Strongyloides stercoralis Infection Causing Obstructive Jaundice and Refractory Pancreatitis: A Lesson Learned from a Case Study

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Abstract

A 58-year-old Japanese woman came to our institution because of leg edema and abdominal distention. She had developed acute pancreatitis 5 times in the past 3 years. Dilation of the bile duct and main pancreatic duct without obstruction was observed on computed tomography and magnetic resonance cholangiopancreatography. The presence of Strongyloides stercoralis was highly suspected from the biopsy sample from the duodenal papilla. Polymerase chain reaction amplification and sequencing of small subunit rDNA from paraffin-embedded specimens identified the worm as S. stercoralis. All of the symptoms were considered to be associated with S. stercoralis infection. Therefore, the patient was treated with oral administration of ivermectin. Subsequently, symptoms and laboratory data improved. There has been no recurrence of the symptoms to date.

Key words: Strongyloides stercoralis, jaundice, pancreatitis, double duct sign, duodenitis

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Introduction

Strongyloides stercoralis, discovered by Normand in 1876 (1), is a common human parasitic nematode in tropical and subtropical regions, and occurs even in temperate zones. Filariform larvae usually infect humans through the skin of bare feet. After the host is infected, larvae migrate to the duodenum, grow into mature female worms, and lay eggs. Rhabditiform larvae that hatch from the eggs are excreted from the host via the stool. However, some rhabditiform larvae develop into filariform larvae, and can reinfect the host through the large intestine or the skin around the anus (i.e., autoinfection). Therefore, once the host is infected, this nematode is able to complete its life cycle and proliferate within the host, and the infection can persist for decades (2). Infection with S. stercoralis is estimated to be approximately 100 million people per year worldwide (3, 4). Of clinical significance, immunocompromised hosts are more likely to develop strongyloidiasis in their lifetime. In Japan, the southwestern islands of Kyushu were endemic areas of S. stercoralis infection. Until quite recently, elderly individuals still showed a high infection rate (5). It has also been documented that the patients who are infected with S. stercoralis are often infected with T-cell lymphotropic virus type 1, resulting in an immunsuppressed state (5). Disseminated strongyloidiasis occurs in such patients, which can cause abdominal pain, diarrhea, nausea, vomiting, and more rarely, functional ileus, malabsorption syndrome, sepsis, bacterial meningitis, jaundice, and pancreatitis (2, 5-8). However, cases of S. stercoralis infection demonstrating both jaundice and pancreatitis are extremely rare. We describe...
here a patient infected with *S. stercoralis*, who presented with both obstructive jaundice and refractory pancreatitis.

**Case Report**

A 58-year-old Japanese woman came to our institution because of leg edema and abdominal distention. She had developed acute pancreatitis 5 times in the past 3 years. She had lived in Okinawa Prefecture, in the southernmost part of Japan, during her childhood. Her childhood medical and social history was unremarkable. On admission, her weight was 39.5 kg. Laboratory analyses showed a white blood cell (WBC) count of 10,200 per mL (eosinophil count 0.2%) and an albumin level of 1.6 g per dL. The levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and γ-glutamyltransferase (γ-GTP) were 2 times higher, and the γ-GTP level was 9 times higher than the upper normal limit.

Jaundice was suspected and magnetic resonance cholangiopancreatography (MRCP) was performed. MRCP showed that the common bile duct and the main pancreatic duct at the pancreatic head were both dilated (11 mm and 6 mm, respectively), without obstruction (Fig. 2). Therefore, esophagogastroduodenoscopy (EGD) and endoscopic retrograde cholangiopancreatography (ERCP) were performed. EGD revealed edematous duodenal mucosa, duodenal erosion, and stenosis with a linear scar at the third portion of the duodenum. Stenosis of the duodenum was observed on duodenography using an endoscope (Fig. 3). Duodenal papilla containing pus was observed upon ERCP and endoscopic nasobiliary drainage (ENBD) (Fig. 4A). On ERCP, dilation of the biliary duct without obstruction was observed (Fig. 4B). After ENBD, the symptoms and laboratory data improved immediately. Histopathological examination of the biopsy specimen obtained from the duodenal papilla revealed a strongly suspected presence of *S. stercoralis* infection (Fig. 5). We therefore performed a DNA analysis of the worm extracted from a paraffin-embedded specimen (Fig. 6). Parasite DNA was extracted from the specimen with TaKaRa DEXPAT Easy (Takara Bio, Tokyo, Japan). The DNA was then amplified using a polymerase chain reaction (PCR) with *S. stercoralis* specific primer sets (9) and the band with expected size (101 bp) was confirmed (Fig. 7). Then the amplified DNA was sequenced. The obtained 34 bp sequence was assigned to be *S. stercoralis* 18S small subunit ribosomal RNA genes by Basic Local Alignment Search Tool (BLAST) analysis (Table 1).

