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Case Report

Huge and ruptured amoebic liver abscess diagnosed by mNGS: A case report

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Background

Amoebic liver abscess (ALA) is caused by the protozoan parasite, *Entamoeba histolytica*, which is the most common extraintestinal presentation of infection with the protozoan.[1] Areas of high incidence of infection worldwide include India, Africa, Mexico, and parts of Central and South America. Although the prognosis of simple abscess is favorable, complex and large abscesses may rupture and be associated with high mortality.[2] The diagnosis of ALA is made through a combination of characteristic findings on imaging and serologic testing (antigen or antibody testing). Colonic carriage can also be asymptomatic. When patients present with ALA, their stool microscopy is often negative for *E. histolytica*. Therefore, clinical history of colitis or stool microscopy cannot be relied upon for a confirmed diagnosis of ALA.[3] Metagenomic next-generation sequencing (mNGS) is being increasingly applied in clinical laboratories for unbiased culture-independent diagnosis, [4] which has been rarely reported in diagnosing ALA. We present a unique case of a massive and ruptured ALA in a male patient without typical symptoms or travel history to endemic areas. The patient was diagnosed by mNGS and had a favorable clinical outcome after metronidazole therapy and liver abscess drainage.

Case Presentation

A 46-year-old White man presented to the emergency department with backache for 2 weeks, which aggravated with right upper abdominal pain for 1 day without fever. He had complained of weight loss for the previous 6 months. He had a medical history of hypothyroidism and denied a history of hepatitis. He was homosexual with normal dietary habits and was a nonsmoker and nondrinker. He came to China 2 years ago for a teaching job. Before that, he was living in Europe for a long time and had no travel history in Africa, India, or other endemic regions of *E. histolytica*.

The physical findings on admission were as follows: body height, 184 cm; body weight, 67 kg; blood pressure, 134/83 mmHg; pulse rate, 120 beat/min; and body temperature, 36.9°C. His heart and respiratory sounds were clear. The abdomen was flat and soft, with mild tenderness of the right upper abdomen but negative peritoneal irritation. Clinical laboratory examination showed elevated inflammatory markers (white blood count [WBC] 19.07 × 10^9/L neutrophil count: 18.06 × 10^9/L and C-reactive protein: 248.1 mg/L); an immunosuppressive status (NK cells: 54 cells/μL, CD4 cells: 503 cells/μL, CD8 cells: 288 cells/μL; and hepatic dysfunction (total bilirubin: 24.4 μmol/L, alkaline phosphatase: 861 U/L, γ-glutamyl transpeptidase: 143 U/L). The albumin concentration was low (29.9 g/L). The patient tested negative for hepatitis B virus (HBV), hepatitis C virus (HCV), and hepatitis E virus (HEV) antigens; human immunodeficiency virus (HIV) antibody; and syphilis. Whole blood was negative for tumor markers. Contrast-enhanced computed tomography (CT) showed a huge mass with several smaller masses underneath occupying the right lobe of the liver, with a large amount of abdominal and pelvic effusion. The right diaphragm was markedly elevated [Supplementary Figure 1].

Considering that the diagnosis was unclear, on the first day after admission, the left lower abdomen was punctured and drained for the pelvic effusion. A large volume (3030 mL) of odorless anchovy-sauce–like fluid was discharged, which suggested the rupture of hepatic lesions [Figure 1]. No bacteria or amoebic protozoa were found by a rapid microscopic examination. The samples of blood and purulent ascites were collected for mNGS assay to detect the pathogen, but the results of both were negative. Based on the characteristics of the drained fluid, liver abscess was suspected. Therefore, we initiated intravenous ceftriaxone and metronidazole administration.

