CLONORCHIASIS-ASSOCIATED PERFORATED EOSINOPHILIC CHOLECYSTITIS

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Abstract. Clonorchiasis, a disease caused by infection with Clonorchis sinensis, is endemic in the Far East. Cholestatis, pyogenic cholangitis, cholecystitis, and biliary tract obstruction are common complications of chronic infection. Although cholecystitis caused by clonorchiasis is common, it is rarely reported as resulting from eosinophilic infiltration. We report a rare case of clonorchiasis-associated perforated eosinophilic cholecystitis and review the relevant literature.

INTRODUCTION

Clonorchis sinensis is one of the most common zoonotic parasites of humans. Humans are infected by ingesting raw or inadequately cooked secondary intermediate hosts, mainly freshwater fish, containing metacercariae. After excysting in the duodenum, metacercariae migrate into the biliary tract through the ampulla of Vater and mature into adult worms.1 The primary lesions are inflammations around the bile ducts that lead to hyperplasia of epithelial cells, metaplasia of mucosa cells, and progressive periductal fibrosis. Hepatobiliary diseases including cholelithiasis, pyogenic cholangitis, cholecystitis, biliary tract obstruction, and cholangiocarcinoma are reported as long-term complications of clonorchiasis.1 Although cholecystitis is common in clonorchiasis and eosinophilia is one of the human immune responses to parasite infestation, only two cases of eosinophilic cholecystitis associated with clonorchiasis are described in the English literature.2 Unlike these two cases, the patient in our report had perforated eosinophilic cholecystitis, and C. sinensis ova were found in the necrotic gallbladder mucosa.

CASE REPORT

A previously healthy 77-year-old Hakkanese man came to a local clinic with upper right abdominal pain for the past three days. The abdominal pain persisted despite medication. Nausea, vomiting, and diffuse abdominal pain occurred and he was sent to an emergency room. The patient lived in Mei-Nung in southern Taiwan and reported a history of occasional ingestion of raw freshwater fish (eaten as sashimi) over a ≥ 30-year period.

The patient had a temperature of 37°C, a heart rate of 118 beats/minute, a respiration rate of 18 breaths/minute, and a blood pressure of 136/51 mm of Hg. Physical examination indicated an acutely ill man with icteric sclera and diffused abdominal tenderness. No active lung lesion appeared on his chest radiograph. An abdominal radiograph showed intestinal ileus without visible free air. He had a white blood cell count of 8,730/μL (89% neutrophils, 7% lymphocytes, 3% monocytes), a hemoglobin level of 13.0 g/dL, and a platelet count of 223,000/μL. Biochemical test showed a blood urea nitrogen level of 52 mg/dL, a serum creatinine level of 3.7 mg/dL, and a alanine transaminase level of 165 U/L, an aspartate transaminase level of 91 U/L, a total bilirubin level of 10.7 mg/dL, a direct bilirubin level of 5.8 mg/dL, a C-reactive protein level of 195 mg/L, and a glucose level of 128 mg/dL. Electrolytes, amylase, and lipase were within normal limits.

Abdominal computed tomography showed dilated peripheral intrahepatic ducts, a hepatic cyst, a distended gallbladder, and fluid accumulation in the pelvic cavity (Figure 1A and B). The patient underwent a laparotomy for possible peritonitis. During surgery, a perforated gallbladder with a thickened wall, turbid bile, and gallstones were found. The common bile duct (CBD) was not dilated. Upon exploring the CBD, numerous parasites were found. Approximately 80 parasites were removed. Each parasite was elliptical in shape and approximately 1.5–2 cm in size. No parasite was found in the resected gallbladder. No CBD stone was found during surgery by choledochoscopy. Approximately 350 mL of bile-like ascites was collected from the abdominal cavity. A 20-Fr T-tube was implanted in the CBD for drainage. Parasite ova were found in drained bile and stool. Several parasites were drained out of the T-tube postoperatively. Infestation with C. sinensis was diagnosed on the basis of the morphology of adult parasites and ova. The patient was treated with praziquantel, 25 mg/kg orally three times a day one day. No parasites were drained from the T-tube by the sixth postoperative day.

Pathologic examination of the resected gallbladder showed diffuse inflammatory necrosis of the mucosal layer and parasite ova (Figure 1C). Additionally, numerous eosinophils infiltrated the submucosal and stromal layers of the gallbladder wall (Figure 1D). Blood, ascites, and bile cultures showed no bacterial growth. Total bilirubin and serum creatinine levels gradually returned to normal values. The postoperative course was uneventful, and the patient was discharged and periodically monitored in the outpatient department. No dilatation or obstruction of intrahepatic or extrahepatic ducts was observed on T-tube cholangiography performed six weeks postoperatively (Figure 2). The T-tube was then removed. The patient has had no recurrence of cholangitis and C. sinensis ova were not found in follow-up stool samples.