All of the patient’s symptoms were considered to be associated with *S. stercoralis* infection. Therefore, the patient was treated with oral administration of ivermectin 6 mg, administered twice with a two-week interval. Subsequently, all symptoms, laboratory data, and intestinal edema on CT improved. There has been no recurrence of these symptoms to date.
Discussion

In the present case, the parasites were found in the duodenal mucosal epithelium and in the vicinity of the crypts. The parasites found in such sites include *S. stercoralis*, *Trichinella* sp., and *Capillaria philippinensis*.

The morphological features of *S. stercoralis* are as follows: 1) adult worms, rhabditiform larvae, and eggs are seen mixed together in the intestinal mucosal villus epithelium; 2) the mean transverse diameter of the adult female worm is approximately 40 μm; 3) muscle cells of the subcuticular layer are indistinguishable; and 4) the uterus of the female worm stains deeply with hematoxylin. *Trichinella* sp. is an ovoviviparous parasite and releases its larvae in the striated muscle cells; eggs are not seen outside of the uterus of the worm. *C. philippinensis* has a morphological similarity with the whipworm *Trichuris trichiura*, namely, it has a long esophagus which has a string of stichocytes (glandular unicellular cells) arranged in a row along the posterior portion of the esophagus, each of which communicates by a single pore with the lumen of the esophagus. Although the eggs in the present case are similar to those of whipworm, they did not have a thick shell and plugs at either end. Thus, *Trichinella* sp. and *C. philippinensis* were ruled out, and *S. stercoralis* was highly suspected.

In the present case, dilation of the biliary duct and pancreatic duct (i.e., double duct sign) without obstruction was observed on CT and MRCP. When ERCP was performed for the acute cholangitis, debris with pus was observed from the
Figure 5. a: Arrow shows a rhabditiform larva hatched from the egg. b: Arrows show the uteri of the parasites. c: Arrows show the intestinal tracts of the parasites. d: Arrows show the eggs.

The extraction of DNA from 5μm × 4 slices of the paraffin-embedded tissues.

1. PCR
   - Enzyme: KOD FX (TOYOBO)
   - Primer: SsF; GAATTCCAAGTAAACGTAAGTCATTAGC
   - SSR; TGCCCTGGAATTTGCTAGTTC
   - Condition; 94°C, 2minutes, (94°C 30 seconds, 60°C 30 seconds, 72°C 30 seconds) ×35, 72°C 2 minutes.

2. Rifining (Exo SAP-IT, Affymetrix)

3. Sequence (bigdye v3.1, 3130xl, life technologies)

Figure 6. The procedure for species identification by PCR using paraffin-embedded tissues is shown.

papilla after cannulation of the catheter, whereas biliary stenosis was not observed on cholangiography. Although *S. stercoralis* was not detected in the bile juice, the parasites were detected in the duodenal papilla biopsy. Moreover, all symptoms were thought to be associated with *S. stercoralis* infection, and there has been no recurrence of acute cholangitis or acute pancreatitis to date. Therefore, acute cholangitis and repeated acute pancreatitis were considered to be the results of papillitis caused by *S. stercoralis* infection, which then caused defects in bile juice and pancreatic juice secretion.

Several reports of jaundice and pancreatitis due to *S. ster-
Coralis infection have been published since the 1950s. Several causes of jaundice have been reported, including extrahepatic stenosis, intrahepatic obstruction due to granulomatous hepatitis, reflex spasm of the sphincter of Oddi, and papillary obstruction. Pijls et al. reported a patient with S. stercoralis infection who had jaundice with extrahepatic stenosis due to an enlarged pancreatic head, and who also had pancreatitis. The extrahepatic stenosis due to an enlarged pancreatic head disappeared after thiabendazole treatment (10). In general, granulomatous hepatitis refers to an inflammatory liver disease associated with granuloma formation in the liver. Poltera et al. reported that 3 out of 5 cases of granulomatous hepatitis due to S. stercoralis had cholestasis (11). Jaundice owing to reflex spasm of the sphincter of Oddi that is caused by S. stercoralis infection is rare, and it can also occur in Crohn’s disease (12).

Yoshida et al. reported a unique case of a patient with S. stercoralis hyperinfection who showed regurgitation of the contrast medium into the biliary and pancreatic duct in a barium meal study (13). Reports on papillary obstruction in jaundice due to S. stercoralis infection are very rare. Astagneau et al. reported a patient with jaundice caused by S. stercoralis infection who did not have papillary stenosis, in whom liver function improved and dilation of the intrapancreatic and common bile ducts resolved after thiabendazole treatment (7).

