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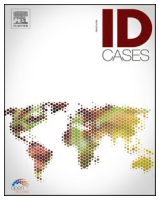

Case report

A case of amebic colitis and liver abscesses that occurred after treatment of coronavirus disease 2019 with dexamethasone

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ABSTRACT

Entamoeba histolytica infections, which can be asymptomatic, are endemic to developing countries; traveling to such countries is a risk factor for contracting these infections. A 65-year-old Japanese man was hospitalized for coronavirus disease 2019 (COVID-19)-associated respiratory distress, and was treated with remdesivir, dexamethasone, and oxygen supplementation. Although his respiratory condition improved and the oxygen support was discontinued, he developed a fever, severe abdominal pain, and diarrhea on day 13 of hospitalization. Fifteen years ago, he was hospitalized for diarrhea of an unknown origin in Suzhou, China, and had a history of passing loose stools for 1 year. Contrast-enhanced abdominal and pelvic computed tomography revealed liver abscesses in both lobes and intestinal edema from the ascending colon to the descending colon. The abscesses were suspected to be amebic based on the characteristics of the drained abscess fluid. The patient was treated with cefotaxime and metronidazole, and his temperature declined and abdominal pain improved. A culture analysis of abscess fluid yielded negative findings; however, polymerase chain reaction analyses of abscess and stool samples were positive for *Entamoeba histolytica*. We speculated that the patient was infected with *Entamoeba histolytica* while in China, and that the corticosteroid usage for COVID-19 had exacerbated the infection. Clinicians should be aware that corticosteroid treatments can lead to recurrent invasive amebiasis in asymptomatic amebic carriers.

Introduction

Coronavirus disease 2019 (COVID-19) has emerged as a global public health concern [1]. The pathogenesis of severe COVID-19 involves an excessive and unregulated pro-inflammatory cytokine storm, which results in immunopathological lung injury, diffuse alveolar damage, the acute respiratory distress syndrome, and death [2]. The RECOVERY trial (a large, prospective, open-labeled, and controlled trial) demonstrated that dexamethasone, a corticosteroid, lowered the 28-day mortality rate among patients hospitalized for COVID-19 who were randomized to undergo mechanical ventilation or oxygen supplementation therapy [3]. Based on the results of this trial, corticosteroids have been increasingly used for treating patients with severe COVID-19. Several common adverse effects of dexamethasone have been recognized. However, there has been little documentation of the development of fatal parasitoses, such as severe amebic colitis, among patients receiving dexamethasone [4]. Thus, we report the case of a patient with COVID-19 who developed amebic colitis and liver abscesses following dexamethasone treatment.

Case

A 65-year-old Japanese man, who had received treatment for chronic obstructive pulmonary disease, developed a fever of 37.8 ℃ 4 days before admission to our hospital. The patient initially visited a local hospital, where he tested positive for severe acute respiratory syndrome coronavirus 2 in a polymerase chain reaction (PCR) assay of his oropharyngeal/nasal swab samples. While the patient was initially treated at home with acetaminophen, he was later hospitalized due to exacerbated respiratory distress. On admission, the patient had a body temperature of 39 °C, blood pressure of 98/64 mmHg, pulse rate of 104 beats/minute, respiratory rate of 16 breaths/minute, and oxygen saturation of 90 % on 2 L/min of supplemental oxygen. Chest computed tomography (CT)revealed consolidation and ground-glass opacities in both lungs. Thus, the patient was treated with remdesivir from days 1–5

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Table 1
The patient's clinical laboratory results at the time of admission and on days 5, 10, 14, 17, and 21 after admission.

