Case report

# Nontravel-related invasive *Entamoeba histolytica* infection with probable heterosexual transmission

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ABSTRACT

*Introduction:* In industrialized countries, amebiasis usually occurs in migrants and travelers returning from areas where the disease is endemic, primarily by ingestion of contaminated food or water. Person-to-person transmission can occur, mainly by fecal-oral contact, but sexual transmission has also been described [1,3–5].
*Presentation of case:* We report a man with *Entamoeba histolytica* colitis and a large liver abscess ($16.5 \times 14$ cm) in Portugal, who had no relevant travel history and whose only risk factor was his heterosexual partner. The abscess required drainage of 1950 mL of "chocolate-milk" purulent fluid, with rapid symptomatic improvement. The diagnosis was established by real-time reverse transcription PCR for *Entamoeba histolytica* in the liver aspirate, with positive IgG antibodies. He received a total of 16 days of ceftriaxone and metronidazole followed by 7 days of paromomycin.
*Conclusion:* As enteric infections may be sexually transmitted, in industrialized countries, even in the absence of travel, sexual history should not be neglected.

## Introduction

Although occurring worldwide, in industrialized countries amebiasis is usually seen in migrants and travelers returning from areas where the disease is endemic, primarily by ingestion of contaminated food or water [1,2]. Person-to-person transmission can occur by fecal-oral contact, most frequently within households [1]. Sexual transmission, mainly via oral and anal sex, mostly in men who have sex with men, has been described [1,3–5].

*E. histolytica* infection is asymptomatic in 90% of cases. Extraintestinal manifestations are present in fewer than 1% of infections, of which amebic liver abscess (ALA) is the most common [6]. Its noncomplicated presentation has low mortality if treated early, yet delays may be fatal [6,7]. Management of uncomplicated ALA relies on medical treatment alone, but invasive procedures may be necessary if complications or a high risk of rupture are present [7].

## Case report

A 63-year-old man sought care at the emergency department in July 2018, reporting a 10-day history of bloody diarrhea (seven to eight bowel movements per day), fever, pain located to the right hypochondrium, anorexia and weight loss. The patient had type 2 diabetes and smoked tobacco. Throughout his life, he only travelled to the United States of America, European countries and Morocco in 1976. A heterosexual with no homosexual contacts, his female partner had traveled to India on March 2018 and received a diagnosis and treatment for amoebic colitis with hepatic abscess on mid-May 2018, after six weeks of symptoms. The couple started having sexual intercourses including oral-vaginal sex in the beginning of May and denied oral-anal contacts or sex toys usage.

Physical examination on admission revealed a tympanic temperature of 39.2 °C, a respiratory rate of 26 cycles per minute, minor signs of dehydration and a globally painful abdomen. On blood panel, marked leukocytosis ($20.2 \times 10^3$ cells/µL) with neutrophilia ($15.1 \times 10^3$ cells/µL), mild eosinophilia ($1.11 \times 10^3$ cells/µL (5%) on admission and a registered maximum of $2.10 \times 10^3$ cells/µL (12.6%)) and an elevated C-reactive protein (2429 nmol/L) were present, along with increased levels of gamma glutamyltransferase (245 U/L on admission and a registered maximum of 359 U/L) and alkaline phosphatase (358 U/L on admission and a registered maximum of 446 U/L) (Table 1). Lactate levels were within normal

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**Table 1**
Serum laboratory data of the patient.

