Approach for Diagnostic and Treatment of Chronic Diarrhea Caused by Hookworm Infection

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ABSTRACT

Chronic diarrhea has various etiologies. One of the causes includes parasitic infection, such as hookworm. Human hookworm infections are caused by the blood-feeding intestinal nematodes (Ancylostoma duodenale and Necator americanus).

A 54-year-old male was admitted to Cipto Mangunkusumo Hospital with a chief complaint of diarrhea since one month before hospital admission. He experienced diarrhea more than five times a day, without blood and mucus. The stool appearance was yellow without bubbles. He also noted decreased appetite and weight loss. The remarkable physical finding was pain in whole abdomen. Laboratory results showed leukocytosis; while the feces analysis showed bacteria, leukocytes and Gram-negative bacilli. Colonoscopy examination revealed a lot of worms in the colon with multiple ulcers. Histopathological findings indicated colitis with plasma and eosinophils cells in the lamina propia. Parasitology analysis confirmed the hookworms (Necator americanus). The patient was given intravenous fluid, albendazole 400 mg in three consecutive days. The patient’s clinical condition was improved and he was subsequently discharged after seven days of hospitalization. During the follow up at outpatient clinic, the patient was in healthy condition.

This is a demonstrative case of human hookworm infection that cause chronic diarrhea. Colonoscopy plays important role for evaluating and finding the etiology of chronic diarrhea. Proper treatment with albendazole has been proven to be effective in eradicating hookworm infection.

Keywords: diarrhea, parasite, hookworm

ABSTRAK

Diare kronik dapat ditimbulkan oleh berbagai macam penyebab. Salah satunya karena infeksi parasit seperti cacing tambang. Infeksi cacing tambang pada manusia disebabkan oleh Ancylostoma duodenale dan Necator americanus.


Pada kasus ini digambarkan bahwa infeksi cacing tambang pada manusia dapat bermanifestasi sebagai...
diare kronik. Pemeriksaan kolonoskopi memegang peranan penting dalam evaluasi dan menemukan penyebab diare kronik. Tatalaksana yang tepat dengan albendazole efektif dalam mengeradikasi infeksi cacing tambang.

**Kata kunci:** diare, parasit, cacing tambang

**INTRODUCTION**

Diarrhea is loosely defined as passage of abnormal liquid or unformed stools on increasing frequency.\(^1\) One of etiologies for chronic diarrhea is parasitic infections and one of the most common infections is hookworm. Hookworm infections are common in the tropics and subtropics.\(^2,3\) The infection rarely occurs in regions with less than 40 inches of rainfall annually. The species of hookworm which are responsible for hookworm disease in humans may vary geographically. *Ancylostoma duodenale* causes infection in Mediterranean countries, Iran, India, Pakistan, and the far east; while *Necator americanus* has infected human in North and South America, Central Africa, Indonesia, Islands of the South Pacific, and parts of India.\(^4,5\)

Human hookworm infection is caused by the blood-feeding nematodes, *Ancylostoma duodenale* and *Necator americanus*, which has infected nearly 740 million people, mostly in rural areas of the tropical countries, resulting in an estimated annual loss of 22 millions disability-adjusted life years (DALYs). These DALYs are the results of a well-established correlation between the intensity of hookworm infection, intestinal blood loss, and anemia.\(^6,7,8\)

Although it was widely prevalent in rural areas of the Southeastern United States, extensive control efforts have diminished hookworm infections within this country in the early 20\(^{th}\) century. Globally, about 740 million people are infected with hookworms. Those at risk for infection include resident children and adults and those with occupational (e.g. infantry troops) or recreational (e.g. tourists walking with barefoot or with open footwear) skin exposures to fecally contaminated soil in endemic areas.\(^7,9\) Hookworm infection is rare in the United States. Prevalence of hookworm infection is as high as 80% in less-developed countries with moist tropical climates, but is only 10-20% in areas with drier climates.\(^7,8\)

The prevalence in Indonesia is high, which is about 40% in rural areas, especially in the plantation. Plantation workers who are often directly related to the soil get infections, i.e. more than 70%.\(^9\) This manuscript would demonstrate a case of chronic diarrhea caused by intestinal worms (*Necator americanus*). It would also discuss about the diagnosis and management.

**CASE ILLUSTRATION**

A 54-year-old male patient came to Cipto Mangunkusumo Hospital with chief complaint of diarrhea since one month before hospitalization. One month before admission, the patient had seen a general practitioner, but he did not feel any improvement. He forgot about the drugs that he had taken. The patient still had diarrhea, which became more often than his previous complaint. He also felt extreme pain in the stomach, especially when he was having diarrhea. Patient also felt nausea and vomiting about three times/day. One day before the admission, the patient still had diarrhea, which occurred more than 10 times/day. His food intake also decreased and he was resting in bed all day. He did not feel fever, headache, and coughing. He had lack of appetite and weight loss in at least one month. The patient worked as a trader in the market with dirty environment and without wearing shoes.

