

Case Report

Diagnosis and management of hepatic fascioliasis mimicking intrahepatic cholangiocarcinoma: a case report

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Abstract: Fascioliasis is a rare zoonotic infection caused by *Fasciola hepatica*, and presents with atypical clinical manifestations including fever, ambiguous gastrointestinal symptoms and right upper quadrant pain. Blood tests often reveal elevated eosinophilia. However, it may be misdiagnosed as intrahepatic cholangiocarcinoma on radiologic findings. In this study, we presented a 41-year-old female patient, with a history of taking raw watercress, presented with right upper quadrant pain, fever and eosinophilia. Magnetic resonance imaging (MRI) studies suggested intrahepatic cholangiocarcinoma. Cholecystectomy and left lateral lobectomy was performed. Due to the dilation of the choledochus, the common bile duct was explored using a fiberoptic cholangioscope; and a leaf-shaped worm was found in the lumen of the lower part of the common bile duct. The worm was confirmed as *Fasciola hepatica* by the Beijing Research Institute of Tropical Medicine. A T-tube was planted in the common bile duct after extraction of the worm using lithotomy forceps. The worm bodies were drained out in the bile through the T-tube for three days after praziquantel tablets were taken. The T-tube was removed two months later. During the 36-month follow-up period after surgical and medical treatment, the symptom of the patient was alleviated. In conclusion, Hepatic fascioliasis should be on the list of differential diagnoses in patients with radiologic findings that mimicking intrahepatic cholangiocarcinoma. Hepatobiliary surgeons should keep in mind the possibility of *Fasciola hepatica* infection in patients with right upper quadrant pain, fever, eosinophilia and a history of the intake of raw aquatic plants. When abdominal exploration is performed, the placement of a T-tube in common bile duct may drain the worm bodies and prevent the development of biliary obstruction, following anti-helminth therapies.

Keywords: Hepatic fascioliasis, intrahepatic cholangiocarcinoma, diagnosis, treatment

Introduction

Hepatic fascioliasis is a food-borne zoonosis caused by *Fasciola hepatica*, which is mainly found in developing countries including South America, Latin America, Africa, Oceania, Europe and Asia; and its overall incidence has increased over the past few decades [1-3]. There are only a few reports of these cases in China [4]. The features of human hepatic fascioliasis are non-specific in most cases. It could be asymptomatic in some patients who suffer chronic parasitic infection in the liver [5].

Furthermore, it is occasionally hard to differentiate this with liver malignant tumors such as

cholangiocarcinoma due to the lack of specific radiologic findings and serum markers [6-9]. Since the treatment and prognosis for cholangiocarcinoma and hepatic fascioliasis are substantially different, it is crucial for the doctors to make the correct diagnosis and manage time.

We presented a case of hepatic masses caused by *Fasciola hepatica*, which was initially diagnosed as intrahepatic cholangiocarcinoma. After abdominal exploration, the diagnosis of hepatic fascioliasis was confirmed. Through the retrospective analysis of the patient's clinical data and literature review, the diagnosis and treatment of hepatic fascioliasis will be discussed.