Measure	Reference range	Day1	Day 5	Day 10	Day 14	Day17	Day 21
White-cell count (per μL)	3500–8500	5600	9470	17,860	24,600	10,330	5660
Red-cell count ($\times 10^4$, per μL)	380–490	494	458	447	478	446	435
Platelet count ($\times 10^4$, per μL)	13–35	20.3	21.2	31.5	33.9	33.5	38.7
Hemoglobin (g/dL)	11.5–15.0	14.9	13.9	13.7	14.3	13.5	13
Hematocrit (%)	34–45	44.8	40.4	40.5	42.4	40.5	39.7
Sodium (mEq/L)	135–147	134	135	135	134	137	138
Potassium (mEq/L)	3.3–4.8	3.8	3.5	3.6	3.5	4.1	4.2
Chloride (mEq/L)	98–109	99	100	97	97	102	105
Calcium (mg/dl)	8.2–10.2	8.3	8.7	8.6	8.7	8.4	8.6
Glucose (mg/dL)	70–110	114	164	136	129	130	141
Blood urea nitrogen (mg/dL)	8–21	18.9	17.9	12.8	15.7	15.2	15.8
Creatinine (mg/dL)	0.3–1.1	0.82	0.61	0.71	0.9	0.69	0.66
Total protein (g/dL)	6.7–8.3	6.3	5.7	5.7			
Albumin (g/dL)	3.9–4.9	3.2	2.9	2.7	2.7	2.4	2.7
Total bilirubin (mg/dL)	0.2–1.2	0.7	0.9	0.8	1.5	0.6	0.5
Alanine aminotransferase (U/L)	0–30	23	18	23	67	44	38
Aspartate aminotransferase (U/L)	0–35	33	25	19	41	37	19
Alkaline phosphatase (U/L)	110–350	146	156	171	308	245	211
Lactate dehydrogenase (U/L)	120–230	360	382	299	248	211	198
Activated partial thromboplastin time (s)	25.0–38.0	34.9	31	29.3	30.2	30.2	33.4
Prothrombin time (s)	10.0–14.0	12	12.2	11.6	12.2	12.6	12.7
International normalized ratio		1.09	1.1	1.05	1.11	1.14	1.15
D-dimer (μg/mL)	0–0.99	0.59	0.57	1.58	4.02	1.43	1.34
Creatine kinase (U/L)	0–200	113	51	22	27	20	31
C-reactive protein (mg/dL)	0–0.3	3.52	3.14	5.29	13.56	3.59	1.14