To further clarify the diagnosis, on the third day after admission, a liver contrast-enhanced ultrasonography (CEUS) that was performed before and after the administration of Sulphur Hexafluoride Microbubbles (SonoVue) with grayscale scanning

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technique in real time revealed a giant mixed echo mass (13.5 × 12.3 cm) in the right hepatic lobe. The mass boundary was hazy and in irregular morphology. After SonoVue contrast administration, there was no enhancement in the peripheral and internal area of the mass [Supplementary Figure 2]. Puncture and drainage were performed successively under the right diaphragm (a total of 1790 mL of odorless anchovy-sauce-like fluid) and crypt effusion of the liver. Routine bacteriological culture and mNGS were inspected, both of which showed negative results. On the fifth day after admission, the huge liver abscess was punctured under the guidance of bedside ultrasound, and the punctured fluid was also like "anchovy sauce" (total volume: 2620 mL). The abscess in the center and the exudate around the abscess cavity were sent for bacteriological culture and mNGS assay. The cultures from pus were negative for any microorganisms. In the mNGS performed on the purulent exudate from the abscess center, five sequences of *Entamoeba* (relative abundance, 94.9%) and three sequences of *E. histolytica* were found. The mNGS of the pus near the wall of the abscess cavity showed 1087 sequences of *Entamoeba* (relative abundance, 99.7%) and 306 sequences of *E. histolytica*, identify confidence is 99.0% [Figure 2]. ALA was diagnosed in combination with the history of homosexuality, drainage fluid and imaging findings, and mNGS results. However, unfortunately, his stool microscopies were consistently negative for five times. At present, there is no literature supporting that mNGS can assist in the diagnosis of ALA. Therefore, further serologic tests were needed. However, there is thus far no hospital or company that tests amoeba antigen or antibody in Shanghai, China.

The patient's condition was stable after metronidazole administration and pus drainage. He was hospitalized in the intensive care unit (ICU) for 18 days and in the general ward for another 24 days. He was discharged thereafter and was prescribed oral metronidazole (500 mg, three times/day).

Figure 1. The drained ascites were an anchovy-sauce-like fluid which indicated the possibility of amoebic liver abscess.

Discussion

ALA is the most common extraintestinal manifestation of infection with *E. histolytica*,[1] which is more commonly found in patients who live in a state of poverty and poor sanitary conditions, have immunocompromised status, or are homosexuals.[5] *E. histolytica* affects about 500 million people worldwide, although the exact prevalence is difficult to discern owing to the high prevalence of colonization with the morphologically identical commensal *Entamoeba dispar*.[2] The incidence rate of ALA is 3–20 times higher in adult men between the ages of 18 years and 50 years than in other age and sex groups.[5] The reason is unclear, but it is thought to be because of factors such as hormonal effects and alcohol consumption.[2] Although the prognosis of most patients with ALA is favorable, the mortality rate may increase to 18% in patients with risk factors including jaundice, hypoalbuminemia, large volume abscess, multiple abscess cavities, and encephalopathy.[6] Our patient had three risk factors of high mortality (hypoalbuminemia, large volume abscess, and multiple abscess cavities). These kinds of patient need to be diagnosed as early as possible to ensure aggressive treatment.

The diagnosis of ALA is made through a combination of the relevant epidemiology and clinical manifestations coupled with radiographic studies and serologic tests.

Individuals can present with ALA months to years after travel to or residency in endemic regions including India, Africa, Mexico, and Central and South America. Therefore, a careful travel history is important for making the diagnosis. Our patient had never visited any endemic area in the past. He had a decent teaching job and always lived in sanitary conditions. In addition to ingesting contaminated food or water, oral and anal sex are other ways for transmission, particularly among men who have sex with men.[7] This patient was homosexual and might have been infected through sexual activity. The patient also had lymphocytopenia on admission, which indicated that may have been immunocompromised. We tested him for HIV thrice, which were all negative. After the treatment, the patient's lymphocyte count returned to normal.

Nearly 80% patients with ALA develop symptoms within 2–4 weeks of exposure.[2] The most common symptoms are fever, pain, and hepatomegaly. In patients with acute onset, the fever is generally present in about 98% of cases. Almost all patients

