A Hospital-Based Study of Intestinal Capillariasis in Thailand: Clinical Features, Potential Clues for Diagnosis, and Epidemiological Characteristics of 85 Patients

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Abstract. Intestinal capillariasis caused by *Capillaria philippinensis*, a fish-borne nematode, is an important, emerging zoonotic helminthiasis. Cases may be fatal if suitable treatment is not administered in time. We reported a hospital-based study of 85 cases in Thailand, most of which were in the northeast. All patients had a history of eating raw or insufficiently cooked fresh water fish or prawns. The clinical manifestations are characterized by chronic diarrhea, borborygmi, abdominal pain, marked weight loss, muscle weakness, fatigue, dizziness, anorexia, and edema, as well as protein and electrolyte loss. Fecal examination revealed *C. philippinensis* in all patients. Although 16 of the total of 85 (18.8%) cases were initially found to be negative for *C. philippinensis* using fecal examination, further examination using an immunoblotting technique found them to be positive for the IgG antibody against *Trichinella spiralis* larval antigen. One day after administration of 400 mg of albendazole, eggs and/or larvae and/or adult *C. philippinensis* were found in 16 fecal samples. After treatment with mebendazole (200 mg twice a day for 30 days) or albendazole (200 mg twice a day for 10 days), all 85 patients recovered. The potential clues for diagnosis are clinical manifestations, history of eating raw contaminated food, and positive serological test, and fecal examinations under professional. Administration of anthelmintic drugs stimulates the excretion of larvae, eggs, and/or adult worms and can be used as a supportive method for the diagnosis of intestinal capillariasis in areas where serological test is not available.

INTRODUCTION

Intestinal capillariasis caused by *Capillaria philippinensis*, a fish-borne nematode, is an important, emerging zoonotic helminth that has become more prevalent in recent years.¹ Fish contract the parasite from water containing the feces of infected birds or humans. Humans are infected by consuming small freshwater fish, either raw or partially cooked. The parasite can reproduce within an individual host, resulting in a large number of worms in the small intestine. Consequently, if the parasite burden increases to massive levels, it can cause disease. This kind of infection was first recorded in the Philippines.^{2,3} Subsequently, cases have been reported in the Philippines,⁴ Indonesia,⁵ the Lao People's Democratic Republic,⁶ Japan,⁷ Taiwan,⁸ India,⁹ Iran,¹⁰ and Egypt.^{11,12} Capillariasis has also been found to be carried from an outside source into Europe.^{5,13,14} In Thailand, the cases have been reported in at least 25 provinces.^{15–21} This report describes the clinical and epidemiological characteristics of a new group of intestinal capillariasis patients (85 cases) from a hospital-based study in Thailand, and potential clues for diagnosis are discussed. The information presented here could possibly be useful for clinicians who care for patients residing in endemic areas. Infection could be avoided by expanding focus on health communication by responsible units. The public health control strategy is still important to break possible morbidity and mortality due to this helminthic disease in this area.

MATERIALS AND METHODS

Between 2000 and 2014, 85 cases of intestinal capillariasis have been diagnosed at Khon Kaen University's Srinagarind

hospital (male:female = 66:19; mean age $\pm$ SD [range] = 43 $\pm$ 15 [10–81] years). All of these patients had experienced chronic diarrhea for more than 1 month and were found negative for human immunodeficiency virus. All patients were hospitalized, treated, and prospectively studied. Epidemiological data, clinical diagnosis, and treatment data were collected and analyzed. Diagnoses were confirmed by eggs and/or larvae and/or adult *C. philippinensis* in the patients' feces. The stool specimens were examined in the same hospital visit using both direct smear³ and formalin-ethyl acetate concentration methods.²² Although 16 of the 85 cases encountered since 2006 were initially found to be negative for *C. philippinensis* using the direct smear and formalin-ethyl acetate concentration methods, they were found positive when subjected to serological examination using an immunoblotting technique against *Trichinella spiralis* larval antigen.²³ All patients received mebendazole at 200 mg twice per day for 30 consecutive days or albendazole at 200 mg twice per day for 10 consecutive days.^{7,24} This retrospective study was approved by the Khon Kaen University Ethics Committee for Human Research (HE 581335).

