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Massive biliary ascariasis: an unusual cause of acute cholangitis

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SUMMARY

Acute cholangitis is a condition of bacterial infection following hepatobiliary tract obstruction, which signifies poor prognosis unless adequately drained. The most common cause of bile duct obstruction is choledocholithiasis, in contrast to parasitic infestation, a rare entity causing acute cholangitis nowadays. Therefore, we reported the case of a 68-year-old Thai man who presented with acute fever, intense right upper quadrant abdominal pain and jaundice for 2 days. His medical history was normal except for the history of intermittent biliary colic for a year. Endoscopic retrograde cholangiography was performed and demonstrated multiple, creamy-coloured roundworms coming out from the ampulla of Vater as well as a tubular filling defect in dilated common bile duct from cholangiography. He was diagnosed with acute cholangitis by biliary ascariasis and underwent endoscopic parasitic removal, which subsequently improved symptoms.

BACKGROUND

Acute cholangitis is a well-established hepatobiliary tract infection, which impacts high mortality unless drainage occurs.[1] The most common aetiologies are choledocholithiasis, benign or malignant biliary stricture, biliary stent obstruction, sclerosing cholangitis and rarely parasitic obstruction in respective order.[2] *Ascaris* is one of the parasites that can cause biliary obstruction and linked to biliary sepsis. To our knowledge, ascariasis is common in both tropical and low-income and middle-income countries, where they are perpetuated by untreated sewage used as a fertiliser and flowing into rivers and lakes. The prevalence of ascariasis in Thailand during 1997 was 0.36% of asymptomatic cases.[3] However, the prevalence has tended to decline over time, in consonance with socioeconomic status improvement, resulting in significant neglect of ascariasis in Thailand. The clinical spectrums are varied, with most being asymptomatic. Therefore, we aim to report the case of a patient with a diagnosis of acute cholangitis; wherein, *Ascaris* worms were found in the bile duct.

CASE PRESENTATION

A 68-year-old Thai man presented with intermittent right upper quadrant pain, nausea and vomiting for 12 months. Two days prior to admission, he had a fever, right upper quadrant pain and jaundice. His medical histories were essential hypertension and a long history of chronic obstructive pulmonary disease (COPD). His current medications were enalapril 5 mg, two times a day; salmeterol/fluticasone propionate (50/250), one puff twice a day and ipratropium bromide/fenoterol two puffs prn. On physical examination, his body temperature was 37.8°C, pulse rate was 99 beats per minute, blood pressure was 140/80 mm Hg and respiratory rate was 18 breaths per minute. He had jaundice with icteric sclera. Abdominal examination revealed mild abdominal distension, normal bowel sound and moderate tenderness at right upper quadrant; liver and spleen were not palpable.

INVESTIGATIONS

Laboratory investigation on admission revealed: white cell count 9.95×10^9/L (4.5–10.0 x 10^9/L), Polymorphonuclear neutrophils 60.9%, lymphocyte 29.2%, eosinophil 5.5%, haemoglobin 147 g/L (130–180 g/L), platelet count 230×10^9/L (150–450 x 10^9/L), total bilirubin 7.25% mg (0%–1.2% mg), direct bilirubin 6.11% mg (0%–0.3% mg), aspartate aminotransferase 60 U/L (10–50 U/L), alanine aminotransferase 114 U/L (10–50 U/L), alkaline phosphatase (ALP) 180 U/L (40–130 U/L), albumin 3.5% g (3.5%–5.2% g) and prothrombin time 11.6 s (control 12.4 s). The ultrasonography of his hepatobiliary system, as shown in figure 1, demonstrated a tubular-shaped hypoechoic lesion filling in the common bile duct (CBD) and a left hepatic bile duct causing bile duct dilatation 8 mm with upstream dilatation of a CBD, intrahepatic bile ducts both lobes of the liver and a subsequently unremarkable pancreas, he underwent endoscopic retrograde

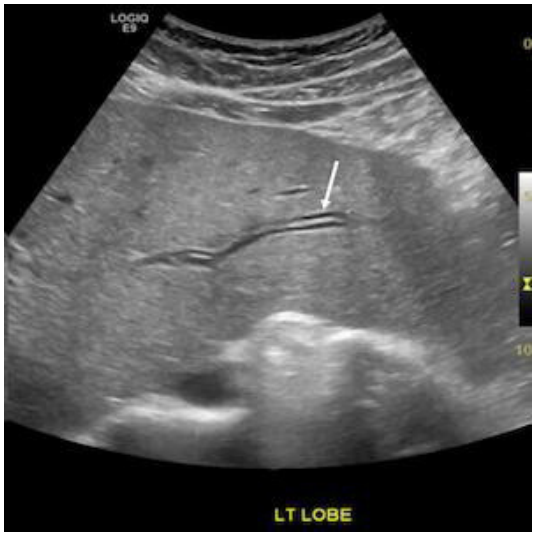

Figure 1 Ultrasonography of hepatobiliary showing a tubular-shaped hypoechoic lesion filling in a common bile duct and a left hepatic bile duct.

