

Endoscopic Management of Biliary Parasitic Diseases

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Abstract *Aim/Materials and Methods* Between January 2000 and June 2007, 3,548 endoscopic retrograde cholangiopancreatography (ERCP) were performed for extrahepatic cholestasis, cholangitis, and choledocholithiasis. The results of ERCPs were evaluated retrospectively and examined carefully to investigate the management and endoscopic therapy of biliary parasites. *Results* Of the 3,548 patients who underwent ERCP, 24 (0.66%) were found to have biliary parasitosis. The mean age of the biliary parasitosis patients (16 women) was 48.6 (15–77) years. Of these 24 cases, 16 patients had hydatid cystic disease (eight with partial obstruction of the biliary tract, and eight with ruptured cysts), four patients had *Fasciola hepatica*, and four patients had *Ascaris lumbricoides* infestation. Endoscopic sphincterotomy was performed, after which the choledochus was examined carefully by balloon catheter and basket procedure. *Conclusion* The ERCP procedure is very useful in the therapy of biliary parasitic infestations.

Keywords Biliary parasitic disease · ERCP ·
Extrahepatic cholestasis · Cholangitis · Choledocholithiasis

Introduction

Parasitic diseases of the biliary tract frequently occur in tropical and subtropical areas and cause high morbidity and mortality. Parasitic infestations rarely occur in the temperate zones, although the incidence seems to be increasing gradually in such areas due to the increasing number of tourists, immigrants, and expatriates [1]. Helminthic infestation from the Metazoa may affect the liver and/or the biliary tract either during passage of worms through these structures or because these organs serve as their natural habitat. Among the many worms present, only nematodes and hermaphroditic trematodes affect the biliary system [2].

Worms in the biliary tree can cause the syndrome commonly referred to as ‘Oriental cholangiohepatitis’. Features of this syndrome include helminthiasis, choledocholithiasis, choledochal obstruction, recurrent cholangitis with stones, and a propensity for stricture of the left hepatic duct [3]. Clinically, oriental cholangiohepatitis includes biliary colic, jaundice, cholecystitis and/or cholangitis [4]. Acute pancreatitis is occasionally seen as a result of worms in the choledochus either due to obstruction of the pancreatic duct or the terminal choledochus [5]. Liver cysts and abscesses occur secondary to ascariasis and liver flukes, whereas hepatocellular carcinoma and cholangio-carcinoma are seen in association with *Clonorchis sinensis* and *opisthorchiasis* [6, 7].

The presence of a parasitic biliary infestation is easily confirmed, most commonly by the identification of the worm in stools or duodenal contents. Ultrasonography (US), computerized tomography (CT), and magnetic resonance imaging (MRI) can be used to demonstrate the flukes, dilatation of the biliary tree due to biliary obstruction caused by the parasites, the presence of stones,

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cholangiocarcinoma, hepatoma, liver abscesses, or cysts [8–13]. The presence of eosinophilia supports the suspicion of the presence of worms. Variable elevations in bilirubin, transaminases, alkaline phosphatase (ALP), and γ -glutamyltranspeptidase (GGT) are seen in severe cases, whereas the level of these liver tests may be normal in mild cases of biliary parasitic infestations.

Endoscopic retrograde cholangiopancreatography (ERCP) is a very useful diagnostic tool for demonstrating the presence of worms in the biliary tree [1]. With the advent of high-resolution US, CT scan, and MRI, the use of ERCP for diagnostic purposes has rapidly declined. At present, ERCP is reserved for already diagnosed cases in which an endoscopic removal of worms is attempted. The aim of this study was to evaluate the endoscopic management of biliary worms.

Materials and Methods

Between January 2000 and June 2007, 3,548 ERCPs were performed for extrahepatic cholestasis, cholangitis, and choledocholithiasis in the Department of Gastroenterology, Ankara University Medical School. ERCP procedure was performed with duodenoscope after premedication with meperidine (50–100 mg,) and midazolam (2–5 mg).

