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## Case Report

# Case report: Intrahepatic cholangiectasis with *Clonorchis sinensis* infection ☆☆☆☆

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## ABSTRACT

*Clonorchis sinensis* infections persist globally among humans. These pathogens mainly inhabit the intrahepatic biliary system. Most individuals with clonorchiasis exhibit mild symptoms. The absence of distinctive symptoms often results in delayed diagnosis and treatment, potentially leading to chronic infection. We herein report a case of a 29-year-old female presented with a year-long history of abdominal distention and dyspepsia. Imaging revealed intrahepatic bile duct dilatation, intrahepatic bile duct cyst, and associated deposits. One month post-cystectomy, the patient developed massive ascites and a significant increase in eosinophil count. After treatment, multiple worms were observed in the drainage tube. Morphological and DNA metagenomic analyses confirmed the presence of *C. sinensis*. Clinical manifestations of *C. sinensis* vary widely. Imaging serves as a valuable diagnostic tool in endemic areas, especially in detecting intrahepatic duct dilation where the flukes reside. In addition to intrahepatic bile duct dilation, abnormal echoes within the bile duct and the presence of floating objects in the gallbladder significantly aid in diagnosis. Clinicians may encounter these parasitic diseases unexpectedly, underscoring the importance of understating such cases in routine practice and contributing to our broader understanding of managing similar cases in clinical settings.

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## Introduction

*Clonorchis sinensis* infection remains prevalent worldwide, notably in regions like China, Korea, northern Vietnam, and eastern Russia. These parasites primarily inhabit the intrahepatic biliary system [1–3]. Most patients with clonorchiasis exhibit mild symptoms such as abdominal pain, diarrhea, nausea, and abdominal discomfort [4,5]. The absence of distinctive symptoms often delays diagnosis and treatment, eventually leading to chronic infection. Cases of *C. sinensis* infections presenting initially with congenital intrahepatic bile duct (IHBD) dilatation are rare. Herein, we present a case highlighting this scenario to enhance understanding of the disease and broaden diagnostic and therapeutic approaches.

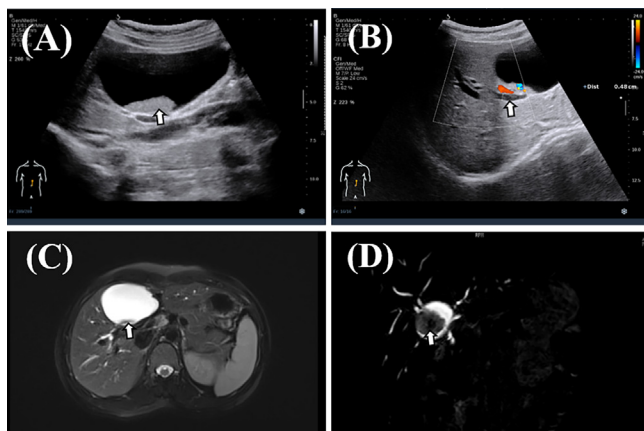
## Case presentation

A 29-year-old female was admitted with “abdominal distension and dyspepsia for 1 year”. Ultrasound examination revealed 88 × 88 × 41 mm cystic lesions in the S4 region of the liver, subsequently confirmed by magnetic resonance cholangiopancreatography (Fig. 1). Mild IHBD dilation and cystic deposits were also observed. No other specific symptoms or signs were observed. Importantly, the patient had a penchant for consuming sashimi and shrimp.

Laboratory tests revealed a leukocyte count of  $6.48 \times 10^9/L$  (normal range,  $3.5\text{--}9.5 \times 10^9/L$ ) with an eosinophil percentage

of 7.4 (normal range, 0.4%–8.0%) and a neutrophil percentage of 38.5 (normal range, 40%–75%) (Figs. 2 and 3) Based on these findings and imaging results, the patient received a preliminary diagnosis of congenital IHBD dilatations. Subsequent procedures included laparoscopic segmental hepatectomy and laparoscopic cholecystectomy.