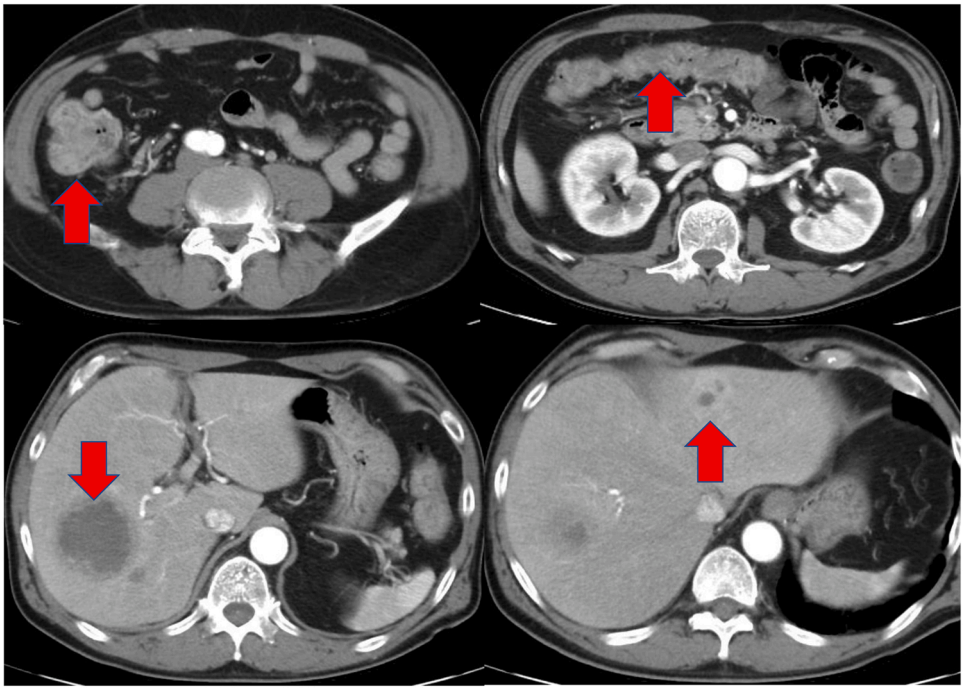

Fig. 1. Computed tomography scan of the patient's abdomen on day 14. The scan reveals severe intestinal edema from the ascending colon to the transverse colon of the large intestine as well as many contrast-enhanced low-density area on the liver.

of hospitalization, and the body temperature dropped below 37.5 ℃ on day 5. However, the patient required oxygen support, and was thus, initiated on oral dexamethasone (6 mg once a day) on day 5. The patient's respiratory status improved, and oxygen administration was terminated on day 9. At midnight on day 13, the patient had a fever of 38.5 °C, severe abdominal pain, and diarrhea. Physical examination revealed right subcostal tenderness. Laboratory examination revealed an elevated white blood cell count (24,600/μL) and elevated levels of C-reactive protein (13.56 mg/dL), aspartate aminotransferase (41 U/L), alanine transaminase (67 U/L), alkaline phosphatase (308 U/L), and gamma-glutamyl transpeptidase (186 U/L) (Table 1). Contrast-enhanced CT of the abdomen and pelvis revealed multiple abscesses in both liver lobes (which were not visible on chest CT on admission) and intestinal edema from the ascending colon to the descending colon (Fig. 1) During further history taking on day 14, the patient denied having a sexual intercourse with commercial sex workers or men. Fifteen years ago, the patient had worked in Suzhou (China), wherein he was hospitalized for diarrhea of unknown origin (DUO) for 10 days. The patient also had a history of passing loose stools for 1 year, which prompted an endoscopic examination at another hospital; however, no

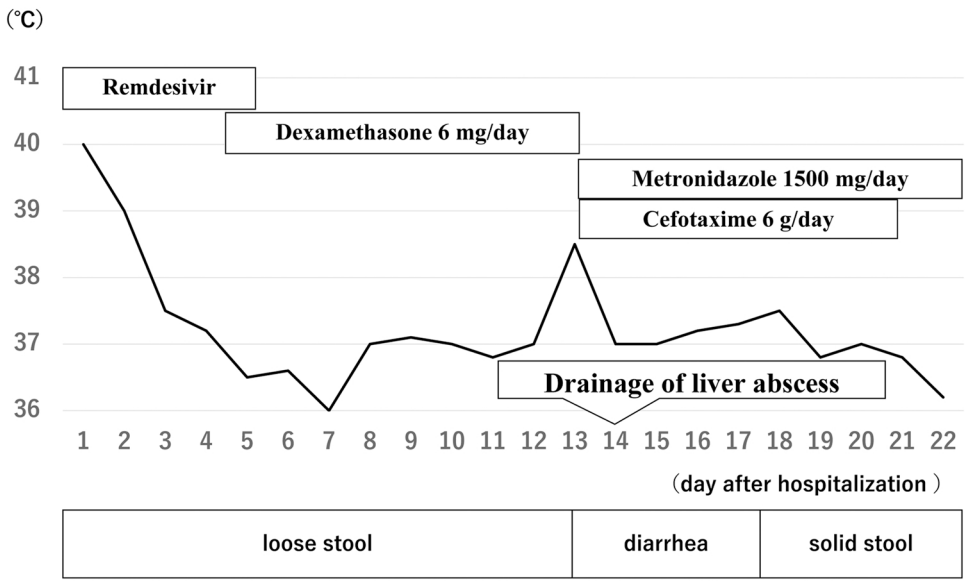

Fig. 2. Clinical course of amebic colitis and liver abscesses. At midnight on day 13, the patient experienced a fever, abdominal pain, and diarrhea. On day 14, he was diagnosed with liver abscesses and colitis using contrast-enhanced computed tomography findings of the abdomen and pelvis. Computed tomography-guided drainage of the liver abscesses was performed, and he was treated with metronidazole and cefotaxime. His fever and abdominal pain were quickly resolved after treatment.