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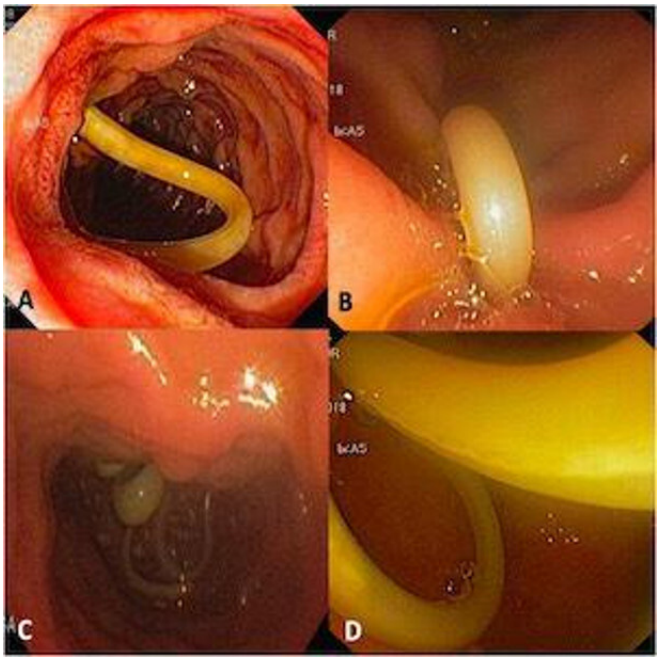

Figure 2 Endoscopic retrograde cholangiography showing multiple creamy-coloured roundworms. (A, B) Roundworms are coming out from the ampulla of Vater and (C, D) in the second part of the duodenum.

cholangiography (ERCP). The findings revealed multiple, creamy-coloured roundworms coming out from the ampulla of Vater, and the second part of the duodenum (figure 2). Cholangiography showed a tubular filling defect with CBD dilatation up to 7.3 mm in diameter, no intrahepatic duct dilatation, patent cystic duct and patent gallbladder (figure 3). He was diagnosed with acute cholangitis from hepatobiliary ascariasis (HBA).

Figure 3 Cholangiography showing a tubular filling defect (white arrow) with common bile duct dilatation up to 7.3 mm in diameter, no intrahepatic duct dilatation, patent cystic duct and patent gallbladder.

Figure 4 *Ascaris* worms which removed from bile ducts.

TREATMENT

Endoscopic removal was performed using balloon sweeping and rat-tooth forcep to remove the *Ascaris* worms (figure 4). He also received albendazole 400 mg once a day, for 14 days until passing all parasites from the stool.

OUTCOME AND FOLLOW-UP

His clinical condition gradually improved, his fever was gone, and he indicated no more abdominal pain. His follow-up liver function test was normal 2 weeks later.

DISCUSSION

Ascaris lumbricoides is one parasite infestation that causes biliary obstruction, and is complicated with acute cholangitis called: 'biliary ascariasis'. Twenty-five per cent of the world's population is estimated to be infested (0.8–1.22 billion people).[4] Ascariasis is common in tropical and low-income and middle-income countries, including Thailand; however, the prevalence has tended to decline over time in consonance with socioeconomic status improvement, resulting in significant neglect of a rare case of acute cholangitis in Thailand, biliary ascariasis.

During the late 80s and early 90s, HBA was a common manifestation of the intestinal ascariasis, particularly in Asian countries and accounted for 36.7% of ascariasis presentation.[5] The prevalence of infestation was directly proportionate with sanitation status, education level and usage of untreated sewage or human excreta as fertiliser. However, the number of reports from several parts of the world has declined over time in accordance with improved sanitation. This reason abated the attention to this entity, especially as a cause of CBD obstruction.