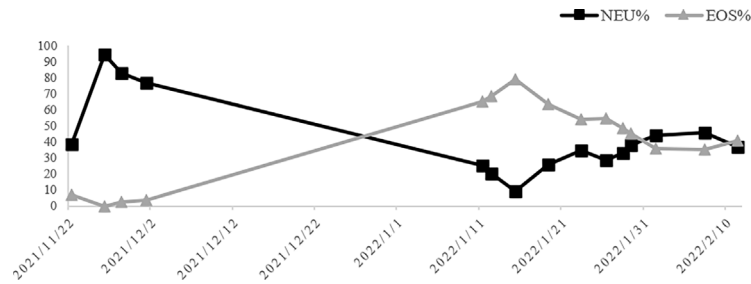
A month later, the patient was readmitted due to increasing abdominal distention accompanied by irregular afternoon fever ranging between 37.5°C and 38.5°C. Physical examination and ultrasound examination confirmed the presence of extensive ascites (Fig. 4). Routine blood tests indicated a leukocyte count of  $16.6 \times 10^9/L$  with an eosinophil percentage of 71.2% and a neutrophil percentage of 20% (Figs. 2 and 3) Ultrasound-guided puncture and drainage in the surgical area (Fig. 4) extracted approximately 2000 mL of bile-containing turbid ascites from the indwelling drainage tube immediately and intermittently. Despite ascites drainage and endoscopic retrograde cholangio-pancreatography for biliary leakage, the abdominal distention and fever persisted. After the exclusion of relevant contraindications, experimental albendazole deworming was initiated, leading to the emergence of numerous worms flowing into the drainage bag 3 days later. Morphologically, these worms resembled *C. sinensis*, exhibiting an anterior oral sucker and a centrally located ventral sucker, dorso-ventrally flattening, a slightly narrow front, and a blunt round rear resembling a sunflower seed (Figs. 6 and 7). A retrospective review of the patient’s surgical pathology confirmed traces of parasites in the bile duct (Fig. 5). However, no parasite eggs were detected in the stool specimen through the direct smear method. Metagenomic analysis of the ascites identified a sequence number of 159 for *C. sinensis* with a relative abundance of 1.72%. The patient underwent standard anthelmintic therapy (praziquantel 60 mg/kg/day for 3 days), resulting in further drainage of *C. sinensis* worms. Subsequently, the patient’s body temperature stabilized gradually, and symptoms such as abdominal distension began to alleviate.



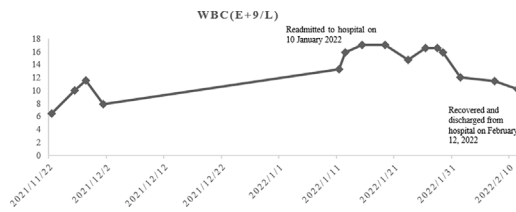
**Fig. 1 – Preoperative imaging.** (A) Ultrasound imaging of the intrahepatic bile duct cyst and its internal deposits: the S4 segment of the liver contained an anechoic area with a clear boundary with an iso-echoic mass inside (arrow), which can be moved by changing the body position with no sound shadows behind. (B) Ultrasound imaging of the dilated intrahepatic bile duct and color Doppler. No blood flow signal could be detected by color Doppler in the iso-echoic area. The arrow indicates the worm in the biliary tract. (C) Magnetic resonance images (MRI) of intrahepatic bile duct dilatation, cysts, and their internal deposits (arrow). (D) MRCP images of intrahepatic bile duct dilatation, cysts, and their internal deposits (arrow).

## Discussion

*C. sinensis* remains prevalent globally, particularly in China [3]. Humans become definitive hosts through the ingestion of raw or undercooked fish carrying the parasite. These organisms usually inhabit the biliary system of mammals, including humans [6], posing a significant risk for cholangiocarcinoma due to chronic inflammation and biliary epithelium damage [7,8]. Clinical presentation varies, including mild fever, epigastric tenderness, abdominal discomfort, malaise, and anorexia, and, in chronic stages, jaundice, diarrhea, liver enlargement, and ascites. Often accompanied by low-grade eosinophilia in peripheral blood [2,6]. Most of the clinical manifestations and, therefore, imaging findings, are contingent on fluke quantity within the biliary tree, often leading to cholangitis (oriental cholangio-hepatitis) due to bile duct obstruction. However, the clinical manifestations of hepatic *C. sinensis* lack specificity, contributing to potential neglect or misdiagnosis. Diagnostic methods such as detecting eggs in fecal samples under a light microscope, the cellophane-thick smear method (Kato-Katz smear), the formalin-ether centrifuge sed-



