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Case Report

Biliary fascioliasis – A rare differential diagnosis of biliary obstruction

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Abstract

Fascioliasis is a zoonotic disease caused by *Fasciola hepatica* or *F. gigantica*. There are two phases of *Fasciola* infection. In the acute phase, the patient has a wide spectrum of clinical manifestations while the later phase of infection is usually related to inflammatory changes in the bile duct and the mechanical effects of the worm, which can lead to biliary obstruction. The presence of *Fasciola* inside the biliary system has rarely been reported in the literature. In this report, we presented a case of bile duct obstruction in a 36-year-old male patient undergoing cholecystectomy for gallstones and with a history of worsening jaundice for one month. Extensive laboratory testing failed to clarify the cause of jaundice. Three living liver flukes were subsequently retrieved from the right hepatic duct and later confirmed as *F. gigantica* by morphology and internal transcribed spacer (ITS2) sequence analysis.

Key words: *Fasciola*; fascioliasis; biliary tract diseases.

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Introduction

Fascioliasis, often considered a zoonosis, is a liver fluke infection affecting ruminants and occasionally humans. An estimated 2.4 million people are infected with the two larger human liver flukes, *Fasciola hepatica,* and *F. gigantica,* and 180 million people are at risk worldwide [1]. This infection typically progresses in two main phases. The acute phase occurs during the migration of the immature flukes through the liver, which may lead to severe symptoms such as fever, abdominal pain, and hepatomegaly. The chronic phase is associated with proliferation, dilatation, and fibrosis of the bile ducts caused by mechanical obstruction [2]. However, the biliary phase is infrequently documented in a human host.

The traditional morphological methods used to distinguish the two species might be unreliable. The development of molecular methods enables species-level identification and provides a powerful tool for identifying potential hybrid species [3]. Currently, there have been several reports of a hybrid of *F. hepatica* and *F. gigantica* in animals worldwide [4]. However, this liver fluke has rarely been detected in humans. In this report, we presented a case of chronic phase fascioliasis diagnosed during exploratory laparotomy and later confirmed as *F. gigantica* by next-generation sequencing.

Case report

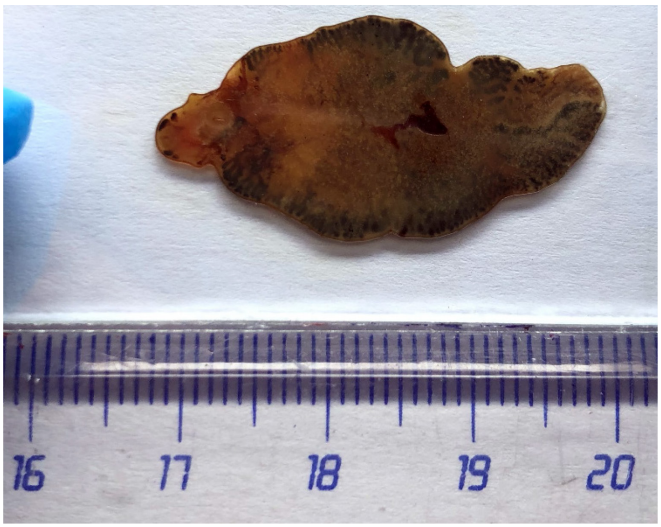
A 36-year-old man was referred to Hue Central Hospital with a history of one-month worsening jaundice. Cholangiocarcinoma was suspected at a private clinic, after which he was referred to the hospital. His past medical history included intermittent right upper quadrant pain and gallbladder stones treated with a laparoscopic cholecystectomy 9 months ago. On physical examination in the Gastrointestinal Surgery Department, he appeared conscious, with a temperature of 37 °C, blood pressure of 120/70 mmHg, and heart rate of 78 bpm. Based on his presentation and history, his differential diagnoses included post-cholecystectomy bile duct stenosis and cholangiocarcinoma. Transabdominal ultrasound revealed mild intra-hepatic biliary dilatation with thickening of the bile duct wall in a 1.2-cm segment at the origin of the right hepatic duct. Blood tests demonstrated an increase in aspartate aminotransferase (77 IU/L) and alanine aminotransferase (134 IU/L). Total and direct bilirubin levels were markedly elevated at 745.4 µmol/L and 374.7 µmol/L, respectively. Tumor

markers were within the normal range. A complete blood count test was obtained, which revealed eosinophilia (4.100/mm^3). Further imaging was indicated to clarify the cause of worsening jaundice. Magnetic resonance imaging (MRI) showed a filling defect distal to the biliary confluence, resulting in upstream biliary dilatation (Figure 1a, b, c).