RESULTS

Over the study period, 85 patients were found to have intestinal capillariasis. Stool examinations found eggs and/or larvae and/or adults of *C. philippinensis* (Figure 1). All of whom had a history of eating raw or insufficiently cooked freshwater fish or prawns. The provinces from which these cases emerged are shown in Figure 2. Eighty-three of the cases were found in the northeastern region. Macroscopic fecal characteristics, signs, and symptoms are presented in Tables 1–3 and Figures 3 and 4. Infected individuals had mainly experienced chronic diarrhea, borborygmi, abdominal pain, and abdominal bloating. Intestinal pseudo-obstruction was found in three cases (3.5%) after treatment. Macroscopic fecal

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FIGURE 1. The representative morphology of *Capillaria philippinensis* in fecal specimens. (A) Adult male and female of *C. philippinensis* indicating stichocyte (Sc), salient vulva (Vu), uterus (UT), larvae (Lv) and eggs (Eg) in the UT (Bar = 100 µm). (B) Adult male *C. philippinensis* spicule (Sp), extended spicule (Ss), and Sc and (C) magnification of the posterior end of *C. philippinensis* adult male from (B, rectangular area) (Bar = 100 µm). (D and E) Adult female of *C. philippinensis* (Bar = 50 µm), (D) indicating Sc, salient Vu, and Eg in the UT. (E) Adult female of *C. philippinensis* whole body indicating Sc, salient Vu, and Lv. (F) The larva and Eg of *C. philippinensis* recovered from fresh feces of a patient, the Eg (the upper right figure) are peanut shaped, flattened bipolar plugs sized about 40 µm long and 20 µm wide (Bar = 20 µm).

characteristics took the form of chronic diarrhea with night time defecation. Clinical signs, such as weight loss, muscle weakness, fatigue, dizziness, anorexia, and edema, were frequently present. Laboratory parameters are presented in Table 4. Anemia, low serum levels of potassium, cholesterol,

FIGURE 2. Map of Thailand showing provinces in which intestinal capillariasis has been discovered. The figures in parentheses indicate the number of cases.

total protein, and albumin, as well as malabsorption of fat were discovered.

Fecal examination revealed *C. philippinensis* in 69 of the 85 patients (81.2%) before treatment with helminthic drugs. Since 2006, some cases ($N = 16$) have been diagnosed as suspected intestinal capillariasis and referred from community and provincial hospitals to the Srinagarind Hospital, the university hospital at Khon Kaen University. In these cases, all stool samples were previously found to be negative for *C. philippinensis* using the direct smear method. Then, the patients had been investigated using several other diagnostic methods (i.e., routine laboratory tests, liver function tests, thyroid function tests, antihuman immunodeficiency virus tests, long gastrointestinal studies, tests for tumor makers for differential gastrointestinal cancer, etc.). All patients presented with the following clinical symptoms: chronic diarrhea, abnormal defecation, nighttime diarrhea, abdominal gurgling for more than 1 month, abdominal pain and bloating, weight loss, and hypoalbuminemia. The patients were prone to eating raw or insufficiently cooked scaled freshwater fish. Repeated

TABLE 1
Macroscopic fecal characteristic of 85 intestinal capillariasis patients*

Characters	
Chronic diarrhea (> 1 month)	85 (100%)
Abnormal defecation	85 (100%)
Night time diarrhea	85 (100%)
Gross blood	1 (1.2%)
Gross Mucous	5 (5.9%)
Foul smell	48 (56.5%)
Food debris in stool	61 (71.8%)

* Out of 85 cases, *Capillaria philippinensis* eggs were found in 39 cases; *C. philippinensis* and *Opisthorchis viverrini* eggs were found in 22 cases; *C. philippinensis* eggs and *Strongyloides stercoralis* larvae were found in 11 cases; *C. philippinensis* eggs, *O. viverrini* eggs, and *S. stercoralis* larvae were found in five cases; *C. philippinensis* and *Echinostome* eggs were found in two cases; *C. philippinensis* eggs, *Echinostome* eggs, and *S. stercoralis* larvae were found in two cases; *C. philippinensis*, *O. viverrini*, and minute intestinal flukes eggs were found in one case; *C. philippinensis* eggs, *S. stercoralis* larvae, and hook worm eggs were found in one case; *C. philippinensis* and *Taenia* eggs were found in one case; *C. philippinensis* eggs, *O. viverrini* eggs, *Taenia* eggs, and *S. stercoralis* larvae were found in one case.