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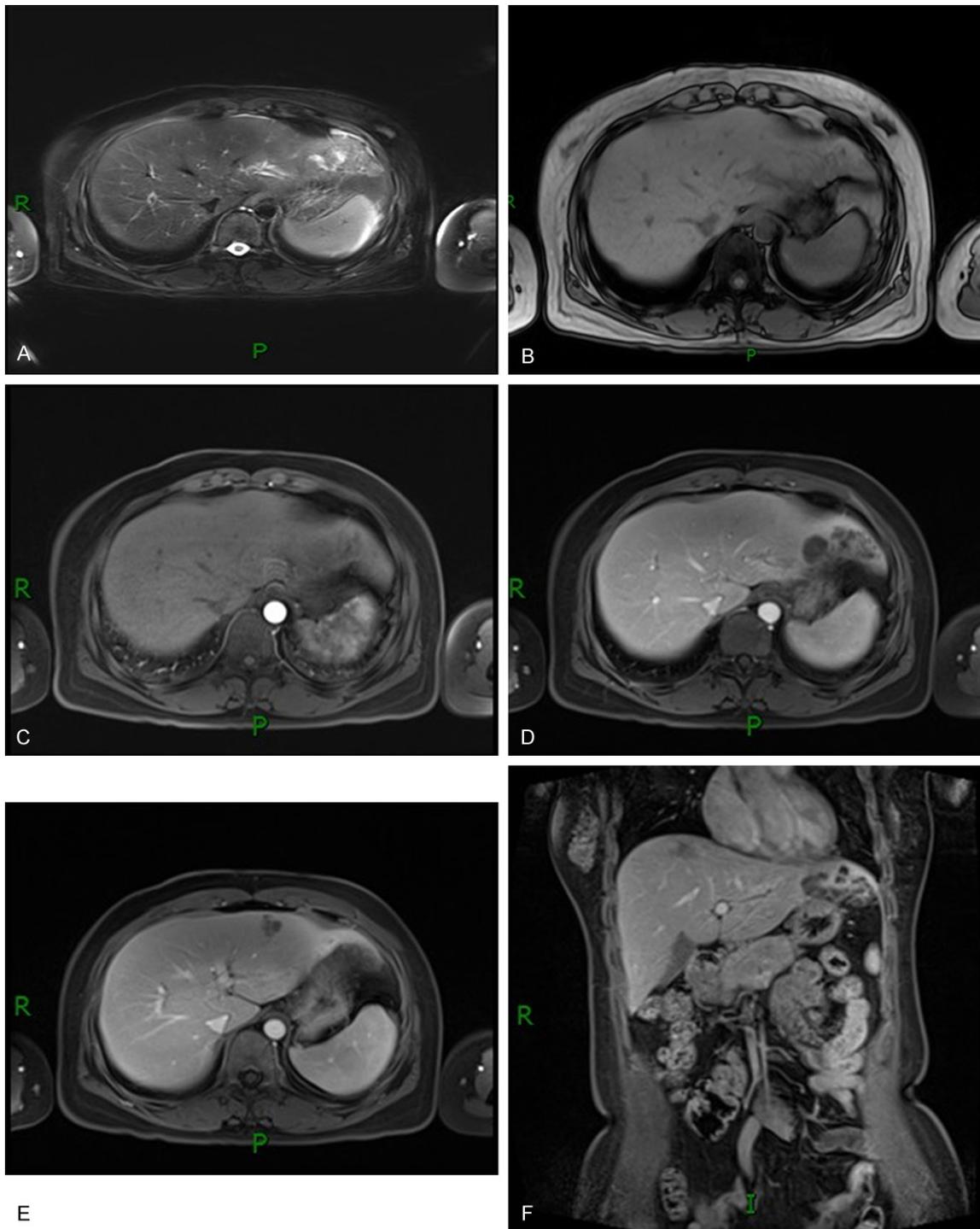


Figure 1. Hypodensity lesions (A) in the left lobe on T1 weighted images, T2 weighted images show hyperdensity lesions (B), no contrast enhancement in arterial phase (C) and peripheral enhancement of the hypodensity lesions in a cluster in portal venous phase (D) and subcapsular irregular tunnel (E), intrahepatic bile duct dilation and hypodensity lesions in a cluster in the left lobe on coronal images (F).

