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Case report

# Plasma next-generation sequencing for diagnosis of amebic liver abscess in a non-endemic area☆

Simon Parzen-Johnson[a,*], Shaunte McKay[b], Nitin Wadhwani[c,d], Saeed Mohammad[b,d], Ben Z. Katz[a,d]

[a] Division of Infectious Diseases, Ann & Robert H Lurie Children's Hospital, USA
[b] Division of Gastroenterology, Hepatology, and Nutrition, Ann & Robert H Lurie Children's Hospital, USA
[c] Division of Pathology and Laboratory Medicine Ann & Robert H Lurie Children's Hospital, USA
[d] Northwestern University, Feinberg School of Medicine, USA

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ABSTRACT

Amebic liver abscess (ALA) is a common condition in the developing world but is rare in the United States without a clear exposure risk. It is even less common to develop in an infant. The diagnosis of ALA can be logistically difficult and often requires invasive procedures and testing with slow turnaround times. We present an 18-month-old boy initially admitted with fever, abdominal pain, and diarrhea with rapid progression to respiratory failure. He was found to have a significant pleural effusion accompanying a large solitary liver lesion with abdominal ascites. There was no infectious exposure history or travel history, and thus pyogenic liver abscess was suspected, and aspiration performed while he was on empiric antimicrobials. The bacterial culture was negative. Molecular testing with 16 s and 18 s rRNA PCR on the fluid were non-diagnostic. The diagnosis of *Entamoeba histolytica* was confirmed within 48 hrs via plasma next-generation sequencing. Serum IgG for *E histolytica* resulted positive multiple weeks after the patient was discharged. The patient made a full recovery after metronidazole and paromomycin. This case illustrates the need to maintain ALA in the differential diagnosis for liver abscess in an infant even in the absence of risk factors. Additionally, plasma next-generation sequencing may play a role in more rapid diagnosis of ALA and has the potential to reduce the need for more invasive testing.

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## Introduction

The differential diagnosis of a liver abscess usually includes pyogenic bacterial (e.g., *Staphylococcus aureus,* anaerobic organisms) and parasitic (*Echinococcus* and *Entamoeba histolytica*) causes, the latter of which are rare in the absence of travel to or immigration from an endemic area. Without risk factors, making a diagnosis of amebic liver abscess is challenging. We present a case of liver abscess due to *Entamoeba histolytica* in a boy born in the United States without a travel history, whose routine diagnostic studies were all negative. Diagnosis was made initially via plasma next-generation sequencing technology.

## Case report

An 18-month-old previously healthy unvaccinated boy presented to the emergency room with 1 week of fever to 105 F, abdominal pain and non-bloody diarrhea. Six weeks prior to presentation he was evaluated for persistent hematochezia occurring 1–2 times per day that lasted for 4–5 weeks. Laboratory evaluation at that time included a negative stool culture, stool ova and parasite examination (O&P) with *Entamoeba coli*, a CBC with WBC count 9800/uL, Hgb 11.9 g/dL, Plt count 278,000/uL and INR1.0. He had no weight loss, vomiting, or history of recurrent infections. His brother had had cough and rhinorrhea the week prior. There were no other sick contacts, travel, or animal exposure other than the presence of a healthy pet dog at home. There was no known contact with men who have sex with men and no known recent travel by close

*Abbreviations:* **ALA**, **(Amebic Liver Abscess)**

☆ 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.

* Correspondence to: Ann & Robert H Lurie Children's Hospital of Chicago, 225 E Chicago Ave., Chicago, IL 60611, USA.
*E-mail address:* sparzenjohnson@luriechildrens.org (S. Parzen-Johnson).

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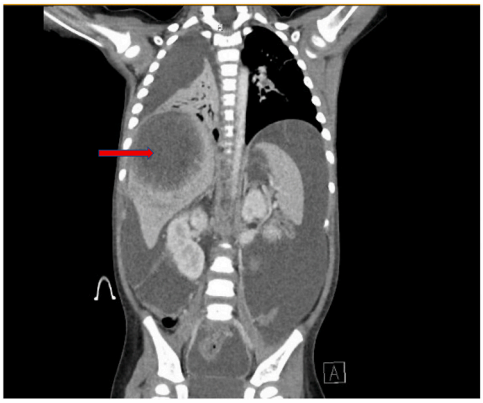

**Fig. 1.** CT coronal image showing 5x5x6cm abscess in the posterior right liver lobe (red arrow), hepatomegaly and ascites fluid. (For interpretation of the references to color in this figure, the reader is referred to the web version of this article.)

relatives. He was exclusively breast fed until 1 year of age and then began a regular diet including pasteurized goat's milk.

