

The Clinical and Cholangiographic Picture of Hepatic Clonorchiasis

Hoi-Hung Chan, M.D., Kwok-Hung Lai, M.D., Gin-Ho Lo, M.D.,
Jin-Shiung Cheng, M.D., Jia-Sheng Huang, M.D., Ping-I Hsu, M.D.,
Chiun-Ku Lin, M.D., and E-Ming Wang, B.S.

Abstract

Background: Hepatic clonorchiasis is endemic in areas of the Far East, including Taiwan, where people commonly eat raw or partially cooked freshwater fish. **Goals:** To analyze and explore the cholangiographic findings of hepatic clonorchiasis with respect to the clinical data. **Study:** From February 1990 to May 1999, 64 patients were diagnosed with hepatic clonorchiasis in the Kaoshiung Veterans General Hospital. Eighteen of the 64 patients were indicated for endoscopic retrograde cholangiopancreatography (ERCP). The final diagnosis was confirmed by identification of ova in bile or worms in the biliary tract. **Results:** Fifteen (83%) of 18 patients had history of raw fish consumption and seven patients (39%) came from an endemic area. Clinically, cholangitis (8 of 18) was the most frequent indication for ERCP. All of the patients were diagnosed by the presence of ova in bile. Only seven (39%) patients had peripheral eosinophilia, and seven (39%) had ova in stool. The most characteristic cholangiographic finding of hepatic clonorchiasis in ERCP is filamentous or elliptic filling defects of the biliary tract (16 of 18). **Conclusion:** When presented with biliary symptoms, a history of raw fish consumption in an endemic area should arouse suspicion of hepatic clonorchiasis. Filamentous filling defects in ERCP with bile analysis may confirm the diagnosis.

Key Words: Cholangiographic pictures—Hepatic clonorchiasis.

Hepatic clonorchiasis is an endemic disease confined to the Far East, especially mainland China, Taiwan, Hong Kong, Japan, Korea, and Vietnam.^{1,2} Humans are the most suitable definitive hosts of *Clonorchis sinensis* and are easily infested by ingestion of the cysts in raw or partially cooked freshwater fish. It is estimated that 19 million people are infected.³ Bile ducts, gallbladder, and pancreatic ducts are involved in cases of heavy infestation.^{4,5} The majority of hepatic clonorchiasis cases are asymptomatic if the number of flukes is less than 100. When the number of flukes increases to more than 100, nonspecific epigastric or right upper abdominal pain, anorexia, nausea, and diarrhea may

occur.⁶ In addition, obstructive jaundice and recurrent pyogenic cholangitis may become visible in cases of severe infestation.⁷ Endoscopic retrograde cholangiopancreatography (ERCP) is indicated for differential diagnosis. The current study assesses the cholangiographic picture of hepatic clonorchiasis on ERCP with regarding to the clinical data.

MATERIAL AND METHODS

From February 1990 to May 1999, 64 patients with *C. sinensis* infestation were diagnosed at the Kaoshiung Veterans General Hospital. Of the 64 patients, 18 had biliary symptoms with indications for a cholangiogram (Table 1). The patients' detailed histories were recorded, including the region in which they lived and the habit of eating raw or partially cooked freshwater fish. Laboratory tests were performed and bile was collected during ERCP for microscopic examination. Final diagnosis was confirmed by identification of ova in bile or worms in the biliary tract.

RESULTS

Among the 64 patients with *C. sinensis* infestation, there were 48 men and 16 women (age range, 24–86 years). The diagnosis was established in 52 patients (81%) by the presence of ova in stool and in 2 patients (3.1%) by the intraoperative finding of worms (Fig. 1) in the biliary tract. Twelve patients (19%) had peripheral eosinophilia. Seven patients (11%) had concomitant hepatic cancers; of those, four had hepatocellular carcinoma and three had cholangiocarcinoma (Fig. 2). Among the four patients with hepatocellular carcinoma, three had concomitant chronic hepatitis B infection and one had hepatitis C infection. None of the three patients with cholangiocarcinoma had viral hepatitis.

