CASE REPORT
HEPATOLOGY

Diseases & Research

Hepatic Paragonimiasis: A Case Report and Literature Review

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Abstract: Paragonimiasis is a parasitic disease caused by paragnonimus, which primarily caused infection in the lung, and ectopic infection was less common. Ectopic paragonimiasis are more likely to be misdiagnosed as malignancy or other inflammatory diseases. Here, we report an ectopic paragonimiasis case initially presented with recurrent fever and abdominal pain. Blood tests suggestive of elevated eosinophil count and the positivity of hydatid immunoglobulin G (IgG) antibodies, additionally, abdominal imaging examination revealed liver space-occupying lesion. A final diagnosis of paragonimiasis was demonstrated through liver puncture biopsy histopathology. This case report reminds clinicians to be aware of ectopic paragonimiasis presented with liver space-occupying lesion. At the same time, we should also pay attention to the mutual identification between parasitic infections.

Keywords: Paragonimiasis; Liver space-occupying lesions; Eosinophil increase.

Introduction

Paragonimiasis is a foodborne parasitic disease, which is mostly caused by consuming uncooked freshwater shrimp and crabs or raw meat from infected hosts containing lung fluke cysts[1]. Clinically, depending on the site of infections, paragonimiasis can be classified into thoracic, abdominal, cerebrospinal, cutaneous, and mixed forms. The most common infectious tissue is the lung, with cough, hemoptysis, chest pain, and shortness of breath as the main manifestations[2,3]. Cases invading the liver are less common. We report a case, mainly manifesting with fever, abdominal pain, elevated eosinophilic granulocyte count and liver occupancy, and finally confirmed as abdominal paragonimiasis by liver punction biopsy.

Case report

A 61-year-old female from Sichuan was admitted to our hospital on March 15, 2022, with recurrent fever for one month and right upper abdominal pain for ten days. One month before admission, the patient had a fever due to a cold, with a maximum temperature of 39.5 ℃, accompanied by chills. Ten days before admission, the patient had newly persistent abdominal pain in the right upper quadrant abdomen. Without coughing, hemoptysis, dyspnea, chest pain, diarrhea or other discomforts in the course. In her local hospital, a complete blood count showed that the white-cell count was 7.69 × 10^9/L with 39.8% of neutrophils and 27.3% of eosinophils, of which the referance ranges were unknown. Enhanced magnetic resonance imaging (MRI) of the upper abdomen revealed a space-occupying lesion (about 4.7 × 3.7 cm) in segment 5 of the liver, which was suspected to be a liver abscess. Antibiotics were prescribed, but she was still with recurrent fever and persistent abdominal pain.

She was in good health before and had no history of hepatitis, tuberculosis, diabetes mellitus, malignant tumor, or other related specific diseases. And she denied any history of consumption of freshwater crabs or crayfish. On physical examination, no abnormality was identified.

After admitting to our hospital, complete blood count showed that white cell count was 7.67 × 10^9/L (normal ranges; 3.5-9.5 × 10^9/L) with 42.2% of neutrophils (normal range; 40-75%) and 21.2% of eosinophils (normal range; 0.4-8.0%). Procalcitonin (PCT) was increased to 0.14 ng/mL (normal range; <0.046 ng/mL). Serum IgG antibodies for hydatid were positive. Total immunoglobulin E (IgE) levels was 177 IU/mL (normal range; 5-150 IU/mL). No parasite eggs were discovered in faeces under microscopy twice. Liver and renal function tests, hepatitis B antigen, hepatitis C antibody, tumor markers including alpha-fetoprotein, IGG4, serum (1,3)-β-D-glucan test (G test) and galactomannan test (GM test) did not show significant abnormalities.