The results of 3,548 ERCP procedures were evaluated retrospectively and examined carefully to investigate the prevalence of biliary parasitosis. The medical records of the hospitalized patients were searched and those patients

found to have biliary parasitosis during ERCP were further examined retrospectively. Patients were evaluated according to age, sex, symptoms, indications for ERCP, treatment strategy (medical, operative, or endoscopic), laboratory tests [complete blood count, eosinophilia in blood smears, serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), GGT, ALP, total and indirect bilirubin levels], and imaging methods. Moreover, antibody levels were noted for patients with cyst hydatid disease and fasciola hepatitis.

Results

Between January 2000 and June 2007, 3,548 ERCPs were performed for different indications in our department. Of the 3,548 patients who underwent ERCP with the diagnosis of obstructive jaundice and/or cholangitis, 24 were found to have biliary parasitosis (mean age 48.6 year, range 15–77, 16 females). All the ERCP records were searched, and the laboratory and the imaging findings of those found to have biliary parasitosis were further examined. All the patients were hospitalized for treatment. The primary symptoms of the patients were right upper quadrant abdominal pain and cholangitis. The characteristics of the patients are shown in Table 1. Of the 24 cases with biliary parasitosis, 16 were found to have hydatid cyst, four *Fasciola hepatica*, and four *Ascaris lumbricoides* infestation (Table 2). About 17 cases were living in rural areas. The remaining seven patients (all of them had hydatid cyst) were living in urban

Table 1 Demographic and laboratory parameters of patients with biliary worms

	N	24
	Sex (female/male)	16/8
	Median age, years	39 (15–77)
Symptoms	Biliary colic	83.3% (20/24)
	Cholangitis	66.6% (16/24)
	Jaundice	66.6% (16/24)
Laboratory results	Median serum GGT level) (N: 5–36 U/l)	241 (72–621)
	Median serum ALP level) (N:35–104 U/l)	349.5 (72–867)
	Median serum AST level) (N: 0–31 U/l)	342.5 (98–746)
	Median serum ALT level) (N: 0–34 U/l)	263 (120–578)
Biochemical test	Median total bilirubin level (N: 0.3–1.2 mg/dl)	8.75 (2.30–18.9)
	Median direct bilirubin level) (N: 0–0.3 mg/dl)	5.4 (1.7–14.3)
Hematological test	Median white blood cell/mm ³	12,000 (6,500–24,000)
	Eosinophilia (%)	87.5% (21/24)
Serologic examination	Positivity of serologic examination	83.3% (20/24)
Hepatobiliary image	Ultrasonography	100% (24/24)
	Computerized tomography	75% (18/24)
	Magnetic resonance imaging	58.3% (14/24)
	MR cholangiography	41.65 (10/24)

Table 2 Distribution of biliary parasites

	<i>N</i>	%
Total number of ERCP	3,548	100
Number of biliary parasites	24	0.66
Hepatobiliary hydatid disease		
Compression by the cyst on the bile duct	8	0.22
Cyst rupture in the biliary tract	8	0.22
Fascioliasis	4	0.11
Ascariasis	4	0.11

areas. All of the seven patients determined to have been living in urban areas were found to have a past history of living in rural or visiting a rural area during holidays. The patients with fasciola and *Ascaris* infestation were found to live in southeast Turkey where poor socio-economic conditions exist.

Of the 16 cases with hydatid cyst, obstruction of the biliary tract was noted in eight cases (due to compression by the cyst on the bile duct; these cases were operated following ERCP). In all patients with hydatid cyst, the diagnosis was

confirmed by ultrasonographic examination and serological laboratory tests. US showed degenerative cysts, which should be suspected of biliary communication in eight patients. ERCP revealed biliary rupture between the cyst cavity and the biliary system in eight patients. After endoscopic sphincterotomy (ES), membranes of the cysts were extracted while the choledochus was examined using the balloon method (Fig. 1). Three of these patients received surgical treatment because of the large communication between the cyst cavities and the hepatic ducts diagnosed with ERCP. Of the eight patients with compression to the bile ducts, the compression was on the right hepatic duct in five patients and on the left hepatic duct in the latter three patients. During ERCP, plastic stents were placed to all patients. Afterwards, operations were performed in all cases.