The reports on pancreatitis associated with S. stercoralis infection are more uncommon compared with jaundice associated with S. stercoralis infection (8, 10, 14, 15) (Table 2). In addition, the mechanism of pancreatitis caused by S. stercoralis has not yet been clarified. In general, an important finding in obstructive pancreatitis is pancreatic ductal dilation. However, the presence of a dilated pancreatic duct was not observed in most reported cases of pancreatitis caused by S. stercoralis. Our patient had repeated pancreatitis, and our findings of obstructive pancreatitis may be very rare and

**Figure 7.** The PCR products amplified with S. stercoralis-specific primers are shown.

### Table 1. The Top 3 BLAST Results of PCR Products Amplified with S. Stercoralis-specific Primers.

<table>
<thead>
<tr>
<th>Description</th>
<th>Max score</th>
<th>Total score</th>
<th>Query cover</th>
<th>E value</th>
<th>Ident</th>
<th>Accession</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strongyloides stercoralis 18S small subunit ribosomal RNA gene, partial sequence</td>
<td>48.1</td>
<td>48.1</td>
<td>94.1%</td>
<td>0.005</td>
<td>91%</td>
<td>AF279916.2</td>
</tr>
<tr>
<td>Strongyloides stercoralis 18S ribosomal RNA gene, complete cds</td>
<td>48.1</td>
<td>48.1</td>
<td>94.1%</td>
<td>0.005</td>
<td>91%</td>
<td>M84229.1</td>
</tr>
<tr>
<td>Strongyloides stercoralis 18S small subunit ribosomal RNA, partial sequence</td>
<td>40.1</td>
<td>40.1</td>
<td>94.1%</td>
<td>1.1</td>
<td>88%</td>
<td>AB923889.1</td>
</tr>
</tbody>
</table>

PCR: Polymerase chain reaction, RNA: ribonucleic acid, E value: expected value

### Table 2. Research on Pancreatitis due to Strongyloides stercoralis.

<table>
<thead>
<tr>
<th>Reference No.</th>
<th>AMY (U/L)</th>
<th>Diameter of main pancreatic duct (mm)</th>
<th>Evidence of S. stercoralis</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>4,367</td>
<td>N.A*</td>
<td>Stool</td>
</tr>
<tr>
<td>10</td>
<td>W.N.L</td>
<td>W.N.L</td>
<td>Stool</td>
</tr>
<tr>
<td>14</td>
<td>430</td>
<td>N.A</td>
<td>Duodenal biopsy</td>
</tr>
<tr>
<td>15</td>
<td>2,100</td>
<td>N.A</td>
<td>Bile juice</td>
</tr>
<tr>
<td>Present case</td>
<td>12**</td>
<td>6</td>
<td>Ampullary biopsy</td>
</tr>
</tbody>
</table>

AMY: amylase level
W.N.L: within normal limits
N.A: not available
*: obvious dilatation
**: amylase count on admission, but having past history of repeated acute pancreatitis
of S. stercoralis was observed in both patients. The biliary duct sign on MRCP, and edema of the duodenal mucosa of the biliary duct and pancreatic duct produced the so-called dou-
tis owing to unknown causes. In addition, dilation of the biliary duct and pancreatic duct have been published to

date (7, 14) (Table 3). Both patients had a history of travel-
ing to endemic areas. These cases had jaundice or pancreati-
tis owing to unknown causes. In addition, dilation of the biliary duct and pancreatic duct produced the so-called dou-
ble duct sign on MRCP, and edema of the duodenal mucosa was observed in both patients.

Our patient had spent most of her life in an endemic area of S. stercoralis infection on imaging. It was speculated that S. stercoralis infection in the duodenum and papilla resulted in

due to unknown causes. In addition, dilation of the biliary duct and pancreatic duct produced the so-called dou-
ble duct sign on MRCP, and edema of the duodenal mucosa was observed in both patients.

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ble duct sign on MRCP, and edema of the duodenal mucosa was observed in both patients.

In conclusion, we suggest the possibility, although rare, of S. stercoralis infection in patients with obstructive jaundice or refractory pancreatitis. Therefore, detailed questioning of a patient’s life history or travel history to endemic areas is important for the accurate diagnosis of S. stercoralis infec-
tion.

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

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script.

<table>
<thead>
<tr>
<th>Reference No.</th>
<th>Diameter of biliary duct (mm)</th>
<th>Diameter of main pancreatic duct (mm)</th>
<th>Evidence of S. stercoralis</th>
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</thead>
<tbody>
<tr>
<td>7</td>
<td>11</td>
<td>4</td>
<td>Stool</td>
</tr>
<tr>
<td>14</td>
<td>N.A*</td>
<td>N.A*</td>
<td>Duodenal biopsy</td>
</tr>
<tr>
<td>Present case</td>
<td>11</td>
<td>6</td>
<td>Ampullary biopsy</td>
</tr>
</tbody>
</table>

N.A: not available
*: obvious dilatation

Table 3. Research on Strongyloides stercoralis Associated with Dilatation of Biliary and Pancreatic Ducts.

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