Of the 18 patients who underwent ERCP, 15 were male and 3 were female. Their ages ranged from 33 to 86 years, with a mean of 61 years. Seven patients (39%) came from the endemic area of southern Taiwan (Mei-Nung and Chi-Shan) and 15 (83%) had a history of raw fish consumption. The laboratory findings are summarized in Table 2. Parasitic ova in bile were identified in all 18 patients (Fig. 3). Seven patients (39%) were positive for stool ova, seven (39%) had peripheral eosinophilia, and nine (50%) had adult worms in their bile collected by nasobiliary drainage (Fig. 4, Table 2). Of all, 15 patients (83%) had filamentous or elliptic filling defects of the biliary tract (Fig. 5), 8 (44%) had intrahepatic ductal dilatation, 7 (39%) had hazy appearance

Submitted March 20, 2001. Accepted July 30, 2001.

From the Division of Gastroenterology, Department of Internal Medicine, Kaoshiung Veterans General Hospital, National Yang Ming University, Taiwan, R.O.C.

Address correspondence and reprint requests to Dr. Kwok-Hung Lai, Department of Internal Medicine, Kaoshiung Veterans General Hospital, 386 Ta-Chung 1st Road, Kaoshiung 813, Taiwan, R.O.C. E-mail: Dadu@ms12.hinet.net

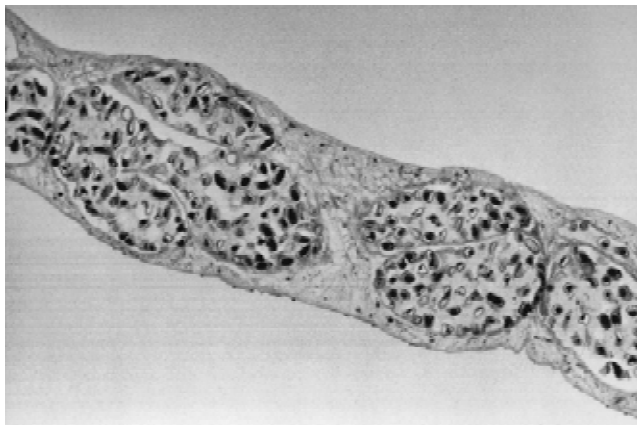
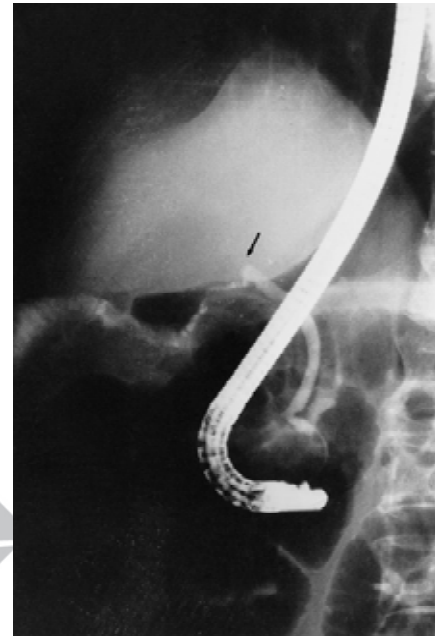
TABLE 1. Clinical features of 18 patients with hepatic clonorchiasis who underwent ERCP

Clinical features	Number of cases	%
Jaundice only	3	18
Jaundice with abdominal symptoms	5	27
Fever	1	5
Body weight loss with abnormal liver function	1	5
Cholangitis	8	45

of the intrahepatic duct, 10 (56%) had a normal diameter of common bile duct including one case with common bile duct stone, 8 (44%) had a dilated common bile duct, and 5 had common bile duct stones (Table 3).

All patients took praziquantel (30 mg/kg/d for 3 days) soon after their diagnosis. Endoscopic treatments, including sphincterotomy, nasobiliary drainage, and endoprosthesis, were done for seven patients, whereas percutaneous transhepatic biliary drainage was done for three. Meanwhile, three patients received both types of procedures because of inadequate relief of jaundice by a single type alone (Table 4). Five patients received surgical intervention for the reasons shown in Table 5.

One patient with liver cirrhosis died of sepsis and hepatic failure during hospitalization. One patient with cholangiocarcinoma and obstructive jaundice died 1 month after biliary endoprosthesis. One patient with cholangiocarcinoma who had undergone surgery died of chronic obstructive pulmonary disease with respiratory failure 6 months later. Another patient died suddenly at home of an unknown cause 1 month later. One patient with hepatocellular carcinoma underwent transcatheter arterial embolization. Four patients were lost to follow-up. Nine patients remained symptom-free after to 26 months of follow-up.