Case presentation

A 41-year-old female from Hebei province, China was referred to our hospital with right

upper quadrant pain and fever that persisted for two months. The pain was blunt in nature with spontaneous onset, but not appearing refer pain. The fever was intermittent and the

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Figure 2. The worm was pale in color, 1.5 cm×0.5 cm×0.1 cm, mobile well.

highest temperature was 38°C. The fever disappeared after a few doses of antibiotic treatment. The patient had poor appetite and slight weight loss in the past two months. There were no diarrhea, hematemesis or melena, and urinary symptoms. There was also no significant past medical history or drug history, and the subject did not smoke or drink alcohol. There was no known tuberculosis exposure. Physical examination revealed a normal clinical appearance with normal vital signs. The right upper quadrant of the abdomen was tender during deep palpation, and liver percussion was positive. Furthermore, there was no lymphadenopathy, and urine and stool tests were all normal. Blood tests revealed a leukocyte count of $4.64 \times 10^9/L$, with an elevated eosinophilia count of $1.14 \times 10^9/L$ (normal: $0.02-0.52 \times 10^9/L$); and accounted for 24.6% (normal: 0.4-8.0%). Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyltransferase (GGT) and total bilirubin (TBil) were all within normal ranges. Serum and urine amylase was also normal. Tumor biomarkers AFP, CEA, CA19-9 and CA72-4 were all normal. Serology for hepatitis B virus (HBV), hepatitis C virus (HCV) and hepatitis E virus (HEV) were negative. Magnetic resonance imaging (MRI) suggested multiple low-signal lesions in the left lobe of the liver on T1-weighted images and peripheral enhancement in the portal venous phase, and intrahepatic bile duct ectasia in the left lobe was observed (**Figure 1**). MRI diagnosis suggested intrahepatic cholangiocarcinoma.

Abdominal exploration was performed on February 28, 2013. Intraoperative exploration

revealed multiple focal lesions in the left lobe with a maximum diameter of 4-cm, cholecyst (9×4×3 cm), and choledochus dilated to 1.1 cm. Fine-needle biopsy for left lobe lesions of the liver revealed eosinophilic granuloma; hence, parasite infection was possible. Cholecystectomy and left lateral lobectomy was performed. Due to the choledochus dilation, the common bile duct was explored by fiberoptic cholangioscopy; and a leaf-shaped worm was found in the lumen of the lower part of the common bile duct. The worm was extracted with lithotomy forceps. A T-tube was planted in the common bile duct. The worm was pale in color, was 1.5×0.5×0.1 cm, and was moving well (**Figure 2**). The *Fasciola hepatica* was confirmed by rgw Beijing Research Institute of Tropical Medicine. Histologically, at postoperative, the bile epithelium was eroded, inflamed and hyperplastic; and the surrounding portal tract was thickened and fibrotic. Large necrotic granulomas could be found within the bile duct and parenchyma. Eosinophils infiltration is typical in all these lesions. Charcot-Leyden crystals formed degranulated eosinophils at the center and between hepatocytes. The gallbladder shows a hypertrophied muscle coat and hyperplastic inflamed mucosal epithelium (**Figure 3**). Blood test revealed the restoration of eosinophil count and eosinophil percentage postoperation, which were $0.06 \times 10^9/L$ and 0.5%, respectively. Praziquantel tablets were given to the patient for further worm eradication (0.6 g bid for two days). Some of the worm bodies were drained out in the bile through the T-tube for three days after taking the praziquantel tablets. The patient was discharged two weeks after the operation. Abdominal CT scan suggested no focal lesions in the liver (**Figure 4**), and fiberoptic cholangioscopy revealed no worms in the biliary tract at two months after the operation. The T-tube was removed afterwards. During the 36-month follow-up after surgical and medical treatment, the symptom of the patient was alleviated.