In our hospital, computed tomography (CT) of the chest showed a little scattered inflammation in both lungs. The contrast-enhanced ultrasound of the liver showed a cyst-solidary space-occupying lesion (about 6.7 × 5.0 cm) in the right lobe of the liver, suggestive of liver abscess (Fig. 1, A and B). Additionally, abdominal enhanced CT was performed and showed slightly hypodense space-occupying lesions (about 6.4 × 5.5 cm) in the anterior inferior segment of the right lobe of the liver, with heterogeneous density, inhomogeneous enhancement, segregation within the lesion, and more obvious enhancement of the liver tissue sur-

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rounding the lesions (Fig. 1, C and D).

Combined with the clinical manifestations and auxiliary examinations, the initial diagnosis was hydatid infection. Therefore, she was prescribed albendazole (400 mg, twice a day) as a diagnostic treatment on March 17, 2022. But after abdominal enhanced CT was finished, the department of liver surgery suggested that the manifestations of abdominal enhanced CT did not support the diagnosis of hydatid disease, serum IgG antibodies for hydatid may be false positive, and diagnosis of hepatic echinococcosis was not considered. Therefore, on March 24, 2022, an ultrasound-guided liver puncture biopsy was performed and the pathological results revealed scattered eosinophils infiltration, focal eosinophilic abscesses with granulomatous inflammation and fibrous tissue encapsulation, and scattered Charcot-Redden crystals, suggesting a parasitic infection (probability of paragonimus).

The pathological results were supportive of liver paragonimiasis, therefore, on April 2nd, 2022, we prescribed praziquantel 1.6g 3 times a day for 3 days. The right liver resection under laparoscopic was performed on April 12, 2022. The gross specimen showed an irregular shape of liver space-occupying lesions without invasion of the envelope (Fig. 2, A and B). After surgery, the complete blood test showed that the eosinophil count was 0.68×10^9/L with an eosinophil ratio of 5.9%, which was significantly decreased and returned within the normal range. The pathology of the surgically resected lesion revealed that the cystsolidary space-occupying lesion was an eosinophilic abscess with a tunnel-like arrangement and a large part of necrosis centrally, with scattered Charcot-Redden crystals, surrounding fibrous tissue hyperplasia, and granulomatous reaction (Fig. 2, C-F), and about 35%~45% of the peripheral hepatocytes showed mixed steatosis in the surrounding liver tissue (Fig. 2, G-H), though worm bodies were not found, suggesting a probability of paragonimus infection. The final diagnosis of liver paragonimiasis was made. After the above treatment, the patient's fever and abdominal pain disappeared, and she was discharged on April 18, 2022.

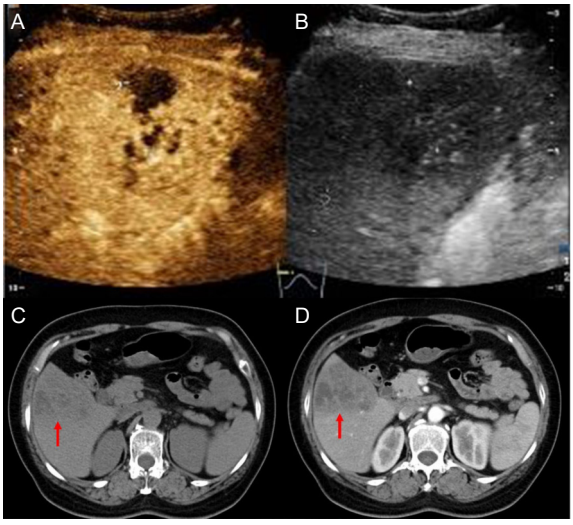

Fig. 1. Imaging examination before surgical excision.
A. The contrast-enhanced ultrasound of the liver.
B. The abdominal two-dimensional ultrasound.
C. The abdominal enhanced CT in plain scan phase.
D. The abdominal enhanced CT in arterial phase.
The red arrows indicate the liver space-occupying lesion.