specific cause was identified. A CT-guided drainage of the liver abscesses was performed, and an odorless anchovy-paste-like fluid was drained. Neither bacteria nor amebic protozoa were detected upon rapid microscopic examination of the fluid. However, amebic liver abscesses were suspected based on the characteristics of the drained fluid. The patient was treated with cefotaxime and metronidazole. Subsequently, his body temperature decreased and his abdominal pain improved. On day 21, cefotaxime was discontinued because the culture test of the abscess sample was negative for bacteria. By day 23, a 10-day course of metronidazole was complete, and the patient was discharged on day 24 (Fig. 2). The patient's abscess and stool samples were subjected to a molecular screening for *Entamoeba histolytica* using a set of universal nested polymerase chain reaction (PCR) primers that targeted the 18 S small subunit of ribosomal RNA gene locus, as described previously [5]. All DNA sequences of the PCR amplicons were read, and the presence of *E. histolytica* was confirmed. Therefore, the patient was diagnosed with amebic colitis and liver abscesses. He was treated with paromomycin for 8 days, following which he experienced no recurrence.

Discussion

Amebiasis is caused by an infection involving the pseudopod-forming, non-flagellated, protozoan parasite *Entamoeba histolytica* [6]. Though endemic in developing countries, amebiasis has been reported to have affected travelers, immigrants, men who have sex with men, and commercial sex workers residing in developed countries [6,7]. Most patients with amebic infections are asymptomatic; 10 % of the patients present with symptoms [6]. Patients usually develop the disease within 5 years of infection, but amebic liver abscesses can occur after a prolonged latency period that can be as long as 32 years [8,9]. Amebic colitis is the most common presentation; however, fulminant amebic colitis is an uncommon complication of amebiasis and is associated with high mortality. On average, more than 50% of patients with severe colitis die [6]. The intake of corticosteroids, commonly prescribed due to their anti-inflammatory and immunosuppressive properties, was identified as a risk factor for fulminant amebic colitis [4]. Misdiagnosis of inflammatory bowel disease and an intent to prevent or treat graft-versus-host disease are the first and second most common reasons for clinicians to prescribe corticosteroids without recognizing an amebic infection, respectively [10]. Corticosteroids remain the standard of care because they have been shown to be effective against severe COVID-19 [11]. The patient in our case had no history of homosexual activity or promiscuity. He was previously hospitalized for DUO while working in China 15 years ago. He also had a 1-year history of passing loose stools, which prompted a consultation at another hospital; however, no specific cause was identified. The patient most likely contracted an amebic infection 15 years ago while working in China, and his symptoms relapsed for 1 year. His recent history of dexamethasone intake for COVID-19 possibly caused the amebic colitis and liver abscess formation. The amebic infection was suspected due to the presence of multiple liver abscesses. Until recently, patients in most cases of amebiasis in Japan were infected abroad; therefore, few physicians consider amebiasis in the differential diagnosis of domestic-onset diarrhea. However, the incidence of domestically acquired amebiasis has been increasing recently, and this condition should be considered even if there is no history of travel to areas where amebiasis is endemic [12]. It should also be noted that in some cases, amebiasis may develop several years after infection. Reactivation of latent tuberculosis or parasitic infections, such as *Strongyloides* infections, are other potentially fatal conditions exacerbated by corticosteroids [13,14]. The increasing use of corticosteroids (such as dexamethasone) for COVID-19 treatment will likely increase the incidence of amebic colitis. Therefore, clinicians need to suspect amebic infections if they encounter abdominal symptoms (such as diarrhea) while administering corticosteroids to patients with COVID-19.