Discussion

Fasciola hepatica is a flatworm that infects the hepatobiliary system of goats, sheep and cattle. Humans may act as accidental hosts via the ingestion of raw watercress, alfalfa juice, lettuce, mint, parsley and similar aquatic vegetables, or drinking water contaminated by the worm; and this infection is termed as, fasciolia-

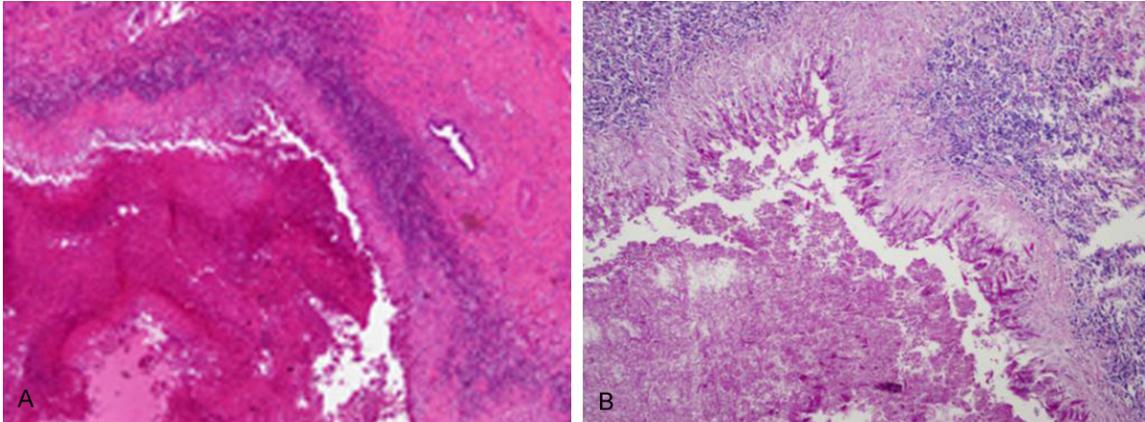


Figure 3. Eosinophilic necrosis (A) necrotic nodule surround by many degranulating eosinophils and some giant cell. H&E $\times 40$ (B) there are numerous purple-staining Charet-Leyden crystals. acid-fast stain $\times 100$.

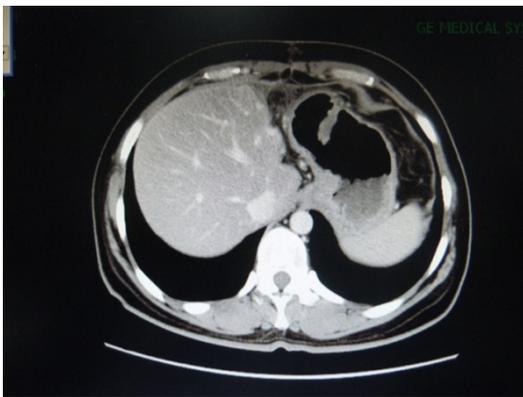


Figure 4. Two months after liver resection. There was no lesions in the liver anymore.

sis [10-12]. Matured *Fasciola hepatica* dwells in the hepatobiliary system of herbivores or humans and lay eggs, which were released through the feces. Eggs hatch into ciliated larvae (miracidia) in freshwater, and multiply within an intermediate host, the freshwater pond snail. From the snail emerge cercariae, which attach themselves onto aquatic plants; and metacercariae is formed. After the ingestion of aquatic plants with metacercariae, immature metacercariae excysts migrate through the digested juice in stomach, duodenum and small intestines. The cercariae penetrate through the intestinal wall, pass into the peritoneal cavity, and migrate towards the liver. After penetrating the liver capsule, the flukes make their way towards the biliary ducts, and finally reach the biliary tree. Maturation takes an average of three months. After that, the mature flukes can release new eggs within the biliary tree [13].

Occasionally, larvae may migrate to and mature in ectopic locations including subcutaneous tissues, the chest cavity, and the brain [14].