TABLE 2
Abdominal manifestations of 85 intestinal capillariasis patients

Abdominal gurgling	83 (97.6%)
Abdominal pain	51 (60%)
Abdominal discomfort	58 (68.2%)
Burning abdomen	17 (20%)
Abdominal bloating	69 (81.2%)

stool diagnosis using the formalin ethyl acetate concentration method was negative in all cases. All patient sera were found positive for the IgG antibody using the immunoblotting technique (Figure 5). One day after administration of 400 mg of albendazole, eggs and/or larvae and/or adult of *C. philippinensis* were found in all fecal samples examined using the direct smear method (Figure 1). All 16 patients were followed treatment with albendazole at 200 mg twice per day until 10 consecutive days. The patients were cured, and no parasites were found in their feces within 2 weeks to 2 months after treatment. The stool consistency changed from watery to form stool within 7 days. Follow-ups revealed no cases of relapse.

DISCUSSION

Food-borne parasites are an emerging public health problem, particularly in Southeast Asian countries²⁵ including Thailand. Importantly, it is possible that *C. philippinensis* may be the cause of symptoms in many cases, especially in patients who present with chronic diarrhea resulting in protein-calorie malnutrition or electrolyte disturbances. This helminthic infection is extraordinary because of its potential severe, or even fatal, consequences in cases of misdiagnosis or improper treatment.⁷ Infection with intestinal capillariasis should be considered in cases of differential diagnosis with malabsorption syndrome.²⁶ More than 2,000 cases resulting in almost 200 deaths have been recorded worldwide, and the cases were mostly from Asia.²⁴ In Thailand, the first case of intestinal capillariasis was reported in a Thai girl from Samut Pragan province in the central region of the country.¹⁵ There have subsequently been sporadic cases reported from different parts of the country. The first outbreak in Thailand was found in Sisaket Province in the northeast, in which there were 20 cases and nine deaths reported.²⁷ A study published in 1983 reported that a total of 100 cases of *C. philippinensis* infection were found in hospitals in the same area between 1979 and 1981 of which 15 cases were fatal.²⁸ Seventy-three percent (73/100) of the patients were aged between 20 and 49 years, and the disease was approximately 2.3 times more common in males.²⁸

TABLE 3
Clinical signs of 85 intestinal capillariasis

Weight loss	84 (98.9%)
Appetite	23 (27%)
Anorexia	52 (61.2%)
Nausea	29 (34.1%)
Vomiting	19 (22.3%)
Fatigue	69 (81.1%)
Muscle weakness	54 (63.5%)
Dizziness	44 (51.7%)
Hypoesthesia	29 (34.1%)
Edema	60 (70.5%)
Fever	9 (10.5%)

FIGURE 3. Clinical image of malnourish patient (no. 1) suffered from chronic intestinal capillariasis showing cachexia with poor skin turgor (A) before treatment, (B) 74 days after treatment, (C) 140 days after treatment. This figure appears in color at www.ajtmh.org.

In the same year, three infected patients who lived in the northeast (Nakhon Ratchasima, Sisaket, and Khon Kaen provinces) were reported at Bamrasnaradura hospital in central Thailand.²⁹ From 1983 to 1991, 17 cases were reported at Khon Kaen University's Srinagarind Hospital in Khon Kaen province with an age range of 21–69 years.¹⁹ Sporadic cases were also reported in the northern (i.e., Prayoa, Phetchabun and Chiang Mai provinces)^{18,30} and central (i.e., Saraburi and Prachinburi provinces)^{16,31,32} regions. In one case, *C. philippinensis* eggs and adult in jejunal content were found using enteroscopy after repeated stool examination.²⁰ In another study in Thailand, Saichua et al.²¹ reviewed a total of 82 cases from 1994 to 2006.

Here, we report 85 new cases of intestinal capillariasis in Thailand from a hospital-based study. It is evident that the disease is not rare in Thailand. The clinical manifestations of intestinal capillariasis commonly present are chronic watery diarrhea, abdominal pain, borborygmus, weight loss, muscle wasting, edema, severe-losing enteropathy, and

FIGURE 4. Clinical image of chronic intestinal capillariasis patient (no. 2) suffered from leg pain due to deep vein thrombosis caused by stagnation. (A) Showing grade 4+ of pitting edema of both legs. (B) Sixteen days after treatment. This figure appears in color at www.ajtmh.org.