The physical examination revealed that the patient was moderately ill. His blood pressure 110/70 mmHg, the pulse rate 88 times/minute, respiratory rate 20 times/minute, and body temperature 37.3\(^{0}\)C. The body height 165 cm, body weight was 60 kg, and the body mass index 21.3 kg/cm\(^2\). The eye examination showed no pale conjunctiva and no jaundice in his sclera, the neck was normal. Heart examination indicated normal heart sounds with no gallop and murmur. The lung examination was normal with vesicular lung sound, no rales and no wheezing was found. The abdomen was flat, supple, and no palpable liver or spleen on the examination. There was increased bowel sound. Abdominal tenderness was detected on whole abdominal region. The extremities were warm with no edema.

The laboratory examination showed following results, i.e. hemoglobin (Hb) level 6.0 g/dL, hematocrite (Ht) 50%, leukocyte counts 24,000/uL, thrombocytes count 413,000/uL. The differential count indicated basophil 0%, eosinophils 21%, segment neutrophils 69%, lymphocytes 8%, and monocytes 8%. The ureum level was 55 mg/dL, creatinine level was 4 mg/dL, blood glucose level was 112 mg/dL, sodium level was 138 mEq/L, potassium level was 3.8 mEq/L, chloride level was 101 Eq/L, albumin level was 3.2 g/dL, globulin level was 4.9 g/dL, aspartate
transaminase (AST) level was 16 U/L, alanine aminotransferase (ALT) level was 26 U/L. The results of urinalysis were leukocytes of 0-2/HPF, erythrocytes of 0-2/high power field (HPF), negative keton, negative blood, negative bacteria, negative nitrite, and negative leukocyte esterase. Chest radiography showed cardiothoracic ratio (CTR) < 50% and no infiltrate in the lungs. Echocardiography showed sinus rhythm (SR), QRS rate 80 times/minute, normo axis, negative T inverted. Macroscopic fecal analysis revealed liquid stool without blood or mucin, no distinctive odor and yellow color. Microscopic analysis showed positive leukocyte count and positive bacteria. Complete fecal analysis demonstrated pH 7, negative glucose, positive results on fat analysis and Gram-negative bacilli.

The patient was considered to have chronic diarrhea with intestinal infection caused by Gram-negative bacteria due to the presence of erythrocytes in his stool specimen. The differential diagnosis was eosinophilic gastroenteritis or colitis. The diagnostic strategies included laboratory investigation, i.e. examination of serial Hb, Ht, leukocytes count and differential count; as well as colonoscopy and biopsy. The therapeutic strategies were administering intravenous fluid of ringer lactate (IVFD RL) of 500 cc/8 hours, therapeutic plans were IVFD RL 500 cc/8 hours, soft food diet of 1,900 kcal/day, 1 g intravenous cefoperazone twice daily, 500 mg ciprofloxacin twice daily, and 2 tablets New Diatab® three times daily.

Acute kidney injury that occurred in this patient was considered due to pre-renal cause and dehydration as there were chronic diarrhea with ureum and creatinine level during early admission of 55 and 4.4 mg/dL; Hb level of 16 g/dL and Ht was 50%. The therapeutic plan included providing balanced fluid status every 24 hours, administering IVFD RL of 500 cc/8 hours and eradicating the cause of diarrhea.

At the third day of treatment, patient had diarrhea, nausea, vomiting and occasionally abdominal pain. Laboratory results showed Hb level of 13.9 g/dL, Ht of 42.7%, leukocytes count of 32,300/uL with 69% eosinophils, ureum level of 42 mg/dL, and creatinine level of 2.2 mg/dL. Moreover, the patient had also undergone colonoscopy and biopsy examinations. The colonoscopy revealed grade II internal hemorrhoids in all colon regions (rectum, sigmoid, descendent, transverse, ascendent colon) with abundant number of worms in cecum segment, that were trying to invade into mucosa. Multiple ulcers were found as the tracks of former worm infection. Biopsy specimens were obtained from rectum and cecum region, including the worms as specimens for parasitological analysis.

No abnormality was found in terminal ileum segment. It was concluded that the patient had grade II internal hemorrhoids, colon helminthiasis and colitis due to worm infection (Figure 1). Biopsy results indicated the colitis appearance, which revealed plasma cells and eosinophilic cells in the lamina propria (> 60 eosinophils/10 HPF), which did not exclude the possibility of eosinophilic colitis (Figure 2).

Furthermore, there was no sign of malignancy. Parasitological examination has provided direct evidence of worm infection, which revealed hookworm infection of male Necator americanus. Based on the abovementioned results, the patient held some problems of chronic diarrhea caused by colitis due to worm infection, grade II internal hemorrhoids,
dyspepsia syndrome and acute kidney injury with differential diagnosis of chronic kidney disease.

The treatment was continued with additional prescription of 400 mg of albendazole orally once daily for three days and other antibiotics were discontinued. Further stool analysis and another colonoscopy and peripheral complete blood examination were scheduled after the patient has completed treatment. On the fifth day of treatment, the patient had normal defecation of three times/day with soft consistency of stool and there was no abdominal pain or nausea. On physical examination, we found no abnormalities.

