Acute Acalculous Cholecystitis Caused by *Giardia lamblia*

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**Abstract**

We report a case of a 70-year-old man with acute acalculous cholecystitis caused by *Giardia lamblia*. Contrast-enhanced computed tomography (CT) showed distention of the gallbladder due to a pericholecystic abscess without gallstones. Magnetic resonance cholangiopancreatography and drip infusion cholecystocholangiography-CT demonstrated a stricture of the hilar bile duct and cystic duct obstruction. We conducted transpapillary bile duct brush cytology and a biopsy of the hilar bile duct stricture; numerous active trophozoites of *Giardia lamblia* were observed without malignant findings. We considered this bile duct lesion to be biliary giardiasis. Biliary giardiasis should be taken into consideration when diagnosing acute acalculous cholecystitis.

**Key words:** *Giardia lamblia*, acute acalculous cholecystitis, biliary giardiasis, metronidazole

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**Introduction**

Acalculous cholecystitis is an acute inflammation of the gallbladder in the absence of gallstones. It comprises from 2-15% of all cases of acute cholecystitis and occurs in critically ill patients (1, 2). The causes of acute acalculous cholecystitis include severe infections, malignant diseases, trauma, surgery, and systemic diseases, and it is frequently associated with more serious morbidities and higher mortality rates than calculous cholecystitis (3, 4).

Giardiasis is caused by the protozoa *Giardia lamblia* and is a travel-related infectious disease, sexually transmitted disease, and opportunistic infectious disease (5). The number of patients with giardiasis is comparatively high in developing countries; however, the condition occurs worldwide (6, 7). *G. lamblia* attaches to the mucosal tissues of the duodenum and upper small intestine and causes persistent diarrhea or malabsorption, which is associated with body weight loss (8). Although many cases of intestinal giardiasis have been reported, few involved the biliary tract. Accordingly, the clinical manifestations of biliary giardiasis have not been fully clarified.

We describe a rare case of acute acalculous cholecystitis due to biliary infection by *G. lamblia*.

**Case Report**

A 70-year-old man was admitted to our hospital in September 2015 because of upper abdominal pain and a fever. His medical history included rheumatoid arthritis and pulmonary emphysema, and he was taking oral immunosuppressive agents, such as methotrexate and adalimumab. He used well water for drinking and had kept a Maltese dog as a pet for 30 years. Moreover, he had traveled to southeast Asian countries about 10 years earlier. On a physical examination, the patient had a body temperature of 38.3°C, pulse rate of 89 beats per minute, and blood pressure of 163/78 mmHg. His abdomen was soft and flat but revealed right-upper-quadrant tenderness with Murphy’s sign. Laboratory
data showed an elevated white blood cell count and serum C-reactive protein level at 12,600/mm$^3$ (normal range, 3,600-9,600/mm$^3$) and 12.9 mg/dL (normal range, ≤0.3 mg/dL), respectively. His serum total bilirubin, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and γ-glutamyl transpeptidase levels were slightly elevated to 0.69 mg/dL (normal range, 0.3-1.2 mg/dL), 50 U/L (normal range, 13-33 U/L), 13 U/L (normal range, 6-30 U/L), 594 U/L (normal range, 100-340 U/L), and 80 U/L (normal range, 10-47 U/L), respectively. Regarding tumor markers, his serum levels of carcinoembryonic antigen and carbohydrate antigen 19-9 were 1.8 U/mL (normal range, <5.0 ng/mL) and 474 U/mL (normal range, <37 U/mL), respectively.