Ascaris lumbricoides was detected in four cases, all of whom were from southeastern Turkey. Of the four cases, three were diagnosed during ERCP while one was suspiciously diagnosed with US before ERCP was performed and one was found to have biliary stones in accordance with the parasitic infestation (Fig. 2). All patients had biliary colic and acute cholangitis. We had to remove the

Fig. 1 **a** Ruptured hydatid cyst in the biliary tract.
b Sphincterotomy.
c–d Membranes of the cysts were extracted while the choledochus was examined using the balloon method

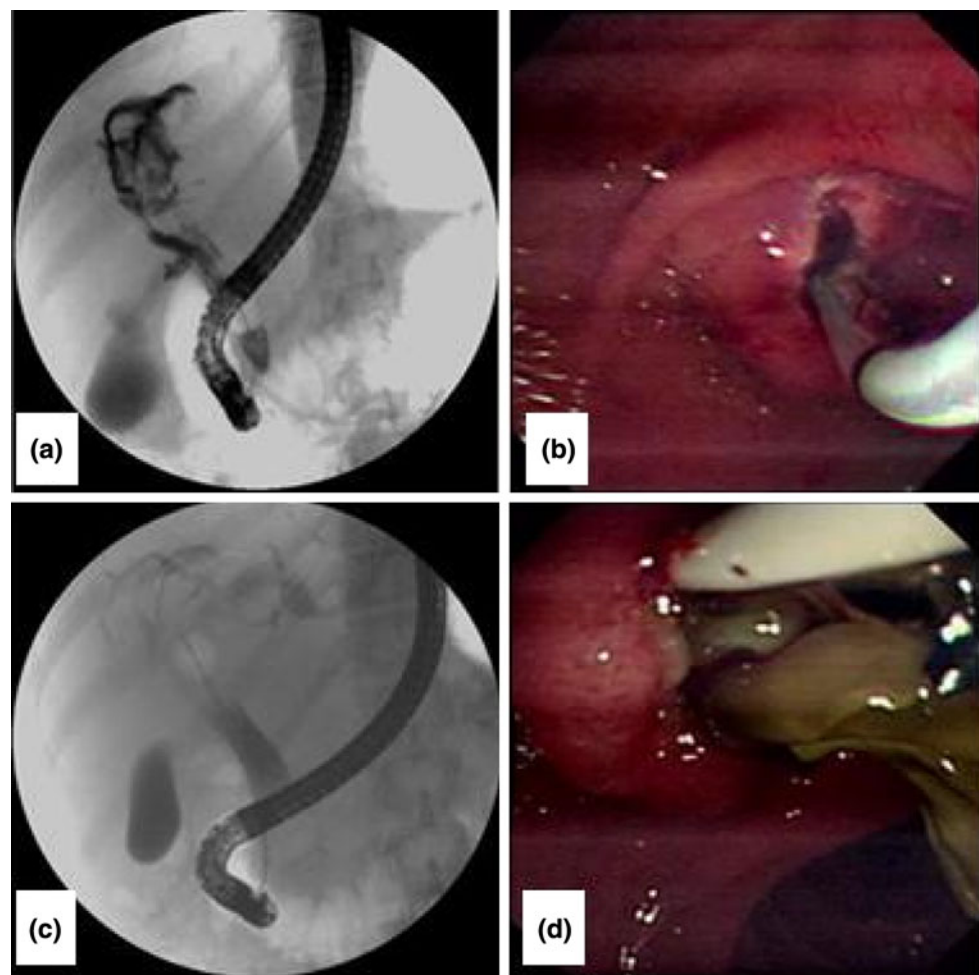




Fig. 2 *Ascaris lumbricoides* extracted by using the balloon method

worm in all cases by wide papillotomy followed by basket extraction. We did not experience any major complications during or following the procedures. After the endoscopic procedure, all patients received mebendazole. At the end of the medical treatment, none of the patients' stool specimens were found to contain *Ascaris* ova.