Endoscopic retrograde cholangiopancreatography (ERCP) was performed in an attempt to diagnose and resolve the cause of biliary stasis. After sphincterotomy, a cholangiogram was obtained, which showed a dilated common bile duct with a diameter of 13 mm and a filling defect at the end of the common bile duct. A Dormia basket was used to remove a small stone from the common bile duct and then a plastic stent was inserted. However, close clinical monitoring for ten days after ERCP revealed worsening jaundice. Eventually, an exploratory laparotomy was indicated. A choledochotomy was performed, and the biliary tree was examined with Mirizzi forceps. No stenosis was observed at the level of Vater's ampulla, and the stent inserted by ERCP was removed. Exploration of the proximal biliary tree revealed a patent left hepatic duct and obstructed right hepatic duct. In a further attempt, three flat and living parasites were removed from the right hepatic duct, which were presumably *Fasciola* spp. (Figure 2).

The patient's serum subsequently tested positive for IgG anti-*Fasciola* spp. antibody (OD: 2.5). Antiparasitic therapy using triclabendazole 10 mg/kg/day for two days was prescribed. After one month of treatment, the symptoms were relieved, and the eosinophil count returned to a normal range. The *Fasciola* spp. IgG titer was reduced by tenfold (OD: 0.25). The *Fasciola* adult worm was then sent to the Vietnam Military Medical University to identify the species by next-generation sequencing. The result suggested that this parasite was *F. gigantica* by ITS2 sequencing (https://www.ncbi.nlm.nih.gov/nuccore/MT429182).

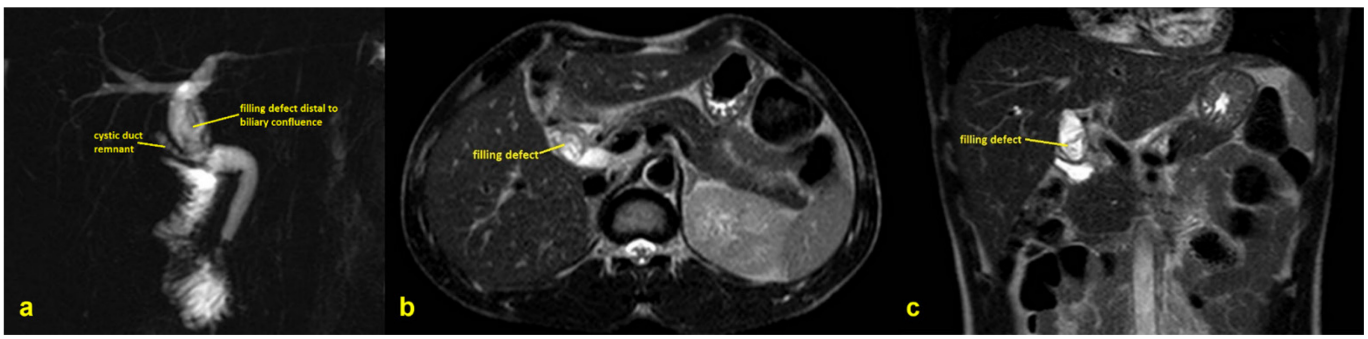
Figure 2. Adult parasites extracted from biliary duct.



Discussion

Fascioliasis is a zoonotic infection caused by *Fasciola* spp. This parasitic disease is commonly observed in Africa, Western Europe, and Latin America. The reservoir of infection is herbivorous animals such as sheep and cattle. Humans are accidental final hosts and usually become infected by eating aquatic plants grown in water that is contaminated with feces from animals harboring *Fasciola* [5]. Fascioliasis may have a wide range of clinical manifestations, from asymptomatic to gastrointestinal complaints. This infection progresses in two phases: the acute hepatic phase and the chronic obstructive biliary phase. However, the later phase is rarely reported in the human host. The classic triad of symptoms in the first phase is abdominal pain, fever, and hepatomegaly. The eosinophil count may be highly elevated during this phase. However, in the later phase, the worms reach the biliary system and cause the symptom of biliary obstruction [6]. In clinical practice, the distinction between the chronic phase of fascioliasis and other causes of biliary obstruction is difficult, as they present

Figure 1. Filling defect on Magnetic Resonance Cholangiopancreatography images: (**a**) filling defect distal to the biliary confluence and upstream biliary dilatation demonstrated on magnetic resonance imaging sequences; (**b**) MRI-T2W axial; (**c**) MRI-T2W coronal.



similar symptoms. In non-endemic areas, the diagnosis of fascioliasis can be difficult and is usually delayed; also, the symptoms may be confused with other hepatic or biliary disorders, as in our case. Since the parasite does not pass eggs in the acute phase of the disease, an ELISA test is faster and more useful than direct examination of the stool.