On physical exam he was tachypneic with a respiratory rate of 32/min, had significant abdominal distension with a fluid shift, and hepatomegaly. CXR showed a right-sided pleural effusion. A respiratory viral panel revealed coronavirus OC43 and parainfluenza virus. He was started on IV ceftriaxone for presumed bacterial pneumonia and admitted to the hospital. Within 24 h he developed respiratory insufficiency requiring BIPAP secondary to worsening abdominal distention. CBC was then remarkable for a WBC count of 10,600/μL, with 29% bands, and PLT 63,000/μL. Liver chemistries showed ALT 36 IU/L and AST 41 IU/L and other laboratory findings showed ESR 12 mm/hr, CRP of 10.4 mg/dL, albumin of 1.8 g/dL, and INR of 1.4. Stool *Entamoeba histolytica* Ag was negative and three stool O&P examinations were also negative. CT scan of the chest and abdomen (Fig. 1) showed a large loculated right pleural effusion, a 5x5x6cm right posterior liver lobe hypoechoic mass with a peripherally enhancing rim extending into the liver capsule, and diffuse free fluid in the abdomen and pelvis. Interventional Radiology was consulted, and they placed two percutaneous drains: one in the peritoneal fluid collection adjacent to the R liver capsule and the other in the liver mass. The child was treated with IV albumin and furosemide which led to resolution of the ascites and respiratory failure. Due to persistent fever despite drainage of 20 mL of purulent fluid from the liver abscess, antibacterials were broadened first to piperacillin-tazobactam and then to ceftriaxone and metronidazole.

Gram stain and cultures from the liver lesion and pleural fluid aspirate were negative. 16 s rRNA PCR was positive for multiple bacterial DNA templates but could not be resolved further. 18 s rRNA PCR was negative. Neutrophil oxidative burst testing was normal. Plasma Next-Generation Sequencing performed by Karius Technologies was positive for *E histolytica.* Biopsy of the liver lesion showed trophozoites in normal liver parenchyma with diffuse inflammatory cells and granulomas (Fig. 2A and B). Peritoneal fluid aspirate had evidence of trophozoites on Papanicolaou (PAP) stain (Fig. 2C). Serum testing for *E histolytica* IgG returned positive three weeks following admission.

He was discharged to complete a 14 day course of metronidazole followed by paromomycin for 7 days. When seen in follow up 6 weeks after discharge, he was well and a follow-up abdominal ultrasound showed a resolving liver lesion. All siblings and his father had negative stool testing for *E histolytica.*

## Discussion

Amebiasis is a clinical entity with variable presentation caused by the protozoan *Entamoeba histolytica.* This organism is endemic in developing countries of Central and South America, Africa, and Asia. Infection with *E histolytica* is uncommon in the United States, and patients diagnosed usually have a history of recent travel or emigration from an endemic region [1]. Although carriage and luminal disease with *E histolytica* occurs at all ages, amebic liver abscess (ALA) predominantly affects adult males [2]. The life cycle relies on ingestion of fecal-shed cysts by new hosts. Once the cysts are consumed, they may undergo excystation in the small intestines where trophozoites can take multiple paths. In most patients, they remain in the lumen of the intestine, multiplying and creating new cysts/trophozoites, leading to asymptomatic shedding. However, the trophozoites can invade locally causing colitis or enter the bloodstream leading to invasive infection in the brain, liver and/or lungs [2].