Fasciola hepatica was found in four cases. All patients were referred to our hospital with the suspicion of obstructive jaundice and choledocholithiasis. US revealed minimal intrahepatic and mild extrahepatic biliary dilatation while other organs were normal, and no stones were observed. Of the four cases with *F. hepatica*, one was suspected to have parasitic infestation during the ultrasonographic examination. However, in the other three patients, no suspicion of parasitic infestation was obtained with US and/or CT. Blood tests revealed mild eosinophilia in all cases.

ERCP demonstrated a small linear filling defect and crescent-like shadows and a jagged appearance in the distal dilated parts. ES was performed, and the living mobile worms were removed from the choledochus by a balloon (Fig. 3). After ERCP, triclabendazole was administered at a dose of 10–12 mg/kg for 1 or 2 days until symptoms disappeared and biochemical values returned to normal. Cholangitis did not occur in any of the patients after the procedure.

Discussion

Parasitic diseases are prevalent in some endemic areas, but such diseases may now have more extensive geographic distribution because of increased travel. Thus, sporadic

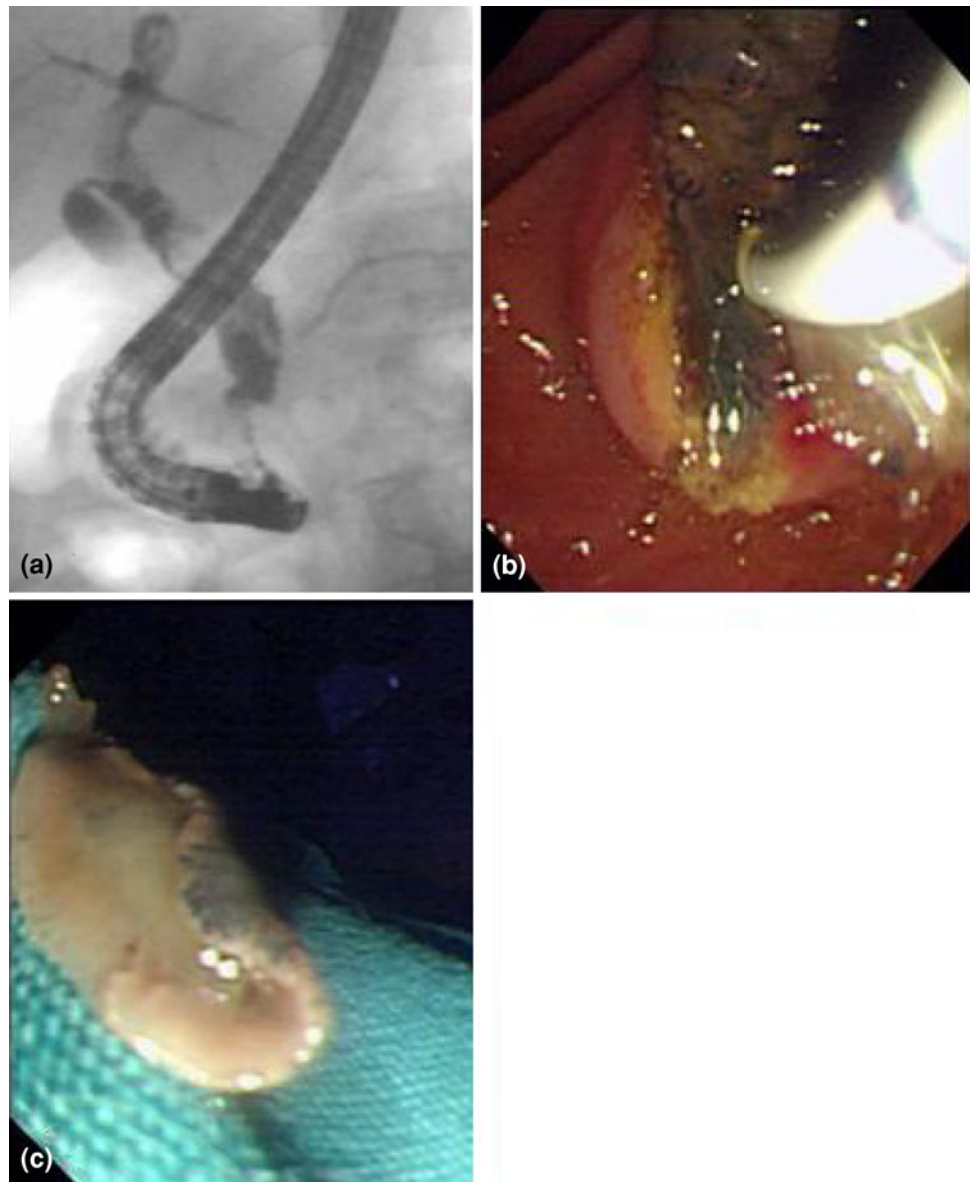
cases are encountered among immigrants in nonendemic areas.