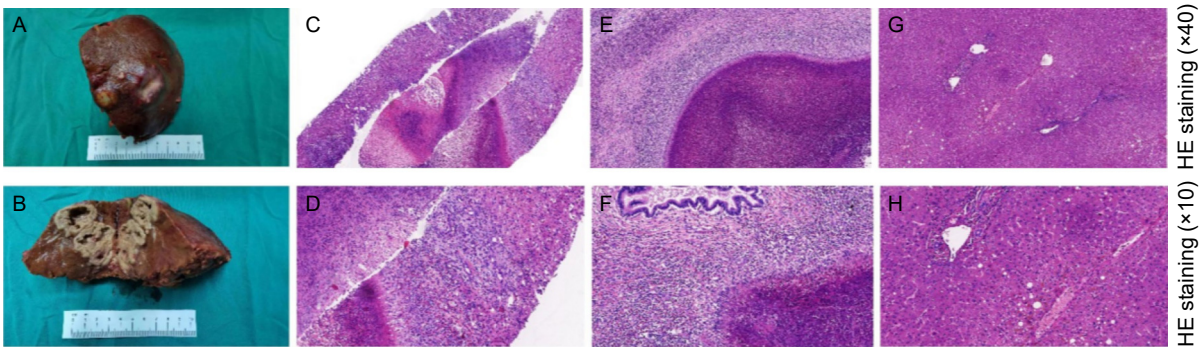

Fig. 2. Macroscopic and microscopic pathologic findings of the liver space-occupying lesion.
A. Macroscopic examination after partial hepatectomy, the space-occupying lesion protruding from the surface of the liver.
B. After dissecting the lesion, irregular shape of liver space-occupying lesions without invasion of the envelope.
C. Under microscopy, eosinophilic abscess, tunnel-like arrangement, and scattered Charcot-Leyden crystals can be seen (HE.×40).
D. Microscopic findings of tunnel-like arrangement of the lesion and granulomatous reaction (HE.×100).
E. Microscopic findings of eosinophilic abscess with large central necrosis, scattered Charcot-Leyden crystals (HE.×40).
F. Peripheral fibrous tissue hyperplasia and granulomatous reaction adjacent to the eosinophilic abscess (HE.×100).
G. About 35%~45% of the hepatocytes showed mixed steatosis in the surrounding liver tissue (HE.×40).
H. Hepatocyte steatosis in peripheral liver tissue with a few inflammatory cells infiltrating in the portal duct area and no obvious proliferation of fibrous tissue (HE.×100).
HE = hematoxylin and eosin.

Discussion

Paragonimiasis is an important zoonotic disease, approximately 50 species of paragonimus are distributed globally and different species of infection were region-specific[4,5]. It is reported that there are 32 species of paragonimus in China[4]. The growth of paragonimiasis involves several stages. The parasite eggs are excreted by the definitive hosts through sputum and faeces, and then eggs are hatched to ciliated miracidium in the freshwater, further develop into cercariae in snails which are deemed as the first intermediate host. The cercariae can move freely in freshwater and evolve to metacercariae inside the crustacean hosts (especially crabs or crayfish). When the definitive hosts consume raw or uncooked crustacean hosts containing metacercariae, metacer-

cariae will locate in the intestine and develop into child larvae which finally migrate through the body. The common migration routine is through the abdominal cavity, diaphragm to the pleural cavity and lungs, and eventually grow into adult worms in the lung. However, child larvae can also migrate to the brain, subcutaneous, liver, heart and other organs and tissues causing ectopic parasitism[6,7].

Cases of liver paragonimiasis are rare and more likely to be misdiagnosed as cancer and abscess. In our patients, significantly elevated eosinophils in routine blood is a suggestion of a high probability of parasitic infection. In a Southwestern study of 123 pediatric patients, 82.9% of paragonimiasis patients were presented with an elevated eosinophil count[8]. Data from a Japanese study showed that 75.5% of 443 paragonimiasis patients had an increased eosinophil ratio and 79.9% had increased IgE levels (>170 IU/mL)[9]. The indexes are similar in our patients. Besides, liver space-occupying lesion is the only imaging finding of the patient, and IgG antibodies for hydatid are positive, combined with clinical presentation, we could not exclude the diagnosis of hepatic alveolar echinococcus (HAE), but the common features of enhanced abdominal CT are that heterogeneous and hypodense lesions (+ 30 to + 40 HU), irregular contours, poorly defined margins, and poor or no enhancement after intravenous contrast injection[10]. The most typical CT feature of HAE is described as "geographic maps", which is pseudocystic necrosis within areas of abnormal hypodensity (0-10 HU). These CT features are not consistent with our patient. Although the results of the serological enzyme-linked immunosorbent assay (ELISA) method on hydatid are positive, it could not exclude false positives due to cross-reactivity caused by other parasitic infections.