TABLE 4
Laboratory parameters of 85 intestinal capillariasis

Blood	
Hemoglobin (gm/dL)	12.2 ± 2.6 (4–18)
Hematocrit (%)	37.1 ± 7.7 (12–54)
WBC/mm ³	8,750 ± 3,901 (4,460–32,300)
Eosinophilia (%)	4.2 ± 3.7 (0–15)
Absolute eosinophil count	333.8 ± 307.2 (0–1,650)
Potassium (mEq/L)	3.4 ± 0.7 (1.5–4.9)
Cholesterol (mg/dL)	118.9 ± 42.3 (51–291)
Total protein (gm/dL)	5.2 ± 1.4 (2.9–7.9)
Albumin (gm/dL)	1.7 ± 0.8 (0.6–4.6)
Globulin (gm/dL)	3.4 ± 1.0 (1.4–5.7)
Stool	
Found red blood cells	4 (4.7%)
Positive occult blood	37 (43.5%)
Positive fat test	22 (25.9%)
Positive Charcot–Leyden crystals	14 (16.4%)

WBC = white blood cell.

malabsorption of fat, as well as low serum potassium, cholesterol, total protein, and albumin levels.^{7,15} Interestingly, in the present report, we found that 3.5% of patients showed intestinal pseudo-obstruction after treatment, as has also been reported in one previous case.³¹ Clinicians who work in endemic areas should be aware that this symptom can be present. The pathological patterns possibly result from a

proteolytic secretion of *C. philippinensis* or direct penetration of the worm, which cause cellular injury and dysfunction.⁷ Another possible mechanism may be atrophy or hypotrophy of the small intestinal muscle with poor contraction from malnutrition (a consequence of chronic diarrhea with malnutrition).³¹

Several kinds of fresh water fish, such as *Cyprinus carpio* (Pla nui), *Puntius gonionotus* (Pla Tapien Khao), and *Rasbora borapelensis* (Pla Sew), which are commonly consumed raw in Thailand, have been reported to be an experimental intermediate host of *C. philippinensis*.³³ People in rural areas of Thailand still consume traditional dishes containing raw fish or prawns, such as *koi pla* or *lap pla* (minced fish with lemon juice and spices) and *koi kung* (raw prawns with lemon juice and spices). The consumption of raw or insufficiently cooked fresh water fish or prawns provides an extremely effective means of *C. philippinensis* transmission.

Presently, intestinal capillariasis remains problematic in clinical practice.³⁴ First, diagnosis is difficult due to atypical clinical symptoms and misdiagnosis as diarrhea caused by gastrointestinal cancer, human immunodeficiency virus infection, or hyperthyroidism. The disease may also be unrecognized by clinicians if it emerges in a nonendemic area. Second, stool examination exhibits low sensitivity, as the parasitic eggs and/or larvae are purged irregularly. Invasive and high-cost diagnostic tools can assist clinicians (i.e., endoscopy and imaging).^{34,35} Here, we revealed another highly effective tool for diagnosis. Albendazole treatment could increase the sensitivity of stool examination methods for diagnosis of intestinal capillariasis. Interestingly, this study revealed that approximately 16 (18.8%) samples which were found to be negative using stool examinations before helminthic drug intake were found to be positive after albendazole intake.

In conclusion, the potential clues for diagnosis of intestinal capillariasis are clinical manifestation of chronic diarrhea and borborygmi, history of eating raw fish or prawns, and positive serological test and stool examinations. In cases with negative stool-examination results but positive serological results, repeated stool examination is required within 1 day after anthelmintic drug treatment on confirmation of diagnosis.

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FIGURE 5. The representative patterns of the immunoblot analysis reacted with individual sera from a pooled positive intestinal capillariasis reference (A), a pooled negative healthy control reference (B), and intestinal capillariasis cases (C and D). The numbers on the left and right sides indicate the molecular masses (kDa). The procedure was conducted as previously described by Intapan and others²³ and the reacted 54, 40.5, and 36.5 kDa bands were used as diagnostic band pattern for intestinal capillariasis.

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