Echinococcosis is the most frequent cause of hepatic cysts, and it is a disease that is endemic in many parts of the world. In Turkey, the most common species is *Echinococcus granulosus*. Hydatid cysts can be asymptomatic, depending on their location and/or size. Cyst growth is expansive, involving a concentric increase in size, and can create pressures of up to 80 cm H₂O. Up to one-third of patients with hepatic hydatid disease experience complications such as rupture into the biliary tree, thorax, or peritoneum; secondary infection; anaphylactic reaction; sepsis; or a need for liver replacement [14].

Cholestasis may also be seen in the liver. Sometimes the rupture of cysts results in cholangitis, pleuritis, peritonitis, liver abscess, or sudden death due to anaphylaxis [15, 16]. The incidence of rupture into the biliary tree varies widely in the literature, ranging from 1.3 to 25% [14, 17, 18]. Ormeci et al. reported that a total of 72 patients were diagnosed with hepatic hydatid disease via ultrasound and serologic tests. ERCP revealed communications between biliary ducts and cyst cavities in nine patients (12.5%) [19]. In our study, cyst rupture into the biliary tract was detected in eight cases; and after ES, membranes of the cysts were extracted while the choledochus was examined using the balloon method. Three of these patients received surgical treatment because of the large communication between the cyst cavities and the hepatic ducts diagnosed with ERCP. During the ERCP procedure, for eight patients detected to have compression to the bile ducts, plastic stents were placed in the proximal segment of the compression region. Afterwards, the patients were operated on. Hydatid disease can be treated surgically when the cysts are uncomplicated and are located at the periphery of the liver. However, surgical treatment has high mortality (0–8%) and morbidity (69%) rates [20, 21]. Medical treatment with mebendazole or even albendazole for the hydatid disease is not effective in 30% of cysts. Another 40% of cysts will recur in a short time after the cessation of treatment [22, 23]. Percutaneous treatment has become very popular over the last two decades due to its lower mortality and morbidity rates [24–28]. Before performing percutaneous treatment, it is very important to know whether there is a relation between the biliary duct and the cyst cavity. Life-threatening complications such as liver abscess, endotoxemia, and cholangitis may develop when there is a relationship between the cyst cavity and the biliary tract.