**FIG. 1.** An adult worm of *C. sinensis* (original magnification, $\times 10$).**FIG. 2.** A case of *C. sinensis* concomitant with cholangiocarcinoma (arrow, obstruction of left intrahepatic duct by tumor mass).

DISCUSSION

In a report by Yen et al.,⁸ 48.0% of people were found to get *C. sinensis* infestation during a screening test at the outpatient clinic of the Kaohsiung Medical College. Thirty-four of them (48.6%) came from the endemic area (Meinung and Chishan). Most of them were Hakkanese and had a habit of consuming raw freshwater fish. In our study, seven patients (39%) came from an endemic area and 15 of them (83%) had history of raw fish consumption. Therefore, coming from an endemic area and having a history of eating raw fish should be seen as risk factors for this disease. Clonorchiasis predominately affected the men in studies by Chou⁹ and Ong and Lu¹⁰ and in the current study.

TABLE 2. Laboratory findings of 18 patients with hepatic clonorchiasis who underwent ERCP

Laboratory findings	Number of cases	%
Peripheral eosinophilia	7	39
Ova in stool	7	39
Ova in bile	18	100
Worms in bile (by drainage)	9	50
Hypoalbuminemia (albumin <3.7 g/dL)	14	78
Elevated GOT (>45 U/L)	13	72
Elevated GPT (>40 U/L)	13	72
Elevated GGT (>60 U/L)	11	61
Elevated alkaline-phosphatase (>95 U/L)	17	94

GOT indicates glutamic-oxaloacetic transaminase; GPT, glutamic pyruvic transaminase; GGT, gamma-glutamyl-transferase.

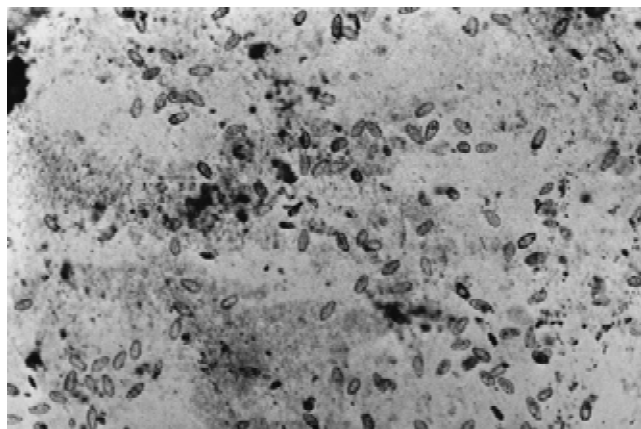


FIG. 3. Ova of *C. sinensis* in bile (original magnification, $\times 120$).

In laboratory examinations, peripheral eosinophilia occurred in 39% (7 of 18) of patients with biliary symptoms and in 10.8% (5 of 46) of patients without biliary symptoms. Less than half of the patients were found to have ova in their stool specimens, even if their bile was positive for parasitic ova. This is probably caused by chronic infestation, in which the number of ova is not large enough. Cholangitis was the most frequent manifestation in our patients with clonorchiasis. However, the concomitance of biliary tract stones or hepatic tumors may also cause similar symptoms. The relationship between clonorchiasis, stones, and tumors is still controversial. The worms can cause biliary obstruction and cholangitis, but they can also act as a nidus for stone formation. In addition, chronic inflammation of the biliary tract by the presence of *C. sinensis* may be a precipitating factor for cancer.^{11,12} Adult worms usually live in the medium-sized and small intrahepatic ducts in which they produce mechanical obstruction and inflammatory re-

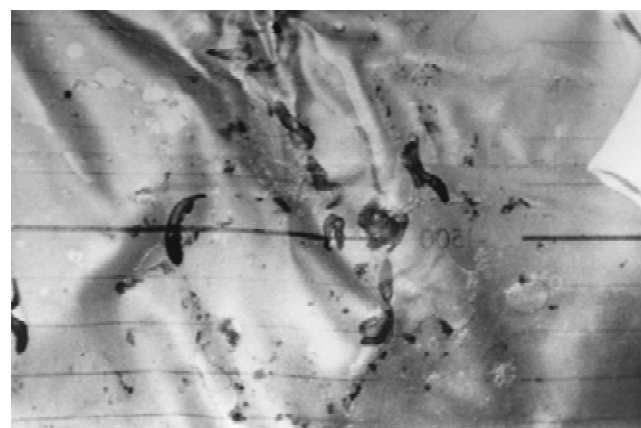


FIG. 4. Adult worms of *C. sinensis* in bile from nasobiliary drainage.