Once in the bile ducts, adult flukes cause inflammation, hyperplasia, and thickening and dilatation of the walls of the duct and gallbladder, as shown in this case. Diagnosis of the cause of jaundice in our case was challenging due to contradictory results of the transabdominal ultrasound, magnetic resonance imaging, and ERCP, and was delayed until exploratory laparotomy. Abdominal ultrasonography findings are generally nonspecific, showing mainly biliary dilatation and bile duct wall thickening. Although MRI has good diagnostic value, no definite conclusion could be drawn. Therefore, ERCP is the better choice for patients in the chronic phase. ERCP and sphincterotomy are sometimes used to remove parasites from the biliary tree [7]. In our patient, ERCP was indicated to resolve long-term cholestasis. Interestingly, the location of obstruction varied among imaging modalities (common hepatic duct on magnetic resonance imaging, common bile duct on ERCP, and right hepatic duct on transabdominal ultrasound). This might be explained by the dynamic movement of the living liver flukes in the biliary tree.

In the literature, it is reported that patients in the biliary phase may also be hospitalized due to acute pancreatitis [2]. This condition was also observed in our patient with an elevation of amylase and lipase to 175 U/L and 809 U/L respectively. Given the uncontrolled overall condition developed by our patient, surgical intervention was indicated, and adult parasites were removed from the right hepatic duct. This case shows that a surgical approach might be necessary for some complicated situations. More often, the biliary phase of fascioliasis is at best managed when the diagnosis is made without surgery using ERCP and sphincterotomy [8,9]. However, the clinical diagnosis of fascioliasis is sometimes difficult because the manifestations in the chronic phase may be indistinguishable from cholangitis, cholecystitis, and cholelithiasis of other origins. Therefore, in some cases, liver fluke infection may remain undetected for several years. Recently, there has been little information available on risk factors by which gallstones form concomitantly with liver fluke infection in humans. The history of cholelithiasis in this patient is more likely associated with fascioliasis. However, it is difficult to distinguish between cause and effect because the life span of the adult fluke can be 9-13 years [10]. A study conducted on an animal model suggested the association between the presence of gallstones and the number of flukes located in the bile duct [11]. A high risk of developing gallstones may be expected in human subjects inhabiting areas where *Fasciola* sp. Is highly endemic.

A single dose of triclabendazole 10-20 mg/kg/day is the recommended treatment for *Fasciola* infection, some reports consider the response to this treatment as a criterion for the diagnosis. While this single-dose therapy is sufficient, multiple doses may be required in some patients with persistent infection [12]. Since surgical intervention might not have completely removed the parasites from the biliary system, a clinical follow-up was required. ELISA was highly effective in diagnosis and post-treatment monitoring. Particularly, the anti-*Fasciola* IgG antibodies in the patient's serum were reduced tenfold (from OD 2.5 to OD 0.25) after one month of treatment. Nevertheless, follow-up after therapy should include monitoring for a resolution of eosinophilia, a clearance of eggs in the stool, and a decrease in serologic titters. It is reasonable to repeat all tests that were initially positive at three months. The disappearance of bile duct lesions on ultrasound after therapy may also be helpful [13].

The adult worm of *F. hepatica* and *F. gigantica* differ in size and other phenotype features. However, the traditional morphological methods used to distinguish the two species may be unreliable, especially in the presence of hybrids that result in intermediate forms in endemic areas where the two species overlap [14]. Previous reports have shown that genetic hybridization can be detected in *Fasciola* species using the ribosomal internal transcribed spacer (ITS) region and mitochondrial DNA as genetic markers [4,14]. In Vietnam, a report, which analyzed 14 samples extracted from humans, presented the majority of *F. gigantica* (9/14). Interestingly, 2 out of 14 specimens in the report were admixed *Fasciola* spp. In another study, out of 120 flukes samples collected from ruminants, 71 were *F. gigantica,* 42 were introgressive hybridization (*F. hepatica* rDNA + *F. gigantica* mtDNA) and 7 were admixed hybrid *Fasciola* spp. [15]. Although the size of the adult parasite taken from the patient in our report is suggestive of *F. hepatica* (3 cm × 1.3 cm) (Figure 2), ITS2 sequencing show rDNA of *F. gigantica.* In fact, *F. gigantica* infects domestic livestock in tropical and subtropical areas, particularly in Africa, the Western Pacific, Hawaii, and Southeast Asia. *F. gigantica* has a similar life cycle and pathology as *F. hepatica* and causes similar clinical manifestations

in the acute and chronic phase. The eggs (190 by 90 microns) and the adult flukes (up to 7.5 cm in length) are larger than *F. hepatica*. Until diagnostic techniques improve, recovery of adult flukes in an appropriate epidemiologic setting can be used to exclude or confirm the diagnosis.

Conclusions

Since biliary fascioliasis is uncommon among the diseases of the hepatobiliary system, physicians should be made aware of this infection in endemic areas. Further studies need to be conducted to optimize the treatment in complicated situations.

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