| Variable | Reference range | Day 0 | Day 2 | Day 6 | Day 9 | Day 13 | Day 17 | Day 27 | Day 34 |
|---|---|---|---|---|---|---|---|---|---|
| Leukocyte count, x $10^9$/L | 4.0–11.0 | 20.2 | 15.5 | 16.4 | 16.7 | 13.7 | 11.1 | 9.4 | 10.1 |
| Neutrophils, x $10^9$/L (%) | 2–7.5 (40–75%) | 15.1 (75%) | 10.0 (65%) | 12.5 (76%) | 12.7 (76%) | 10.2 (75%) | 6.7 (60%) | 3.1 (33%) | 4.8 (48%) |
| Eosinophils, x $10^9$/L (%) | 0.04–0.40 (1–6%) | 1.11 (6%) | 1.64 (11%) | 0.43 (3%) | 2.10 (13%) | 0.42 (3%) | 0.62 (6%) | 1.49 (16%) | 0.71 (7%) |
| Hemoglobin, g/L | 130–170 | 126 | 122 | 118 | 107 | 100 | 114 | 122 | 131 |
| Platelets, x $10^9$/L | 150–400 | 314 | 300 | 303 | 330 | 633 | 838 | 609 | 428 |
| CRP[a], nmol/L | 0–50 | 2314 | 2429 | 1933 | 600 | 419 | 105 | 10 | 10 |
| Creatinine, μmol/L | 35–100 | 71 | 77 | 61 | 55 | 55 | 72 | 71 | 70 |
| Total bilirubin, μmol/L | 0–24 | 19 | 19 | 41 | 23 | 14 | 9 | 7 | 5 |
| ASAT[a], U/L | 10–34 | 18 | 18 | 89 | 19 | 17 | 20 | 21 | 20 |
| ALAT[a], U/L | 10–44 | 37 | 27 | 43 | 20 | 12 | 11 | 16 | 15 |
| ALP[a], U/L | 45–122 | 358 | 244 | 321 | 368 | 446 | 394 | 204 | 139 |
| GGT[a], U/L | 10–66 | 245 | 161 | 245 | 296 | 359 | 343 | 281 | 196 |
| Albumin, g/L | 35–50 | NA | 29 | NA | NA | 24 | NA | 37 | NA |
| INR[a] | 0.9–1.1 | NA | NA | NA | NA | 1.8 | 1.5 | 1.1 | NA |

[a] CRP, C-reactive protein; ASAT, Aspartate aminotransferase; ALAT, Alanine aminotransferase; ALP, Alkaline phosphatase; GGT, Gamma glutamyltransferase; INR, international normalized ratio; NA, not available.

limits. HIV, HCV and HBV serologies were negative and the patient was immune to HAV. A nodular heterogeneous subcapsular lesion of the right lobe of the liver, with 8.4 cm of diameter, was observed on ultrasound. The patient was admitted to the Infectious Diseases ward and started on ciprofloxacin (500 mg twice a day orally). Stool cultures were negative; cysts or trophozoites were not observed on three fecal samples.

On day 6, further characterization of the lesion by computed tomography (CT) disclosed enlargement (14.3 × 9.5 cm), with characteristics of an abscess, as liquid content and peripheral septa were present (Fig. 1). A continuous thickening of the ascending colon, of part of the transverse colon and of the rectal wall, denoting colitis and proctitis, was also observed. Because of lack of clinical and radiologic improvement, with sustainably high inflammatory markers (Table 1), therapy was switched to ceftriaxone and metronidazole (2 g per day intravenously and 750 mg three times a day orally, respectively).
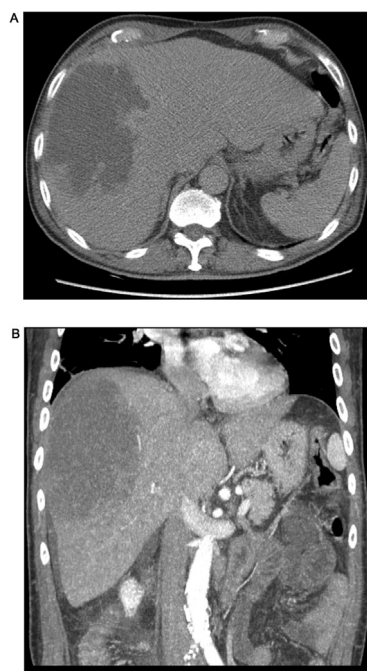
Reevaluation ultrasound on day 13 displayed further expansion of the mass (Fig. 2), with 16.5 × 14 cm, and perihepatic fluid (2 cm thickness), prompting CT-guided drainage of the abscess with a pigtail catheter. A total of 1950 mL of "chocolate-milk" purulent fluid was drained during the following days, with rapid symptomatic improvement.