Fig. 1 provides a timeline of the patient’s clinical course as described in this article. Abdominal ultrasonography and contrast-enhanced computed tomography (CT) showed distention of the gallbladder with peripheral cholecystic and perihepatic fluid collections without gallstones (Fig. 2). Pericholecystic fluid collection was irregularly rounded with peripheral rim enhancement and a hypodense lesion in segment 5 of the liver, which communicated with the gallbladder. Based on these findings, we diagnosed the patient with acute cholecystitis with pericholecystic abscess. We considered performing percutaneous trans-hepatic gallbladder drainage (PTGBD). However, there was a possibility of acute acalculous cholecystitis due to malignant biliary dis-
ease at the time of hospital admission. PTGBD was considered at risk for abdominal dissemination via a PTGBD tube; therefore, we started conservative therapy without gallbladder drainage. The patient received empirical antibiotic therapy with cefozopran 2.0 g per day intravenously from the date of hospital admission for 14 days and experienced clinical improvement with amelioration of his abdominal pain and overall condition on Day 7. Magnetic resonance cholangiopancreatography (MRCP) on Day 7 and drip infusion cholecystochoangiography (DIC)-CT on Day 11 demonstrated a stricture of the hilar bile duct and cystic duct obstruction (Fig. 3). As gallstones were not noted on these imaging examinations, we performed endoscopic ultrasonography (EUS) on Day 11 to rule out cholangiocarcinoma. However, we could not detect the hilar bile duct, and a detailed observation of the target lesion was impossible by EUS. Thus, endoscopic retrograde cholangiopancreatography (ERCP) was necessary to rule out malignant biliary disease.

Figure 3. Magnetic resonance cholangiopancreatography (MRCP) (A) and drip infusion cholecystochoangiography (DIC) -CT (B) findings before metronidazole treatment. The images demonstrated a stricture of the hilar bile duct and cystic duct obstruction.

ERC on Day 13 revealed a slightly stenotic lesion of the hilar bile duct with a smooth luminal surface (Fig. 4A), and transpapillary intraductal ultrasonography (IDUS) of the bile duct indicated a continuously thickened wall from the upper to the lower bile duct with a smooth circular symmetric outer margin, a smooth inner margin, and a homogenous internal echo pattern. We conducted transpapillary bile duct brush cytology and a biopsy of the hilar bile duct stricture. (B) Transpapillary intraductal ultrasonography of the bile duct indicated a continuously thick wall from the upper to the lower bile duct with a smooth circular symmetric outer margin, a smooth inner margin, and a homogenous internal echo pattern.

Figure 4. (A) Endoscopic retrograde cholangiography revealed a slightly stenotic lesion of the hilar bile duct, and we conducted transpapillary bile duct brush cytology and a biopsy of the hilar bile duct stricture. (B) Transpapillary intraductal ultrasonography revealed a continuously thickened wall from the upper to the lower bile duct with a smooth circular symmetric outer margin, a smooth inner margin, and a homogenous internal echo pattern.
formed a random duodenal biopsy, and G. lamblia was detected in both a stool sample and biopsy specimens of the duodenum. Therefore, we considered this bile duct lesion to be biliary giardiasis and ultimately made a diagnosis of acute acalculous cholecystitis caused by G. lamblia.

The patient was discharged from our hospital on Day 15. After the diagnosis of biliary giardiasis on Day 19, the patient was treated with metronidazole 250 mg 3 times per day on Day 25 for 7 days. Three months after initiation of metronidazole therapy, follow-up MRCP and DIC-CT were conducted to validate the efficacy of metronidazole therapy for biliary tract and disprove malignant disease. MRCP and DIC-CT demonstrated dramatic improvement in the hilar bile duct stricture, and a cystic duct was clearly detected (Fig. 6). Furthermore, the pericholecystic abscess had disappeared, and the gallbladder exhibited a normal appearance. The patient is currently undergoing outpatient follow-up, and no relapse has occurred to date.