Fasciola hepatica infection in humans can be divided into two stages: acute stage and chronic stage. During the acute (hepatic) stage, the immature fluke penetrates the liver capsule to migrate through the liver parenchyma; causing inflammation and tissue necrosis. The symptoms are non-specific, which include anorexia (sometimes associated with nausea and vomiting), and might lead to weight loss, abdominal pain in the right upper quadrant, fever, night sweats, urticaria and arthralgia; and these can last for many months. Other findings that were less frequently reported include splenomegaly, ascites, subcapsular hepatic hematoma, intra-abdominal hemorrhage, pleural or pericardial effusion, and respiratory symptoms [15]. The chronic (biliary) stage reflects the arrival of the adult fluke in the biliary tree, and symptoms represent biliary obstruction and inflammation. It is rarely observed with the icterus, which is caused by the obstruction of the common bile duct. Gulsen *et al.* reported five patients with obstructive jaundice due to *Fasciola hepatica*, who were diagnosed and managed with endoscopic retrograde cholangiopancreatography (ERCP) [16]. Echenique-Elizondo M *et al.* reported a patient who complained of acute pancreatitis. ERCP reveals distinct features, and sphincterotomy allows for the extraction of multiple *Fasciola hepatica* [17]. Ectopic fascioliasis in other localizations has been reported in subcutaneous tissues, eyes, the brain, lungs, epididymis, inguinal lymph nodes, the stomach,

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cecum and the colon. Some have been mistaken with metastatic tumors [18, 19].

The major laboratory abnormality is eosinophilia and anaemia [16, 20]. A history of the recent consumption of raw watercress and other aquatic plants is an important finding. However, the source of infection remains obscure in some patients [15]. For our patient, she admitted that she took watercress several months ago. The diagnosis mainly relied on egg finding in stool examinations, followed by serology, intradermal reaction, surgery, and mobile fluke observation [21].

The diagnosis of *Fasciola hepatica* infection can be performed through the identification of *Fasciola hepatica* eggs in fecal samples. Since eggs appear in feces only after the parasite has entered the bile duct and matured, early infections cannot be diagnosed. Serological detection by enzyme-linked immunosorbent assay (ELISA) is the most helpful test, but is not available in many countries. The detection of anti-fluke antibodies in serum by ELISA is considered a sensitive and reliable method for the diagnosis of acute infections, and it can also be used as an adjunct to fecal analysis for the diagnosis of latent and chronic infections. Figueroa-Santiago reported that FhSAP2-based ELISA was more specific (95.6%) than FhES-ELISA (91.9%). FhSAP2 can be used in the serodiagnosis of chronic human fascioliasis, with the additional advantage of being relatively cheap and easy to produce [22]. Kim suggested that the 8-kDa protein of *Fasciola hepatica* is one of diagnostic antigens in human fascioliasis that does not have a cross-reaction with other human trematodiasis [23].

Ultrasound examinations have shown multiple hypoechoic nodules or parenchyma heterogeneity. Ductal dilatation appears as thin hypoechoic lines parallel to the portal areas at the beginning of the ductal phase, followed by an increase in biliary dilatation and tortuosity of the bile ducts after the 12th week post-infection. In some instances, ultrasound can demonstrate mobile flukes in dilated bile ducts and the gallbladder.

Computed tomography findings in the acute phase of hepatic fascioliasis include multiple, small, round, or oval clustered hypodense le-

sions, with peripheral contrast enhancement. Hypodense nodular lesions arise in the subcapsular area during the first weeks after ingestion of metacercariae, which progress to tortuous clustered lesions by the 6th week. CT demonstrates dilated biliary ducts with periportal tracking.

On T2-weighted images, capsular hyperintensity can be demonstrated on axial and coronal images, as a penetrating area of the parasite. Early migration routes appear in patients as hypointense and hyperintense lines in the subcapsular area on T1- and T2-weighted MRI images, respectively. Parenchymal clustered lesions show hyperintensity on T2-weighted and hypointensity on T1-weighted images, with peripheral enhancement after contrast administration. Mild dilated bile ducts appear on T2-weighted images as hyperintense areas parallel to hypointense lines, which correspond to the portal vessels. Capsular and subcapsular fibrotic scars develop during the ductal phase and appear as an irregular heterogeneity on MRI. Intermediate signals of filling defects represent worms that can be observed in dilated ducts on MRI [24, 25].