CRediT authorship contribution statement

H. Motobayashi was responsible for the coordination and writing of this clinical cases. T. Mizuno and M. Tokoro performed the polymerase chain reaction analysis to detect *Entamoeba histolytica*. All authors contributed to the writing of the final manuscript and agreed to be accountable for all aspects of the work. All authors meet the ICMJE authorship criteria.

Ethical approval

Written informed consent was obtained from the patient, and consent for the publication of this case report.

Consent

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Declarations of interest

None.

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References

[1] Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. J Autoimmun 2020;109:102433. https://doi.org/10.1016/j.jaut.2020.102433.
[2] Fadel R, Morrison AR, Vahia A, Smith ZR, Chaudhry Z, Bhargava P, et al. Early short-course corticosteroids in hospitalized patients with COVID-19. Clin Infect Dis 2020;71:2114–20. https://doi.org/10.1093/cid/ciaa601.
[3] Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, Linsell L, et al. Dexamethasone in hospitalized patients with Covid-19. N Engl J Med 2021;384:693–704. https://doi.org/10.1056/NEJMoa2021436.
[4] Shirley DA, Moonah S. COVID-19 and corticosteroids: unfamiliar but potentially fatal infections that can arise following short-course steroid treatment. Am J Trop Med Hyg 2021;104:790–3. https://doi.org/10.4269/ajtmh.20-1471.
[5] Matey EJ, Tokoro M, Nagamoto T, Mizuno T, Saina MC, Bi X, et al. Lower prevalence of Entamoeba species in children with vertically transmitted HIV infection in Western Kenya. AIDS 2016;30:803–5. https://doi.org/10.1097/QAD.0000000000001002.
[6] Shirley DT, Farr L, Watanabe K, Moonah S. A review of the global burden, new diagnostics, and current therapeutics for amebiasis. Open Forum Infect Dis 2018;5:ofy161. https://doi.org/10.1093/ofid/ofy161.
[7] Nagata N, Shimbo T, Akiyama J, Nakashima R, Nishimura S, Yada T, et al. Risk factors for intestinal invasive amebiasis in Japan, 2003–2009. Emerg Infect Dis 2012;18:717–24. https://doi.org/10.3201/eid1805.111275.
[8] Hoffbrand BI. Amoebic liver abscess presenting thirty-two years after acute amoebic dysentery. Proc R Soc Med 1975;68:593–4.
[9] Zurauskas JP, McBride WJ. Case of amoebic liver abscess: prolonged latency or acquired in Australia? Intern Med J 2001;31:565–6. https://doi.org/10.1046/j.1445-5994.2001.00117.x.
[10] Shirley DA, Moonah S. Fulminant amebic colitis after corticosteroid therapy: a systematic review. PLoS Negl Trop Dis 2016;10:e0004879. https://doi.org/10.1371/journal.pntd.0004879.
[11] Agarwal A, Rochwerg B, Lamontagne F, Siemieniuk RA, Agoritsas T, Askie L, et al. A living WHO guideline on drugs for covid-19. BMJ 2020;370:m3379. https://doi.org/10.1136/bmj.m3379.
[12] Ishikane M, Arima Y, Kanayama A, Takahashi T, Yamagishi T, Yahata Y, et al. Epidemiology of domestically acquired amebiasis in Japan, 2000–2013. Am J Trop Med Hyg 2016;94:1008–14. https://doi.org/10.4269/ajtmh.15-0560.
[13] Song WM, Zhao JY, Zhang QY, Liu SQ, Zhu XH, An QQ, et al. COVID-19 and tuberculosis coinfection: an overview of case reports/case series and meta-analysis. Front Med 2021;8:657006. https://doi.org/10.3389/fmed.2021.657006.
[14] Lier AJ, Tuan JJ, Davis MW, Paulson N, McManus D, Campbell S, et al. Case report: disseminated strongyloidiasis in a patient with COVID-19. Am J Trop Med Hyg 2020;103:1590–2. https://doi.org/10.4269/ajtmh.20-0699.