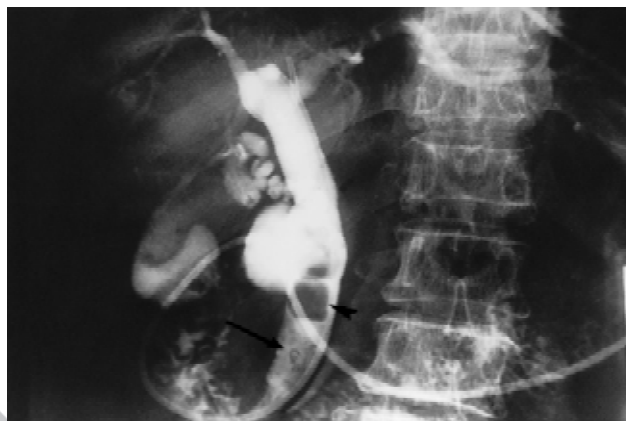


FIG. 5. Filamentous filling defect in bile duct indicating the possibility of clonorchiasis (arrow) shown by cholangiogram in a case of common bile stone concomitant with such infection (arrow head).

TABLE 3. Cholangiogram of 18 patients with hepatic clonorchiasis who underwent ERCP

	Number of cases	%
Filamentous or elliptic filling defects	15	83
IHD dilatation	8	44
Hazy appearance of IHD	7	39
Normal common bile duct	10	56
Without stone	9	50
With stone	1	6
Common bile duct dilatation	8	44
Without stone	3	16
With stone	5	28

IHD indicates intrahepatic duct.

TABLE 4. Endoscopic or percutaneous treatment for patients with *C. sinensis* who underwent ERCP

Methods of treatment	Number of cases
Endoscopic treatment	7
EPT only	3
NBD only	1
EPT + NBD	2
EPT + NBD + stent	1
PTCD only	3
Both types of procedures	3
EPT + PTGBD	1
NBD + PTCD + stent	1
EPT + PTCD	1

EPT indicates sphincterotomy; NBD, nasobiliary drainage; stent, biliary endoprosthesis; PTCD, percutaneous transhepatic biliary drainage; PTGBD, percutaneous transhepatic gallbladder drainage.

TABLE 5. Reasons of surgical intervention for patients with *C. sinensis* infestation who underwent ERCP

Causes for surgical intervention	Number of cases
Acute cholecystitis	1
Primary liver cancer	2
Incomplete removal of common bile duct stones by ERCP	2

action,¹³ which may result in malignant transformation of the bile ducts.^{14,15}

In our study, 7 of 64 patients with clonorchiasis had primary liver cancer. Three patients with hepatocellular carcinoma also had hepatitis B infection, which is a well-known cause of hepatocellular carcinoma. In patients with cholangiocarcinoma, no other cause except clonorchiasis was found. Therefore, biliary clonorchiasis should be considered as a cause of primary liver cancer, particularly cholangiocarcinoma.¹⁶ Furthermore, for those patients with hepatic clonorchiasis, follow-up may be needed for long-term sequelae, such as cholangiocarcinoma.¹⁷

Filamentous filling defects shown during cholangiography is characteristic of clonorchiasis, but the defects can be obscured by the contrast medium. The other cholangiographic findings of hepatic clonorchiasis include small irregular filling defects, intrahepatic ductal dilatation (especially of the peripheral ducts), and hazy appearance of the intrahepatic duct.¹⁸ Filamentous wavy and/or elliptical appearance of the worm is a pathognomonic finding on ERCP examination.¹⁹ Careful observation and the use of diluted contrast medium may increase the diagnostic accuracy. Presence of stones or bile duct obstruction cannot exclude the possibilities of clonorchiasis, as these two conditions may be complications of clonorchiasis. In patients with a history of raw fish intake and the presence of biliary symptoms, bile analysis should be routinely performed to rule out the possibility of clonorchiasis.

Besides the endoscopic or percutaneous means of relieving the obstructive jaundice caused directly or indirectly by the worm, the first choice of treatment of *C. sinensis* infestation is praziquantel. When taken at a dosage of 30 mg/kg three times daily for 2 days, efficacy reaches 100%.²⁰ However, in a study by Niels et al.,²¹ the efficacy of praziquantel 25 mg/kg/d for 3 days was unsatisfactory, indicating the

possibility of resistance and cautioning against low-dose regimens. Perhaps, the most effective preventive means are to stop consumption of raw fish, even when it has been kept in a freezer or heavily salted²² and to avoid establishing pig farms in the vicinity of water reservoirs.²³

Acknowledgments: The authors thank Mr. Andy Wilson for revision of English Grammar.