There is no gold standard for the diagnosis of pulmonary paragonimiasis. Clinical epidemiological history is important but not necessary, not every patient can be traced to a definite history of consuming freshwater crabs or crayfish. A Japanese study survey found that about 22.6% of patients had no definitive dietary history data[9]. Similarly, a report from Chongqing showed that about 32% of patients had no clear causative dietary history[11]. Commonly used diagnostic methods for paragonimiasis are discovering eggs in sputum or faeces, but the positive detection rates are low. Besides, pathology of liver puncture or surgical resection specimens can also be used to confirm the diagnosis, mainly manifesting as coagulative or liquefactive necrosis within the lesion, infiltration of a large number of eosinophils with the formation of chronic eosinophilic abscesses and distribution of Charcot-Leyden crystals[12,13]. But Histopathological analyses are based on invasive processes, limiting their usage in clinical routine practice.

Additionally, ELISA is an easy and convenient screening test to detect parasite infection, primarily focused on antibodies of IgG. However, we can not distinguish a current infection from a previous infection based on IgG antibodies, and a false positivity may be shown owing to cross-reactivity. Recently, a newly assay that is loop-mediated isothermal amplification (LAMP) combined with a lateral flow dipstick (LFD) for detecting paragonimus westermani was performed in blood samples of dogs, and the results demonstrated its superiority over polymerase chain reaction (PCR) and its sensitivity for rapid detection[14]. More molecular assays are needed for parasite infection detection efficiently and accurately.

Besides, abdominal imaging findings are also helpful in identifying the diagnosis of paragonimiasis. The contrast-enhanced ultrasonography of hepatic paragonimiasis mainly represent lesions in subcapsular locations with hypoechoic, rim enhancement and tract-like nonenhanced internal areas[13]. Enhanced abdominal CT images features are illustrated as low-attenuation, rim-enhancing lesions located in the peripheral regions of the liver parenchyma, tubular structures enhancement, mutually connected cysts with tortuous tract formation; and perihepatic enhancement and wedge-shaped peri-lesion enhancement can also be revealed[12]. A rim-enhancing cysts in subcapsular location of the liver can also manifest in MRI, with low signal intensity on T1-weighted images and bright signal intensity on T2-weighted images[15,16].

We also find a few previously reported cases of liver occupy caused by paragonimiasis[17–21]. Ectopic paragonimiasis of the liver are still rarely reported until now. No matter with or without a history of consuming freshwater crabs or crayfish, patients with liver space-occupying lesions and elevated eosinophil count should be taken into consideration for paragonimus infection, especially when patients come from an endemic area of paragonimiasis.

Abbreviations

CT, computed tomography; ELISA, enzyme-linked immunosorbent assay; G test, (1,3)-β-D-glucan test; GM test, galactomannan test; HAE, hepatic alveolar echinococcosis; HE, hematoxylin and eosin; IgE, immunoglobulin E; IgG, immunoglobulin G; LAMP, loop-mediated isothermal amplification; LFD, lateral flow dipstick; MRI, magnetic resonance imaging; PCR, polymerase chain reaction; PCT, procalcitonin.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Authors' contributions

EQC designed the study; LQL, TL and YJH collected the data; LQL and TL wrote the manuscript; EQC edited the manuscript. All authors received the manuscript.

References

[1] Yoshida A, Doanh PN, Maruyama H. Paragonimus and paragonimiasis in Asia: An update. Acta Trop, 2019, 199: 105074.