In humans, the life cycle of this parasite begins by ingestion of *A. lumbricoides* ova, which then hatch in the small intestine. These larvae invade the small bowel mucosa, migrate through the systemic circulation to the lungs, ascend the bronchial tree, and then are swallowed into the small intestine, where they mature into their adult form.[6] *A. lumbricoides* has a natural preference to migrate and seek out a small orifice. Consequently, it tends to enter the hepatobiliary system, via the ampulla of Vater, to

lodge: in the (1) ampulla, (2) CBD and (3) hepatic ducts. There is also a relatively rare proportion of gallbladder and pancreatic duct lodging.[7]

There is a female predominance (female/male ratio of 3:1) of ascariasis, comparatively with other nematode infestations.[8] The exact reason for this is unknown, but the effect of progesterone might play an essential role in the relaxation of the Sphincter of Oddi.[9] The affected age ranged from forty-to-seventy years and is usually around the mid-thirties.[10] Childhood manifestation of ascariasis usually presents with a clinical presentation of gut obstruction, intestinal colic, volvulus and intussusception as a result of the accretion of worm load and the small calibre of the biliary system.[10] Adult onset of ascariasis usually presents with various hepatobiliary manifestations, as in our case. Several factors that might increase HBA infection are the following; (1) Those who had a prior history of hepatobiliary surgery (cholecystectomy, choledocholithotomy, sphincteroplasty, endoscopic sphincterotomy,[10 11] (2) Pregnancy, probably owing to progesterone effects on ampulla during pregnancy,[12] (3) Perturbation of the environment surrounding the worm; for instance, fever, anaesthetics, and tetrachloroethylene used to treat hookworm infestation during the early 20th century.[9] However, we hypothesised there were no known risk factors in our case and that our patient's medical history of poorly controlled COPD and receiving corticosteroids during an exacerbation, may have led to an immunocompromised status, and might have been a risk factor for developing massive biliary ascariasis. There are various clinical manifestations and complications of HBA, depending on which organs are involved. Biliary colic is the most common HBA presentation, accounting for 56% of cases.[9] This is consistent with our patient's presentions as intermittent, dull aching pain located at the right, upper quadrant pain, either; recurrent or continuously lasting for a few days. Followed by acute cholangitis (25%), which was diagnosed by the evidence of systemic inflammation, cholestasis and imaging according to Tokyo guideline 2018.[13] Once the diagnosis has been established, the severity must be assessed. Various domains are evaluated for severity of instances, organ failure, white cell count, high-grade fever, age, bilirubin level and hypoalbuminaemia. Our aforementioned patient presented with three domains of diagnostic criteria and severity assessment showed mild severity. Acute cholecystitis (13%) in HBA presented with fever, right hypochondrial pain, which might be referred to the right scapular, and a palpable cystic mass might be present. The ultrasonography usually revealed a thick wall, distended gall bladder with biliary sludge.[9 11] Acute pancreatitis (6%) in HBA presented with acute abdominal pain, referring to the back, nausea and vomiting.[9] Liver abscess was a rare HBA presentation, which could present with either solitary or multiple abscesses. These abscesses might result from the dead ova released by female producing worms. Granulomatous inflammatory reaction with subsequent breakdown of eosinophilic infiltration.[7] The long-term complication of HBA is associated with biliary lithiasis and recurrent pyogenic cholangitis, as biliary sludge is often demonstrated. This provides an appropriate milieu for future stone formation. Indeed, part of macerated worms are formed in the nidus of such stones when followed-up in several years and these stones compose of calcium bilirubinate layers.[14] For an unexplainable reason, the biliary stone tends to occur in the intrahepatic duct, as reported in one large study from India.[7] This led to strong epidemiological correlations between ascariasis and the entity. The definite diagnosis depended on the direct visualisation of the worms in the biliary tree, especially in the endemic zone. However, this was not always straightforward as a consequence of the worm's nature to frequently move in-and-out of the duct within 7 days of presentation.[7] The diagnosis was based on clinical findings and abdominal ultrasonography in clinical practice, then confirmation by an endoscopic procedure.

Basic laboratory investigations, including complete blood count, liver function test and stool examination, were obtained for diagnosis. Peripheral eosinophilia and leucocytosis are common in ascariasis. Elevation of serum bilirubin, transaminases, ALP and gamma-glutamyltransferase could be present, depending on the extent of biliary involvement. Stool examination might also show the *A. lumbricoides* ova. Some patients, especially children who presented with gut obstruction, might pass the adult worms via vomitus. Although antibodies against ascariasis developed in infected patients, there was a low yield in immune-diagnosis because of the extensive cross-reactivity with other helminthic antigens.[7 11]

Ultrasonography is the imaging of choice, owing to its sensitivity and specificity to demonstrate both worms and their mobility in the biliary system over time.[9 11] The findings revealed a typical longitudinal image of a hyperechoic tubular structure, without acoustic shadow or a round hyperechoic structure, with a hypoechoic centre (parallel echoic strip). Other findings described were 'strip', 'inner tube' and 'spaghetti' signs.[15] A worm that did not change its position after 10 days was usually dead and macerated. The drawback of ultrasonography is its inability to not being able to detect the worms in the duodenum and the ampullary orifice. Therefore, ultrasonography was reported to miss up to 50% of HBA cases.[11] CT and MR cholangiography (MRCP) will demonstrate the intraductal linear filling of the worm, described as 'bull's eye' and 'eye-glass' signs.[16] In the presence of coexisting stones or dead or decaying worms, CT and MRCP had better visualisation because they could reveal the duodenum and the ampullary orifice, while ultrasonography could not. ERCP plays a fundamental role in HBA, as its role is both diagnostic and therapeutic, making for direct visualisation and extraction.