REFERENCES

- Rim HJ. The current pathobiology and chemotherapy of clonorchiasis. *Korean J Parasitol* 1986;24(suppl):7-20.
- Sun T. Pathology and immunology of *Clonorchis sinensis* infection of the liver. *Ann Clin Lab Sci* 1984;14:208-15.
- Manson-Bahr PEC, Bell DR. Manson's tropical diseases, 19th ed. London: Bailliere Tindall, 1987.
- Lee SH, Shin TS, Lee SM, et al. Studies in pathological changes of the liver in Albino rats infected with *Clonorchis sinensis*. *Korean J Parasitol* 1978;16:148-55.
- Chan PH, Teoh TB. The pathology of *Clonorchis sinensis* infestation of the pancreas. *J Pathol Bacteriol* 1967;93:185-9.
- Lin AC, Chapman SW, Turner HR, et al. Clonorchiasis: an update. *South Med J* 1987;80:919-22.
- Lim JH. Radiologic findings of clonorchiasis. *AJR Am J Roentgenol* 1990;155:1001-8.
- Yen CM, Chen ER, Fang AH, et al. Human clonorchiasis in new endemic areas of Taiwan, an epidemiological survey. *Kaohsiung J Med Sci* 1988;4:538-46.
- Chou LP. Epidemiological studies of clonorchiasis at Meinung township in southern Taiwan. *Formosan Sci* 1960;14:135-65.
- Ong SJ, Lu SC. Protozoan and helminthic infections among the government workers and students of Miao-Li district in Miao-Li County: a highly endemic area of clonorchiasis in Taiwan. *Zhonghua Min Guo Wei Sheng Wu Xue Za Zhi* 1979;12:13-20.
- Fernando VO, Joseph NT. Clonorchis-associated cholangiocarcinoma: a report of two cases with unusual manifestations. *Gastroenterology* 1991;101:831-9.
- Hou PC. The relationship between primary carcinoma of the liver and infestation with *Clonorchis sinensis*. *J Pathol Bacteriol* 1956;72:239-46.
- Hou PC. The pathology of *Clonorchis sinensis* infestation of the liver. *J Pathol Bacteriol* 1955;70:53-64.
- Hou PC. Pathological changes in the intrahepatic bile ducts of cats (*Felis catus*) infested with *Clonorchis sinensis*. *J Pathol Bacteriol* 1965;89:357-64.
- Seel DJ, Park YK. Oriental infestation cholangitis. *Am J Surg* 1983;146:366-70.
- Shin HR, Lee CU, Park HJ, et al. Hepatitis B and C virus, *Clonorchis sinensis* for the risk of liver cancer: a case-control study in Pusan, Korea. *Int J Epidemiol* 1996;25:933-40.
- Liu LX, Harinasuta KT. Liver and intestinal flukes. *Gastroenterol Clin North Am* 1996;25:627-36.
- Okuda K, Emura T, Morokuma K, et al. Clonorchiasis studied by percutaneous cholangiography and a therapeutic trial of tolurene-2-4-diisothiocyanate. *Gastroenterology* 1973;65:457-61.
- Leung JWC, Sung JY, Chung SCS, et al. Hepatic clonorchiasis—a study by endoscopic retrograde cholangiopancreatography. *Gastrointest Endosc* 1989;35:226-31.
- Chen CY, Hsieh WC. *C. sinensis*: epidemiology in Taiwan and clinical experience with praziquantel. *Arzneimittelforschung* 1984;34:1160-2.
- Niels T, Nguyen VD, Ha VV, et al. Little effect of praziquantel or artemisinin on clonorchiasis in northern Vietnam: a pilot study. *Trop Med Int Health* 1999;4:814-8.
- Fan PC. Viability of metacercariae of *Clonorchis sinensis* in frozen or salted freshwater fish. *Int J Parasitol* 1998;28:603-5.
- Ooi HK, Chen CI, Lin SC, et al. Metacercariae in fishes of Sun Moon Lake which is an endemic area for *Clonorchis sinensis* in Taiwan. *Southeast Asian J Trop Med Public Health* 1997;28(Suppl 1):222-3.