[2] Ahn CS, Shin JW, Kim JG, et al. Spectrum of pleuropulmonary paragonimiasis: An analysis of 685 cases diagnosed over 22 years. J Infect, 2021, 82(1): 150-158.

[3] Donato RA, Donato RJ. Pulmonary, liver and cerebral paragonimiasis: An unusual clinical case in Colombia. Travel Med Infect Dis, 2022, 46: 102253.

[4] Zhou XJ, Yang Q, Tan QH, et al. Paragonimus and its hosts in China: An update. Acta Trop, 2021, 223: 106094.

[5] Blair D. Lung flukes of the genus Paragonimus: ancient and re-

emerging pathogens. Parasitology, 2022, 149(10): 1286-1295.

[6] Liu Q, Wei F, Liu W, et al. Paragonimiasis: an important food-borne zoonosis in China. Trends Parasitol, 2008, 24(7): 318-323.

[7] Blair D. Paragonimiasis. Adv Exp Med Biol, 2019, 1154: 105-138.

[8] Gong Z, Miao R, Shu M, et al. Paragonimiasis in Children in Southwest China: A retrospective case reports review from 2005 to 2016. Medicine (Baltimore), 2017, 96(25): e7265.

[9] Nagayasu E, Yoshida A, Hombu A, et al. Paragonimiasis in Japan: a twelve-year retrospective case review (2001-2012). Intern Med, 2015, 54(2): 179-186.

[10] Didier D, Weiler S, Rohmer P, et al. Hepatic alveolar echinococcosis: correlative US and CT study. Radiology, 1985, 154(1): 179-186.

[11] Peng X, Zhang J, Zhang J, et al. Incidence of paragonimiasis in Chongqing China: a 6-year retrospective case review. Parasitology, 2018, 145(6): 792-796.

[12] Li XM, Yu JQ, Yang ZG, et al. Correlations between MDCT features and clinicopathological findings of hepatic paragonimiasis. Eur J Radiol, 2012, 81(4): e421-425.

[13] Lu Q, Ling WW, Ma L, et al. Contrast-enhanced ultrasonographic findings of hepatic paragonimiasis. World J Gastroenterol, 2013, 19(13): 2087-2091.

[14] Xunhui Z, Qingming K, Qunbo T, et al. DNA detection of Paragonimus westermani: Diagnostic validity of a new assay based on loop-mediated isothermal amplification (LAMP) combined with a lateral flow dipstick. Acta Trop, 2019, 200: 105185.

[15] Kim EA, Juhng SK, Kim HW, et al. Imaging findings of hepatic paragonimiasis: a case report. J Korean Med Sci, 2004, 19(5): 759-762.

[16] Yao A, Hammond N, Alasadi R, et al. Central hepatic involvement in paragonimiasis: appearance on CT and MRI. AJR Am J Roentgenol, 2006, 187(2): W236-237.

[17] Yoo BH, Kim SH, Baek YJ, et al. Hepatobiliary and Pancreatic: Liver abscess not responding to drainage and antibiotics. J Gastroenterol Hepatol, 2021, 36(4): 851.

[18] Liu F, Zhang J, Lei C, et al. Feasibility of laparoscopic major hepatectomy for hepatic paragonimiasis: two case reports. Medicine (Baltimore), 2016, 95(38): e4939.

[19] Gong Z, Xu Z, Lei C, et al. Hepatic paragonimiasis in a 15-month-old girl: a case report. BMC Pediatr, 2017, 17(1): 190.

[20] Jin WX, Li TH, Zhu H, et al. A case of hepatic paragonimiasis was misdiagnosed as hepatocellular carcinoma with rupture and haemorrhage. J Int Med Res, 2021, 49(6): 3000605211012668.

[21] Lin YX, Jia QB, Fu YY, et al. Hepatic Paragonimiasis Mimicking Hepatocellular Carcinoma. J Gastrointest Surg, 2018, 22(3): 550-552.