The treatment of HBA requires multimodalities and aspects

All patients with HBA infestation should be hospitalised because their degradation products and excreta could cause marked bowel oedema. There are three treatment aspects for biliary ascariasis.[11] First, the conservative treatment for acute cholangitis or cholecystitis played a crucial role for all HBA patients, which included broad-spectrum antibiotics in acute cholangitis, analgesics and intravenous fluids. Second, the treatment of helminthic included oral antihelminth, which acted as a paralysing agent to the adult worm, but none could affect the larval stage. The worm clearance was usually completed after 3 days of oral antihelminth, depending on gut transit time, pre-existing diarrhoea and worm load. Direct instillation of antihelminth to the biliary tree via endoscopically or nasobiliary tube infusion was not recommended because the degradation products would lead to further inflammation. The treatment regimens with a single dose of albendazole (400 mg) or a 3-day regimen of mebendazole (200 mg/day) have the highest efficacy (100%).[11] Other medications including pyrantel pamoate, levamisole, piperazine citrate and thiabendazole can be used as well with an efficacy of 90%–100%.[11] Other modalities were the Chinese study involving 50 cases, using Chinese herbal medicine and acupuncture that claimed 96% efficacy.[17]

Lastly, endoscopic and surgical management; usually indicated in one-fourth of patients, who did not respond to conservative treatment. Usually, clinical and ultrasonographic monitoring was indicated at 72 hours; if the symptoms persisted, endoscopy

was mandatory. ERCP for biliary drainage and decompression by snares, Dormia basket, and biopsy forceps is the treatment of choice in biliary ascariasis. Endoscopic worm extraction, from the ampullary orifices, rapidly relieved the symptoms in biliary colic.[5] Sphincterotomy could facilitate the remigration of the worm into the biliary tract. For this reason, the balloon dilatation of Oddi's sphincter is preferred. Almost 100% of endoscopic worm extraction cases from the ampulla were successful using grasping forceps, even if multiple sessions might be required. Those that were entirely within the bile duct were stimulated to migrate out to the papilla after contrast injection or could be extracted using a balloon, with a 90% Dormia basket succession rate. The complications of endoscopic procedures were hypotension and cholangitis, which were relatively low (6%).[10]

The surgical approach was usually indicated in patients with endoscopic failure, or whom had coexisting obstructive jaundice and intestinal obstruction. The surgical procedures included choledochotomy and removal of worms, cholecystectomy. In particular cases, choledochoduodenostomy, hepaticojejunostomy and pancreaticojejunostomy had also been performed.

In conclusion, *A. lumbricoides* is an unusual cause of acute cholangitis, despite their low prevalence. Ultrasonography has been advocated as a soft and quick diagnostic modality in suspicious cases, but there is a risk of false negative due to active migration of the worm. Endoscopic approach for bile duct clearance along with pharmacotherapy is the mainstay of treatment. Surgical approach is the alternative method spared for non-responder cases. However, such procedures usually require high technical expertise.

Learning points

- *Ascaris lumbricoides* is an unusual cause of acute cholangitis, despite their prevalence being as low as 0.04% in Japan and developed countries. The diagnosis of hepatobiliary ascariasis (HBA) is based on clinical suspicion. For example, a history of intermittent jaundice is a consequence of the worm's nature, which moves in-and-out of the duct, and compatible risk factors.
- The diagnosis of HBA is challenging because the worm is not always present inside the duct. The radiological modalities are the mainstay of the diagnostic approach. CT and MR cholangiography can demonstrate the pathology at the duodenum and ampullary orifice, while ultrasound cannot.
- Oral antihelminth acts as a paralysing agent to the adult worms and leads to spontaneous parasitic clearance by the peristalsis. Direct instillation is not recommended, as the worm's debris may lead to further inflammation.
- Endoscopic retrograde cholangiography plays a fundamental role in HBA, as its role is both diagnostic and therapeutic, making for direct visualisation and extraction.

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