe inflammatory cell infiltration throughout the intestinal wall layer. No amoebic invasion was observed in the colon. The patient had no history of international travel, amoebiasis, sexual intercourse with homosexual individuals, commercial sex workers, or an unspecified number of people. The source of an infection is unknown. Metronidazole was given by the 14th day after the surgery after which his general condition improved, and the liver abscess shrunk on abdominal CT. The patient was discharged on the 36th postoperative day. Subsequently, gastric cancer surgery was performed and the patient was discharged without postoperative complications. The clinical course of the patient was demonstrated in Figure.5.

Discussion

We use the PubMed search engine, and two papers of fulminant amoebic colitis during preoperative chemotherapy for cancer have existed in the past [5, 6]. It is important to check the travel history and medical history before preoperative chemotherapy, and they recommend suspecting amoebic enteritis for gastrointestinal signs and symptoms during preoperative chemotherapy.

Approximately 90% of the people infected with *Entamoeba histolytica* have asymptomatic infections or mild diarrhea. Amoebiasis is sometimes activated under immunosuppressive conditions, such as chemotherapy for cancer or steroids, or as a result of acquired immunodeficiency syndrome, leading to FAC or amoebiasis-related death [5, 6]. Although the exact route of infection was unknown in this case, it is possible that the patient was infected with *Entamoeba histolytica* and became an asymptomatic carrier. Subsequently, he developed amoebic colitis under immunosuppressive conditions caused by chemotherapy.

Direct fecal smears in stool test are a non-invasive technique to detect amoebic trophozoites and cysts. It requires a fresh specimen within 3–4 hours of collection, kept at 37°C and examined by a speculum to avoid the autolysis of amoebiasis; however, the detection rate of amoebic trophozoites and cysts is relatively low, up to 25–60% [1, 7, 8]. Colonoscopy and subsequent biopsy examination of the lesion are reported to be the most reliable and sensitive methods for the pathological detection of amoebic trophozoites and cysts. In addition to routine HE staining, the detection of amoebic trophozoites and cysts is facilitated by PAS and Grocott staining, [9]. As a serological approach, anti-amoebiasis antibody titer measurements have been widely used for diagnosis, with a detection rate of 61–95% in amoebic colitis, reaching 91–100% in extraintestinal amoebiasis, such as liver abscesses [10]. However, reports indicate that it does not

necessarily correlate with disease progression or severity [10]. Although there are other methods to detect amoebiasis antigens by ELISA (enzyme-linked immunosorbent assay (ELISA) or DNA by polymerase chain reaction) [11], the number of institutions or hospitals that implement these methods is limited. Therefore, direct intraluminal observation by endoscopy and lesion biopsy is the most reliable and useful approach for the definitive diagnosis of amoebic colitis. It is reported that biopsy for amoebic colitis should be taken from the bottom of the ulcer [12].

In this case, although amoebic enteritis was diagnosed preoperatively, no amoebae were detected in the resected specimens after surgery. We thought the cause of this is that metronidazole was significantly effective.

Antiprotozoal agents such as metronidazole are the mainstay of treatment for both intestinal and extraintestinal amoebiasis. Approximately 90% of the patients with amoebic colitis respond to metronidazole therapy. In the case of FAC, broad-spectrum antibiotics are the first choice for treating enteric bacteria that may spill into the peritoneum [1]. Tomino reported that the perioperative use of metronidazole in patients with FAC may improve mortality rates [13]. Therefore, patients should be treated immediately with metronidazole once if amoebic colitis is suspected based on medical history and clinical findings.

In summary, we presented a successful case of fulminant amoebic colitis during systemic chemotherapy for gastric cancer. Routine inquiries about the travel history and medical history should be considered before initiating chemotherapy. Additionally, amoebic colitis should be listed as a differential diagnosis when enteritis occurs during chemotherapy.

Acknowledgments

This study was conducted according to the principles of the Declaration of Helsinki.

Conflict of Interest Statement

The authors declare that this study was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

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