Blood and urine cultures were negative. Examination of the drained fluid revealed no cysts or trophozoites; Gram stain was negative and cultures sterile; pathologic examination exhibited cellular debris and necrotic material, along with polymorphonuclear neutrophils and some macrophages. IgG antibodies against *Entamoeba histolytica* were detected (2.50 index) by ELISA on day 15, but the patient maintained ceftriaxone and metronidazole until real-time reverse transcription PCR for *E. histolytica* was reported positive in the liver aspirate on day 22, as there were concerns about bacterial infection.

He received a total of 16 days of combined antimicrobial therapy followed by 7 days of paromomycin (750 mg three times a day orally). End-of-treatment CT scan showed a residual 6.8 × 5.8 cm lesion. The patient was discharged after a 5-week admission and remained asymptomatic to date. One month after discharge, CT scan exhibited a remaining 6.8 × 5.6 cm lesion.

## Discussion

The differential diagnosis of amebiasis with hepatic involvement includes pyogenic liver abscess (PLA). Patients with PLA are more likely than patients with ALA to be older and to have diabetes [6] (Table 2), as our patient. Clinical manifestations of PLA and ALA are similar, including fever and right hypochondrium pain, but patients with ALA may be sicker, possibly (but not frequently) reporting dysentery concomitantly or within the previous months [8,9]. In contrast to ALA, in PLA a left shift on leukocytes and elevated serum bilirubin concentration are usually present, as in our patient. Radiology is not specific for differentiating between
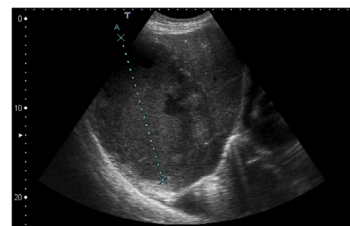


**Fig. 1.** Computed tomography scans unveiling a large abscess in the right lobe of the liver of a 63-year-old man with nontravel-related *Entamoeba histolytica* infection in Portugal. **A)** Axial reconstruction. **B)** Coronal reconstruction.



**Fig. 2.** Ultrasonography image displaying an augment of the liver abscess size of a 63-year-old man with nontravel-related *Entamoeba histolytica* infection in Portugal. $\overline{A}$ = 165 cm.

**Table 2**
Comparison of the clinical characteristics of pyogenic vs. amebic liver abscess.

|  | Pyogenic liver abscess | Amebic liver abscess |
|---|---|---|
| Age | Older adults | Younger adults |
| Gender | Men and women equally affected | Male predominance |
| Relevant history | Diabetes mellitus | Exposure to regions where amebiasis is endemic |
|  | History of gallstones |  |
| Clinical features | Right upper quadrant pain | Right upper quadrant pain |
|  | Fever | Fever |
|  | Jaundice usually present | Jaundice usually absent |
|  | Diarrhea absent | Diarrhea may be present |
| Blood panel | Neutrophilia usually present | Neutrophilia usually absent |
|  | Serum bilirubin often elevated | Serum bilirubin usually within normal limits |
| Ultrasound findings | Highly variable echogenicity (solid appearance in the early stage; increasingly cystic as necrosis and liquefaction develops; intense echogenicity if gas present) | Hypoechoic, homogeneous |
|  | Posterior acoustic enhancement | No noteworthy wall echoes |
|  |  | Subcapsular location |
|  |  | Diaphragm disruption |
|  |  | Target sign[a] |
|  | Walls generally irregular and well-defined | Treated lesions may become anechoic |
|  |  | or calcified or may persist with cystic-appearance |
| CT findings | Well-defined, low-attenuation mass | Low-attenuation mass |
|  | Single nonloculated, single | May contain internal septa |
|  | multiloculated or multiple lesions | Enhancing rim or capsule, 3–15 mm |
|  | Enhancing rim | May be surrounded by a rim of edema |
|  | Gas-containing | Elevated right hemidiaphragm |
|  | Cluster sign[b] | Extension beyond liver may be present (right pleural effusion, right basilar atelectasis, thickening of the wall of the cecum) |
|  | Double target sign[c] |  |
|  | Septal breakage sign[d] |  |
|  | Turquoise sign[e] |  |
|  | Hair ball sign[f] |  |