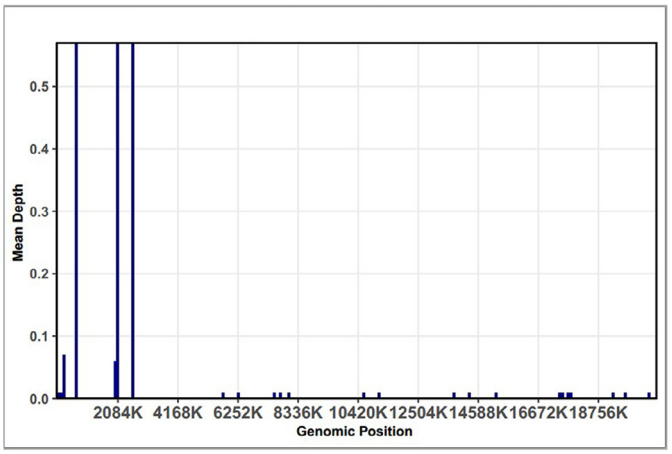

Figure 2. The mNGS of the pus showed the coverage of *Entamoeba histolytica*was 0.18%. mNGS: Metagenomic next-generation sequencing.

suffer from abdominal pain, which is the earliest and most frequent complaint. ALA arises from hematogenous spreading through the portal circulation. The right lobe is a frequent location, most likely owing to its large volume, and receives most of the venous drainage from the right colon, a segment of the bowel frequently affected by intestinal amoebiasis.[5] Therefore, most patients feel pain in the right upper quadrant of the abdomen. In abscesses of the left lobe, the pain is located in the upper abdomen and left hypochondria, which may lead to pericardial effusion and even cardiac tamponade.[8]

CEUS is a new advanced method to study the liver and detect abscesses. After contrast administration, ALA is reported as a slight strengthening of the parietal portion of the lesions, with no further findings of solid contextual components.[9] The CT feature in cases with ALA is a round or oval low-attenuation mass that may contain internal septations. The wall of the abscess typically measures 3–15-mm thick, enhances with contrast, and may be surrounded by a rim of edema.[10] However, the ultrasound, CEUS, and CT findings of this patient were inconsistent with previous reports owing to the huge and ruptured liver abscess with multiple cavities, and they therefore could not help to make the diagnosis.

Amoebic serology is highly sensitive (>94%) and highly specific (>95%) for the diagnosis of ALA, although the test may be negative during the first 7–10 days of the illness.[11] In non-endemic areas like Shanghai, there is no hospital or company that currently tests for amoeba antibody or antigen.

We used mNGS to detect the pathogen in blood and purulent ascites from the ruptured abscess, but the results were all negative. Samples obtained from the center and the edge of the abscess cavity showed the presence of only *E. histolytica* sequences. Interestingly, there were far more sequences detected at the edge of the abscess cavity than in the center. The reason might be that ALA is not a true abscess but a pocket of necrotic debris. Amoebic lysis of neutrophils at the edge of the lesion releases mediators, which leads to hepatocyte death, extending the damage to distant hepatic cells, and increasing the number of small lesions that coalesce to develop a larger hepatic lesion. The reddish-brown color of the abscess content is due to the digestion of liver tissue and red blood cells, which might be the characteristic of ALA. Although the trophozoites can be found at the edge of the lesion, they are rarely detected in the pus or within the abscess cavity itself.[8] The negative results of blood and ascites samples also indicated the low possibility of bacterial liver abscess. Currently, mNGS assays come to the clinical forefront usually in the event of a failure to identify causal agents by means of traditional methods. It performs well in detecting uncommon, novel, and coinfecting pathogens and provides new diagnostic clues for difficult-to-diagnose infections in critically ill or immunodeficient patients.[4] Cost is another significant concern regarding the use of mNGS in infectious disease diagnostics. This strategy could be interesting in high-income countries, where the prevalence of ALA appears low.

Treatment entails the use of metronidazole at a dose of 500–750 mg by mouth or intravenously three times per day for 7–10 days; the cure rate for which is >90%. There is no drug resistance in amoebiasis. Most patients treated with metronidazole improve within 72–96 h. Drainage should only be considered in cases with a high risk of ruptured abscess (diameter: ≥5 cm or lesions in the left lobe), which have no clinical response to antibiotics within 5–7 days, and in cases of bacterial coinfection of ALA.[5] This patient was given metronidazole empirically based on the "anchovy sauce" color of the ascites with close monitoring of his clinical condition. Drainage of his huge abscess was necessary for both diagnosis and treatment.

Conclusions

Our case highlights the use of mNGS for rapid diagnosis of huge and ruptured ALA in non-endemic areas that lack serologic tests.

Consent to Publish

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

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Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jointm.2021.11.007.

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