**Fig. 2 – Fluctuations of eosinophils (EOS%) and neutrophils (NEU%).**

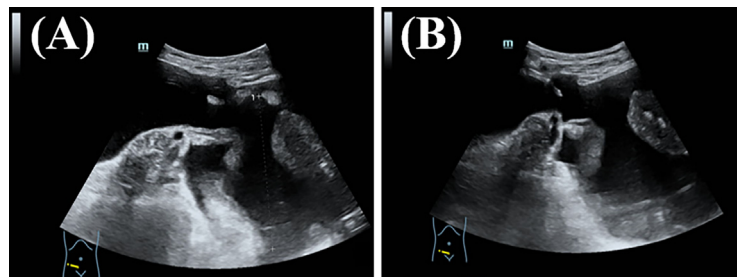


**Fig. 3 – A graph depicting the leukocyte fluctuation (WBC).**

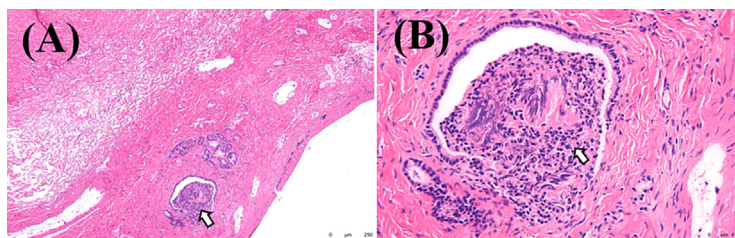
imentation method, the enzyme-linked immunosorbent assay, and imaging modalities like ultrasonography, computed tomography, and magnetic resonance imaging serve as adjuncts but lack specificity. DNA detection for *C. sinensis* aids in confirmation but is impractical for screening due to cost and time constraints [3]. Liao, G et al. reported that *C. sinensis* eggs were significantly higher in bile than in fecal samples, indicating bile as a preferable specimen in case of biliary obstruction [9]. Currently, diagnosis often hinges on routine examinations like diffuse IHBD dilation, peri-bile duct echo, and gallbladder floating objects, alongside a significant eosinophil elevation in routine blood examination [8,10]. However, as demonstrated in this case, patients may initially lack evident symptoms or abnormal eosinophil counts, complicating timely diagnosis. Several diseases, including congenital intrahepatic cholangiectasis, cholangiolithiasis, and cholangiocarcinoma, can mimic IHBD dilation, leading to diagnostic challenges. Misdiagnosis or oversight may result in complications like gallstones, biliary stones, casts inside dilated bile, pyogenic cholangitis, liver abscesses, cholecystitis, hepatitis, cirrhosis, or even cholangiocarcinoma.

In this case, we report a *C. sinensis* infection presenting with congenital IHBD dilation, a rarity attributed to aberrant ductal plate development, belonging thus to the spectrum of congenital bile duct cysts (BDC) [11–13]. Congenital IHBD dilations correspond to type V BDC according to the Todani et al. classification [14,15]. Congenital IHBD dilations are often asymptomatic in children or young adults and often manifest after a biliary tract infection caused by chronic cholestasis. Other symptoms include abdominal pain, chills, fever, and jaundice. Owing to its similarity to cholelithiasis and cholangitis, it is easy to misdiagnose this disease [12]. Congenital IHBD dilations may present themselves in a localized form limited to one hepatic lobe or segment to a bilobar and diffuse form involving the entire intrahepatic biliary tree equally [11]. Thus, such challenges and disease similarities make it difficult to diagnose *C. sinensis* infection.

Initial symptoms, in this case, were subtle, primarily occasional indigestion and abdominal discomfort. Preoperative and postoperative blood tests did not indicate eosinophilia or other abnormalities. Although imaging suggested multiple bile duct dilatation and floccus in cysts, they were initially overlooked. Surgical intervention was performed based on the assumption of simple IHBD dilation. However, within a month post-surgery, the patient experienced severe abdominal discomfort, massive ascites, and fever. Despite attempts to manage biliary leakage and fever with antibiotics and drainage, a significant increase in eosinophils indicated a potential parasitic infection. Experimental deworming with albendazole led to the removal of worms, followed by praziquantel administration, resulting in gradual symptom improvement. After this diagnosis, we examined the patient's stool, which yielded negative results, possibly due to low egg detection rates [16]. Fi-



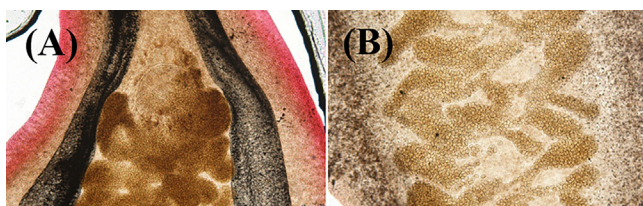
**Fig. 4 – Postoperative imaging. (A) Ultrasound imaging showing massive ascites. (B) Puncture and drainage in the surgical area performed under the guidance of ultrasound.**



**Fig. 5 – Pathological section. (A and B) The arrow indicates the worm in the biliary tract.**



**Fig. 6 – Sinensis worms drained from bile.**



**Fig. 7 – The fine structure of *C. sinensis* worms.**

nally, *C. sinensis* infection was confirmed by next-generation sequencing (NGS) and histopathology. Following the diagnosis, we reviewed the patient's preoperative imaging and found abnormal echogenic foci in the bile duct and deposits in the cyst. We did not investigate why we had these imaging findings, either pre- or postoperatively. Until postoperative complications such as biliary leakage, irregular fever, and elevated eosinophils developed.

## Conclusions

In summary, the protean nature of *C. sinensis* infection warrants suspicion upon observing a history of raw freshwater fish consumption, recurrent cholangitis, obstructive jaundice, peripheral eosinophilia, and IHBD dilation on radiographic

imaging. While imaging aids in diagnosis, it may not provide definitive evidence alone but offers crucial cues in daily practice, practically in endemic areas [17,10], especially regarding the dilation of the intrahepatic ducts where the flukes are lodged without extrahepatic obstruction [8,18]. Recognition of hepatobiliary symptoms alongside imaging findings suggestive of IHBD dilation should prompt a thorough investigation into potential causes such as bile duct cancer, IHBD stones, or parasites. Especially, in this case, the patient had congenital dilatation of IHBDs, which made our diagnosis more difficult. Therefore, in addition to IHBD dilation, abnormal echoes in the bile duct and floating objects in the gallbladder aid better in the diagnosis process, as they reveal definite signs of *C. sinensis* infection. Clinicians may unexpectedly face some of these parasitic diseases in their practice, and it is hoped that this case will shed some light on our daily work.

## Patient consent

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

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