Differential diagnosis is needed for hepatic fascioliasis with intrahepatic cholangiocarcinoma. The mass-forming subtype intrahepatic cholangiocarcinoma appears in CT scans as a hypodense lesion with irregular margins. In most cases, a rim-like enhancement in the arterial phase is shown, followed by a progressive hyperattenuation in the portal venous phase and a typical maximum enhancement in the delayed phase [26].

Yeşildağ A *et al.* reported a case of hepatobiliary fascioliasis, and presented unusual radiological findings that revealed hepatic cystic pouches communicating with intrahepatic bile ducts. Snail-like, oval shaped and conglomerated echogenic particles with no acoustic shadowing, which suggest *Fasciola hepatica*, were detected in these cystic pouches [27]. Furthermore, Adachi S suggested that laparoscopy with liver biopsy is very important for diagnosing human fascioliasis, particularly for asymptomatic fascioliasis [5].

Chronic biliary fascioliasis may be asymptomatic or may present with biliary obstruction,

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cholangitis, or portal fibrosis. Furthermore, some patients also presented with cholangitis. Endoscopic sphincterotomy and ERCP is considered as the optimal approach for treating biliary parasitosis, including biliary fascioliasis, biliary ascariasis, and biliary hydatid disease. Previous reports have revealed that ERCP and sphincterotomy have a role in the differential diagnosis for symptoms of right upper quadrant pain and common bile duct dilatation [28].

For our patient, her MRI finding mimicked intrahepatic cholangiocarcinoma, and the radiologist's diagnosis was "intrahepatic cholangiocarcinoma possible". Although radiological findings play an important role in the differential diagnosis of the disease, since it may clinically mimic several hepatobiliary and systemic diseases, the combination of illness history (administration of raw aquatic plants), typical clinical manifestation, eosinophilia, serological testing and radiologic findings can help in providing a correct diagnosis.

Medical therapy to treat fascioliasis can be useful in the hepatic stage of the disease, and a variety of anti-helminth therapies can be attempted. The administration of albendazole, triclabendazole, praziquantel and artesunate are feasible, safe and efficacious public health interventions [29, 30].

Other treatments include endoscopic retrograde cholangiopancreatography with sphincterotomy and the extraction of adult flukes. This can be very effective for treating patients in the biliary stage of infection with *Fasciola hepatica*, in which cholestasis and biliary tree inflammation predominates. Gulsen MT confirmed the diagnostic and therapeutic role of ERCP in patients with obstructive jaundice caused by biliary fascioliasis [16]. Serial serological testing can provide a useful tool to monitor individual patient response to therapy together with radiological evidence of improvement in the lesions.

For our patient, when we found the fluke in the common bile duct, we planted a T-tube in common bile duct to prevent biliary obstruction when worm eradication medicine was given to the patient. Some worm bodies were drained out in bile through the T-tube for three days after praziquantel tablets were taken, and no biliary obstruction developed.

Hepatic fascioliasis should be on the list of differential diagnoses in patients with radiologic findings that mimic intrahepatic cholangiocarcinoma [31]. For a non-endemic area such North China, hepatobiliary surgeons should keep in mind the possibility of *Fasciola hepatica* infection for patients with right upper quadrant pain, fever, eosinophilia and a history of intake of raw aquatic plants. The early serological testing of these patients may prevent a wrong diagnosis. Furthermore, specific radiological findings would be very helpful in its diagnosis. Eggs in the stool samples, serological testing and the extraction of live flukes from bile ducts can confirm the diagnosis. Anti-helminth therapies to treat the hepatic stage of fascioliasis can be useful, and ERCP may play a role in the biliary stage of fascioliasis. When abdominal exploration is performed, the placement of a T-tube in the common bile duct may drain the worm bodies and prevent the development of biliary obstruction following anti-helminth therapies.

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Disclosure of conflict of interest

None.

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