DISCUSSION

Clonorchiasis is endemic in the Far East, especially in South Korea, China, Vietnam, Japan, and Taiwan.3 Clonorchiasis has been observed since 1915, and the overall human infection rate is approximately 1.5% in Taiwan.4 Miao-Li County in northern Taiwan, the Sun-Moon Lake area in central Taiwan, and Mei-Nung township in southern Taiwan are the three most highly endemic areas, with human infection.
rates of 57%, 52%, and 52%, respectively. A higher incidence of clonorchiasis is found among the Hakkanese ethnic group, possibly because raw freshwater fish is a common food eaten at feasts. Our patient is Hakkanese, lives in Mei-Nung, and has a history of eating raw freshwater fish, which predisposes him to clonorchiasis.

Although cholecystitis and eosinophilia are common in clonorchiasis and human parasitic infestations, respectively, only two cases of eosinophilic cholecystitis caused by clonorchiasis have been reported. Table 1 summarizes the clinical characteristics of eosinophilic cholecystitis associated with clonorchiasis. Unlike the previously reported cases, the gallbladder of our patient was perforated and *C. sinensis* ova were found in the gallbladder mucosa (Figure 1C). No eosinophilia was found in the peripheral blood of our patient, which suggests that eosinophilic infiltration in the gallbladder wall was a local reaction to parasite infestation. In addition, *C. sinensis* ova found in gallbladder mucosa might have been the cause of eosinophilic cholecystitis.

Eosinophilic cholecystitis is rare, with an incidence of 0.5–6.4% in cholecystectomy specimens. Although more than 90% of transmural infiltrating inflammatory cells are eosinophils, the etiology of eosinophilic cholecystitis is not clearly understood and might be associated with hypersensitivity to antibiotics, other drugs, herbal medicines, hepatic echinococcosis, or as a variant manifestation of eosinophilic gastroenteritis. The possible pathogenesis of clonorchiasis-induced eosinophilic cholecystitis might be an allergic reaction to the metabolites released from the adult worm in the CBD and gallbladder.

*Clonorchis sinensis* and *Ascaris lumbricoides* are the two most common parasites that involve the biliary system in humans and are associated with hepatolithiasis. In addition, cholelithiasis is one of the common complications of chronic clonorchiasis. However, only gallstones were found in our patient. The relationship between gallstones and clonorchiasis is controversial. Teoh reported that the worm or egg can cause biliary tract obstruction and serve as a nidus for stone formation. However, in studies conducted by Hou and
others in Taiwan\textsuperscript{13} and Choi and others in South Korea,\textsuperscript{14} gallstones were found in 85 (9\%) of 947 and 14 (4\%) of 316 in infested groups, respectively. However, there were no statistically significant differences when compared with the non-infested groups. Without further examination of the gallstones found in our patient, it would be difficult to determine that gallstones were caused by clonorchiasis or were just an incidental finding.

Our patient had dilated peripheral intrahepatic ducts, but the extrahepatic ducts and CBD were not dilated, as shown by abdominal computed tomography (Figure 1A); this is one of the characteristic imaging findings of clonorchiasis.\textsuperscript{15} The discrepant dilatation of the peripheral intrahepatic ducts and extrahepatic biliary tract might be due to the smaller size of the intrahepatic ducts. These ducts would be easily obstructed by parasites, resulting in dilatation.\textsuperscript{16} The dilated intrahepatic ducts of our patient returned to normal size after treatment (Figure 2). In addition, jaundice is uncommon in cholecystitis without biliary tract obstruction. Thus, clonorchiasis should be one of the differential diagnoses of patients with cholecystitis, jaundice, and dilated peripheral intrahepatic ducts without extrahepatic duct dilatation, especially in regions where clonorchiasis is endemic or if the patient immigrated from an disease-endemic region.

In summary, clonorchiasis-associated eosinophilic cholecystitis is rare. The true prevalence and pathogenesis of eosinophilic cholecystitis caused by clonorchiasis requires further study.

Received August 20, 2006. Accepted for publication October 24, 2006.

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REFERENCES


### TABLE 1
Clinical characteristics of eosinophilic cholecystitis associated with clonorchiasis*

<table>
<thead>
<tr>
<th>Age, years/sex</th>
<th>Clinical presentation</th>
<th>Blood examination</th>
<th>Gallbladder</th>
<th>Dilated CBD</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>65/M</td>
<td>Epigastric pain</td>
<td>Leukocytosis (−)</td>
<td>Gallstone (+)</td>
<td>No</td>
<td>2</td>
</tr>
<tr>
<td>50/M</td>
<td>RUQ pain</td>
<td>Eosinophilia (−)</td>
<td>Worm (−), ova (−)</td>
<td>Yes</td>
<td>2</td>
</tr>
<tr>
<td>77/M</td>
<td>Nausea, vomiting, RUQ pain</td>
<td>Leukocytosis (−)</td>
<td>Gallstone (+)</td>
<td>No</td>
<td>PR</td>
</tr>
</tbody>
</table>

*RUQ = right upper quadrant of abdomen; PR = present report.