[a] Dense echogenic center with a hypoechoic periphery.
[b] Aggregation of multiple small low-attenuation lesions.
[c] Low-attenuation central area surrounded by a high-attenuation inner ring and a low-attenuation zone.
[d] Arborizing patterns of septa.
[e] Numerous septal breakages.
[f] Tangled pattern of blurring amorphous hairlike content in the abscess fluid.

the two; in comparison with PLA, ALA are more likely to be solitary, subcapsular, located to the right lobe of the liver and to cause elevation of the hemidiaphragm, but these findings are not pathognomonic [9,10]. In the present case-patient, ALA presented on ultrasound as a heterogeneous mass, but a homogeneous appearance is typical [9].

Considering the above factors, the atypical presentation of amebiasis in this case-patient and, moreover, the absence of travel to countries where the disease is endemic, this diagnosis was initially assumed very unlikely, justifying the initial ciprofloxacin therapy and the maintenance of both ceftriaxone and metronidazole combined therapy even after a positive IgG against E. histolytica.

Complications of ALA include rupture with extension into the peritoneum, pleural cavity, pericardium [11,12], colon or biliary tree [6], hepatic vein or inferior vena cava thrombosis and hematologic spread to other organs [10]. Untreated ALA are usually fatal, yet routine aspiration or drainage is not generally required [6,13]. These should be considered in the presence of complications or high risk of rupture (cavities with a diameter superior to 5 cm, less than 1 cm between the abscess wall and the liver surface, or lesions located to the left lobe) [6,8], in case of lack of response to medical therapy within five to seven days, if bacterial co-infection is present, and if there is uncertainty in diagnosis [11,12]. In the presented case-patient, the abscess continued to enlarge and the patient remained symptomatic through the 13 initial days despite combined antimicrobial therapy, with presence of perihepatic fluid and altered liver function, presumably by liver compression. Furthermore, the etiological diagnosis was not yet established at that time. Drainage of the abscess permitted not only therapeutic management but also confirmation of the diagnosis.

Nontravel-related Entamoeba histolytica infection is uncommon in countries where it is not endemic. However, enteric infections may be sexually transmitted, particularly through oral-anal activity [3,4]. Although more frequent in men who have sex with men [1,12], heterosexual transmission of E. histolytica has also been rarely reported [14,15]. The couple did not live together and described strict hygiene measures because of the woman's symptoms and recent diagnosis. Albeit denying oral-anal sexual activity, repeated oral-vaginal contacts were reported, which we assume as the most likely form of transmission. Hence, even in industrialized countries, where E. histolytica infection is not endemic, and in patients without travel history, amebiasis should be considered in the presence of fever and hepatic abscesses with relevant sexual contacts, either homosexual or heterosexual.

### Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

### CRediT authorship contribution statement

**Sofia R. de Valdoleiros:** Conceptualization, Writing - original draft. **João Abranches Carvalho:** Conceptualization, Writing - original draft. **Celina Gonçalves:** Conceptualization, Writing -

review & editing, Supervision. **Olga Vasconcelos:** Conceptualization, Writing - review & editing, Supervision. **Rui Sarmento-Castro:** Conceptualization, Writing - review & editing, Supervision.

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