In cases of colitis, severe diarrhea can develop often associated with hematochezia. It is uncommon for patients with amebic colitis to have fever [2]. On the other hand, patients with amebic liver abscess typically have fever along with RUQ abdominal pain, with only a minority presenting with concurrent or antecedent GI symptoms. Other symptoms, such as tachypnea, as was seen in our patient, are associated with local spread to the pleural space, lungs, and pericardium. Younger, elderly, and immunocompromised patients tend to have more severe presentations. Our patient had hematochezia and diarrhea in the weeks prior to presentation, likely due to amebic colitis with incipient liver abscess formation. Interestingly, he was diagnosed with *Entaemoeba coli* at that time by another medical group. We were unable to contact this group, but it is possible the organisms seen were misidentified and were *E histolytica.*

Diagnosis of intestinal amebiasis was historically performed by stool wet mount, but stool PCR has been shown to have significantly higher sensitivity. Additionally, although the organism can be visualized by light microscopy, the sensitivity is typically low for *E histolytica* (10–40%) [3]. Stool antigen is performed at some centers but has significantly less sensitivity than PCR, as was the case with our patient [4]. Although *E histolytica* serologic testing has a sensitivity of 70–80% in acute disease, it can take up to 7 days to become positive, as was the case in our patient [5]. Serology is very sensitive and very specific but does not distinguish between acute and prior infection and thus is more helpful in areas of low incidence [2,5]. It is unusual for abscess aspirates to show trophozoites unless cyst wall sampling occurs [6]. PCR of combined samples from urine and saliva has excellent sensitivity and specificity but is not widely available [7]. Serum next-generation sequencing can make the diagnosis of ALA, as it did in our patient, but is expensive and thus not practical for use in developing countries [8]. There is published literature using Karius cell-free DNA blood testing for *pyogenic* liver abscess, but we were unable to find other published literature utilizing it for diagnosis of ALA [9]. The use of non-invasive testing modalities could prove helpful when determining the need for invasive sampling.

Treatment of amebiasis depends on the location of disease. Asymptomatic excretion of cysts requires only infection control measures. Amebic colitis and extraintestinal infections should be treated first with metronidazole to kill trophozoites followed by an intraluminal amebicide (paromomycin or diiodohydroxyquinoline/iodoquinol), because metronidazole is not effective against cysts. In most cases, ALA will resolve without surgical intervention, although if there is risk of rupture or poor response to antibiotic therapy, drainage is needed [2].

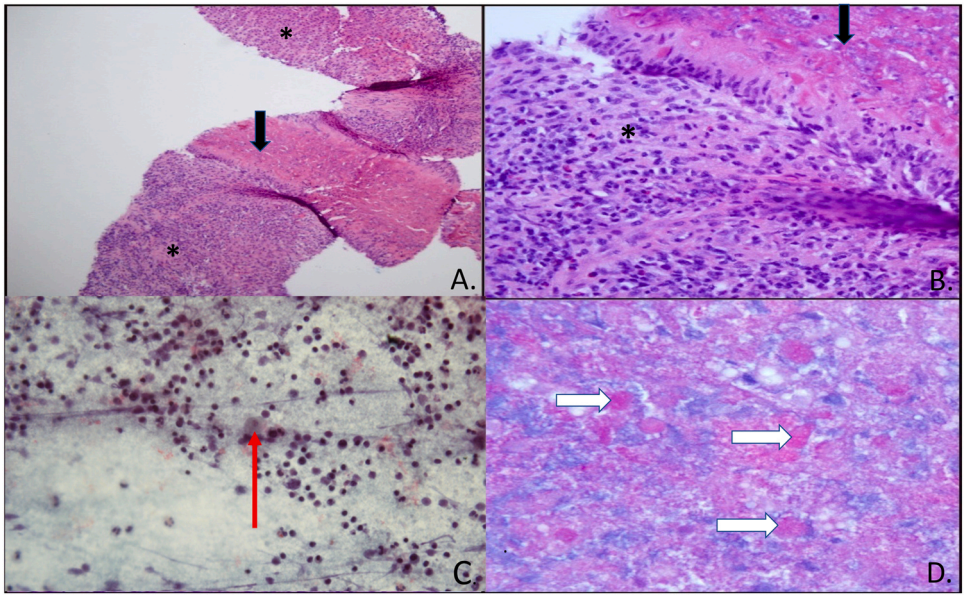


**Fig. 2.** A&B Granuloma formation (black arrow) and normal hepatic parenchyma with mixed inflammatory cells consistent with abscess formation (black asterisk) C. PAP stain of peritoneal fluid with trophozoite (red arrow) D. Trophozoites on liver parenchyma (white arrows). (For interpretation of the references to color in this figure, the reader is referred to the web version of this article.)

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## Consent

Signed consent has been obtained and is available if needed.

## Ethical approval

Signed consent has been obtained and is available if needed.

## Conflict of interest disclosures

The authors have indicated they have no conflicts of interest relevant to this article to disclose.

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