Discussion

We describe a case of acute acalculous cholecystitis due to G. lamblia. Giardiasis is a diarrheal disease caused by G. lamblia, which is a common intestinal protozoan parasite of humans. The prevalence of giardiasis is 2-5% in developed countries and 20-30% in developing and underdeveloped countries, largely due to unsanitary conditions (8, 9). G. lamblia infects approximately 2% of adults and 6-8% of children in developed countries worldwide (5). Accordingly, giardiasis is a global disease. The lifecycle of G. lamblia comprises an active form known as a trophozoite and an inactive form called a cyst. Trophozoites can be found in feces but rarely survive for a prolonged period outside the host. In contrast, cysts are the infectious and resistant form and can survive for several months outside the host. Giardiasis can be spread by ingestion of G. lamblia in feces from an infected person or animal, drinking water from sources contaminated with G. lamblia, such as untreated water from
lakes or wells, and contact with a person suffering from giardiasis (5, 8). Hence, travel to countries in which giardia-
sis is common is associated with a risk of infection. In the
present case, the patient frequently drank water from wells
in a mountainous area and had a pet dog. Moreover, he had
traveled to southeast Asian countries about 10 years earlier.
Therefore, the ingestion of contaminated water or food con-
taining G. lamblia was likely the source of his infection. Immunodeciency, hypochlorhydria, and achlorhydria in-
crease the susceptibility to giardiasis (10) and may be asso-
ciated with persistent infection. The patient did not have a
history of proton pump inhibitor or histamine H2 receptor
antagonist intake; however, he had been taking methotrexate
and adalimumab regularly for rheumatoid arthritis, which
might have led to the development of giardiasis.

A definitive diagnosis requires the microscopic identifica-
tion of cysts or trophozoites of G. lamblia (11). However,
Giardia infection is rarely diagnosed because organisms are
excreted only intermittently. Therefore, multiple stool speci-
mens collected over several days are usually required to de-
tect G. lamblia. Gardner et al. reported that one stool sam-
ple facilitates the detection of 60-80% of infections, two
stool samples 80-90%, and three stool samples enable detect-
one of >90% of infections (5, 12, 13). In patients who can-
not be diagnosed by an examination of the stool, endoscopy
with duodenal fluid sampling and a biopsy should be per-
formed (5). In this case, G. lamblia was detected in duode-
nal and biliary biopsy specimens, which facilitated the diag-
nosis of giardiasis.

Giardia infection has various clinical intestinal manifesta-
tions, including diarrhea, abdominal cramps, and upset
stomach or nausea (5, 10, 14, 15). Active trophozoites attach
to the mucous membrane of the duodenum and upper jeju-
um, the alkaline pH of which favors their growth, which is
responsible for the manifestations of giardiasis. These symp-
toms can last for 1 to 2 weeks or longer and may lead to
weight loss. Concerning biliary giardiasis, few cases have
been reported. The literature in the MEDLINE database was
searched for English-language papers from the year of data-
base inception to August 2016. The search strategies in-
cluded terms for Giardia lamblia, biliary, cholangitis, chole-
cystitis, and biliary giardiasis. The literature search in the
database generated only 6 articles with an abstract available
after reviewing the titles and abstracts for eligibility (16-21).
In the present case, the pathogenesis of biliary giardiasis in-
volves access to the bile duct by the active trophozoite via
the ampulla of Vater, followed by attachment to the bile duct
wall. An imaging examinations showed no gallbladder
stones but did reveal a biliary stenosis at the hilar bile duct
with acute cholecystitis. The distended gallbladder might
have partially compressed the hilar bile duct. Therefore, one
cause of biliary stricture is thought to be a Mirrizzi syn-
drome, in a broad sense. However, we suspected that cho-
langiocarcinoma may have been the cause of cholecystitis;
therefore, ERCP was performed to detect malignant disease.
Bile duct brush cytology and a biopsy of the hilar bile duct
striction revealed numerous active G. lamblia trophozoites,
which resulted in a diagnosis of biliary giardiasis. On com-
paring Fig. 3 (MRCP) and Fig. 4A (ERC), we found that
these cholangiography results were slightly different from
each other. A severe stenotic lesion was observed in the hi-
lar bile duct with MRCP despite the presence of mild hilar
biliary stricture with ERC. The bile duct wall of biliary
 giardiasis is flexible and relatively easy to expand using the
pressure of contrast medium during the ERC procedure.
This elasticity of the thickened bile duct wall may have
been the cause of the discrepancy between the MRCP and
ERC findings. The cystic duct was occluded by cholangitis
with giardiasis at the time of admission, which was consid-
 ered to be the direct cause of acute cholecystitis. The cystic
duct obstruction and hilar bile duct stricture were amelio-
 rated after recovery from cholangitis due to metronidazole
treatment.