F. hepatica is a trematode that infects cattle and sheep; humans are accidental hosts. Hepatic fascioliasis manifests as clusters of microabscesses arranged in a characteristic tract-like fashion, usually in the subcapsular regions, and shows slow evolution of the lesion on follow-up examinations [29, 30]. On cholangiograms, biliary fascioliasis is

Fig. 3 **a** Small linear filling defect and crescent-like shadows in the distal part of the choledochus. **b** *Fasciola hepatica* removed from the choledochus by a balloon. **c** Appearance of *Fasciola hepatica* after the procedure



characterized by nonspecific biliary dilatation and single or multiple small filling defects that represent flukes themselves [29]. The majority of patients are asymptomatic, with symptoms limited mostly to heavily infected persons.

Infections occur worldwide in areas where sheep and cattle are raised, including Europe, Australia, and other developed countries. In one study from Spain, 37 hepatobiliary fascioliasis cases were reported between 1975 and 1999. Thirty-two were in the liver invasive stage and in five the biliary tree was invaded [31]. Although *F. hepatica* infestation is not common in Turkey, this infestation is recently being more frequently reported in patients [32, 33]. In our study, *F. hepatica* infestation was determined in only four of the cases who underwent ERCP for extrahepatic cholestasis. In these cases, medical treatment was

applied after ES and balloon retrieval and the infestation was entirely eradicated.

Ascariasis is one of the most common helminthic diseases in humans [12]. Clinical manifestations of ascariasis are often vague and non-specific. *Ascaris lumbricoides* residing in the small intestine may migrate into aberrant sites, mostly into the bile duct through the duodenal papilla, and cause biliary colic and obstructive jaundice. Hepatobiliary and pancreatic ascariasis is a frequent cause of biliary and pancreatic disease in endemic areas. It can cause biliary colic, acute cholecystitis, acute cholangitis, acute pancreatitis, and hepatic abscess [34]. Ascariasis can also cause postcholecystectomy syndrome [35]. Parasitic diseases usually present with characteristic imaging findings. US is the imaging method of choice for diagnosis as well as for

the follow-up of hepatobiliary ascariasis [36]. CT is valuable in showing the extent of possible complications of biliary ascariasis. MR imaging and MRCP with 3-D MIP of the biliary tree are excellent non-invasive means of showing biliary ascariasis. ERCP show a long tubular filling defect in the bile duct or gallbladder [37]. ERCP may be mainly used for endoscopic removal of worms in an already diagnosed case [38]. Prevalence of hepatobiliary ascariasis during ERCP procedure in endemic areas has been reported at rates of 18–30%. More than 80% of patients with biliary ascariasis are treated successfully by ERCP [34, 39]. In our study of the 3,548 ERCP procedures, only four patients were diagnosed as having biliary ascariasis. All of them presented with acute cholangitis. In one patient, ultrasonographic examination of the abdomen led to suspicious diagnosis of the condition. Worms were removed with the help of a Dormia basket after ES in four patients. In one of the patients, choledocholithiasis was determined simultaneously. No complications of endoscopic therapy were observed. After the ERCP procedure, all patients receive medical treatment. Pyrantel pamoate, mebendazole, albendazole, and levamisole are effective drugs and can be used for mass therapy to control ascariasis in endemic areas [37]. ES application is still controversial in patients with biliary ascariasis. Sandouk et al. reported 300 pancreatic-biliary ascariasis patients. Most patients (232 patients; 77%) had previously undergone an ES. They suggested that in endemic countries, ascariasis should be suspected in patients with pancreatic-biliary disease, especially if a cholecystectomy or sphincterotomy has been performed in the past [34]. Alam et al. documented 77 consecutive patients with hepatobiliary and pancreatic ascariasis over 5 years. In 94.8% of the cases, they had to remove the worm by wide papillotomy followed by basket extraction. They did not experience any major complications during or following the procedures. They suggested that endoscopic extraction was a safe and effective procedure for the treatment of hepatobiliary and pancreatic ascariasis [40]. Likewise, recurrence after ES did not occur in our patients.

In conclusion, in our study, biliary parasitosis found incidentally during ERCP procedure was ~0.66%. Hydatid cyst was predominant. According to the results of this study, we suggest that ERCP should be used for the diagnosis and treatment of biliary parasitic infestations.

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