The most common antibiotics used for the treatment of
 giardiasis are the 5-nitroimidazoles, which include metroni-
dazole, tinidazole, secnidazole, and ornidazole, with metro-
idazole being the most common (5, 22, 23). The efficacy
rate of monotherapy with a single course of treatment varies
from 60% to 100%, with an average of over 80% (5, 7).
Metronidazole is typically administered at a dose of 250 mg
3 times per day for 5-7 days for adults and has few side ef-
effects. The patient was administered metronidazole after ame-
lioration of acute cholecystitis, and the abnormal lesions in
the biliary tract showed almost complete improvement. Ac-
cordingly, metronidazole is considered to be efficacious as a
first-line treatment for biliary giardiasis. However, several
cases of treatment failure with nitroimidazoles for giardiasis
have also been reported (7, 24, 25). The treatment of such
cases of refractory biliary giardiasis should be reconsidered.

In summary, we report a case of acute acalculous chole-
cystitis with bile duct stricture due to G. lamblia. A c u t e
acalculous cholecystitis is generally associated with major
cardiac and abdominal surgery, malignant disease, severe
trauma, burns, prolonged fasting, and long-term total par-
enteral nutrition. However, biliary giardiasis should be con-
sidered as a cause as well. Because it is impossible to diag-
nose biliary giardiasis from only imaging findings, the first
step to diagnose it is to ask patients detailed questions.
Therefore, taking a thorough medical history, including in-
quiries into their habits, pets, travel history, and medications,
is fundamental and essential for diagnosing biliary giardia-
sis. The accumulation of further similar cases is necessary to
clarify the pathophysiology of biliary giardiasis.

The authors state that they have no Conflict of Interest (COI).

References

1. Ganpathi IS, Diddapur RK, Eugene H, Karim M. Acute acalculous
cholecystitis: challenging the myths. HPB (Oxford) 9: 131-134,
2007.
2. Poddighe D, Cagnoli G, Mastricci N, Bruni P. Acute acalculous
cholecystitis associated with severe EBV hepatitis in an immuno-
acalculous cholecystitis by Epstein-Barr virus infection: a rare as-
4. Savoca PE, Longo WE, Zucker KA, McMillen MM, Modlin IM. 
The increasing prevalence of acalculous cholecystitis in outpa-
with metronidazole as treatments for infections with Giardia duod-
9. Farthing MJ. Diarrhoeal disease: current concepts and future chal-
and Cryptosporidium organisms in fecal specimens. J Clin Micro-
12. Hiatt RA, Markell EK, Ng E. How many stool examinations are 
necessary to detect pathogenic intestinal protozoa? Am J Trop 
13. Goka AK, Rolston DD, Mathan VI, Farthing MJ. The relative merits of faecal and duodenal juice microscopy in the diagnosis 
14. Farthing MJ. Giardia comes of age: progress in epidemiology, immu-
nology and chemotherapy. J Antimicrob Chemother 30: 563-
ment of giardiasis in chronic diarrhoea and malnutrition. Arch Dis 
acidocalcious cholecystitis and duodenitis. Am J Gastroenterol 67: 265-
269, 1977.
17. McGowan JM, Nussbaum CC, Burroughs EW. Cholecystitis due 
to Giardia lamblia in a left-sided gallbladder. Ann Surg 128: 
1032-1037, 1948.
papillary stenosis due to Giardia lamblia in a patient with hyper-
immunoglobulin M immunodeficiency syndrome. Gastrointest En-
19. Aronson NE, Cheney C, Rholl V, Burris D, Hadro N. Biliary 

giardiasis in a patient with human immunodeficiency virus. J Clin 

granules: main pathologic bile component in patients with idi-
21. el Sheikh Mohamed AR, al Karawi MA, Yassew MI. Modern 
techniques in the diagnosis and treatment of gastrointestinal and 
22. Pasupuleti V, Escobedo AA, Deshpande A, Thota P, Roman Y, 

Hernandez AV. Efficacy of 5-nitroimidazoles for the treatment of 
giardiasis: a systematic review of randomized controlled trials. 
23. Zaat JO, Mank TG, Assendelft WJ. A systematic review on the 
TA. Treatment of patients with refractory giardiasis. Clin Infect 
giardiasis in Spanish travellers. Travel Med Infect Dis 11: 126-
129, 2013.