On the seventh day of treatment, the patient had normal bowel sound, with defecation of three times/day and solid stool, no nausea or vomiting, no stomach pain and no other complaints. The physical examination revealed no abnormalities and the laboratory results showed that he had Hb level 13 g/dL, Ht 40%, leukocytes 12,000/uL and thrombocytes count of 435,000/uL, mean corpuscular volume (MCV) was 84 fl, mean corpuscular hemoglobin (MCH) was 28 pg/cell, mean corpuscular hemoglobin concentration (MCHC) was 33 g/dL. The differential counts showed 0% basophils, 9% eosinophils, 3% band neutrophils, 57% segments, 30% lymphocytes and 1% monocytes. The urea level was 40 mg/dL and creatinine 1.0 mg/dL. The patient was subsequently discharged from hospital.

During treatment and for take-home message, the patient had received explanation about his disease and he has been encouraged to maintain good sanitation and healthy environment, especially about the use of footwear when he is working.

Two weeks later, patient visited our gastroenterology clinic. He had no more diarrhea, no abdominal pain or nausea. Laboratory results showed Hb level 14 g/dL, Ht 43%, leukocytes 8,700/uL and thrombocytes counts 435,000/uL, MCV 84 fl, MCH 28 pg/cell, MCHC 33 g/dL. The differential count showed basophils 0%, eosinophils 1%, band neutrophils 3%, segments 58%, lymphocytes 37% and monocytes 1%. Fecal analysis showed no abnormality was found. Two months later, the patient had another visit to our gastroenterology clinic. He was suggested to have further colonoscopy examination to evaluate the healing process and the success of treatment. We explained that although he already had a complete review and fecal analysis, which showed negative results (Figure 3), colonoscopy should be performed to evaluate whether there is any existence of worm infestations throughout the colon.

DISCUSSION

Colonoscopy in this patient has revealed infestation of worms along the colon, which subsequently identified as the hookworm infection of *Necator americanus*. *Necator americanus* was first discovered in Brazil and then was found in Texas. Later it was found in indigenous in Africa, China, Southwest Pacific Islands, India and Southeast Asia. This parasite is a tropical parasite and is the most common species in humans. There are about 30-50% hookworms in Indonesia, especially in rural areas. Roughly 95% of hookworms found in the Southern region of the United States are *Necator americanus*.9,10 *Necator americanus* is a parasitic nematode worm that lives in the small intestine of hosts such as humans, dogs and cats. It is responsible for necatoriasis. This parasite has two dorsal and two ventral cutting plates around the anterior margin of the buccal capsule. The typical life span of these parasites is three to five years. They can produce anywhere between 5,000 to 10,000 eggs per day.11,12

*Necator americanus* transmits through penetration of skin causing abdominal discomfort, diarrhea and cramps, anorexia, weight loss and iron deficiency anemia. *Ancylostoma duodenale* and *Necator americanus* are small, off-white worms. Males are 8-11 mm in length, and females are 10-13 mm. Walking barefoot on soil contaminated with feces (the source of hookworm eggs and larvae) is the most common method of exposure. After skin penetration, the venous circulation carries larvae to the pulmonary bed, where they lodge in pulmonary capillaries.
Within 3-5 days, the larvae break through into alveoli and travel up the ciliary escalator from the lungs into the bronchi, the trachea, and the pharynx. Upon reaching the pharynx, larvae are swallowed and gain access to the gastrointestinal (GI) tract. Once in the GI tract, worms attach to the wall of the intestine and begin to feed on the blood of the host. A *Necator americanus* adult worm consumes approximately 0.3 mL of blood/day, while the *Ancylostoma duodenale* consumes approximately 0.5 mL of blood each day. Chronic loss of blood and serum proteins leads to hookworm anemia and impaired nutrition.\(^{13,14}\)

The abovementioned facts are in accordance with the conditions of this patient. The patient worked as a trader in the market with dirty environment and without wearing any footwear while he was working. It is very possible that the worms easily penetrate into the patient’s skin. The potential manifestations reflect the four phases of hookworm infection including the dermal penetration by infecting larvae, transpulmonary passage, acute gastrointestinal symptoms and chronic nutritional impairments.\(^{13,15}\)

The daily losses of blood, iron and albumin, especially in patient with heavy infections, can lead to hookworm anemia and contribute to impaired nutrition. Therapy of intestinal hookworm, *Trichuris*, and *Ascaris* infections in those with marginal nutrition has been proven to have salutary effects of growth, exercise, and cognitive function and is the basis for on going mass treatment programs in countries where these geohelminth infections are prevalent. Even in those without impaired nutrition, anthelmintic therapies can improve hemoglobin levels.\(^{16,17}\)

Hookworms cause trouble for their human host when the worms attach their mouths to the lining of the small intestine and suck the person’s blood.\(^{18}\) An itchy, slightly raised rash called “ground itch” may appear around the area where the larvae first bored through the skin. The skin in this area may become red and swollen. This lasts for several days and commonly occurs between the toes. When the larvae are in the lungs, the patient may have a fever, cough, and some wheezing. However, some people have none of these symptoms.\(^{19,20}\)

Once established within the intestine, the adult worms can cause abdominal pain, decreased appetite, diarrhea, and weight loss. Most importantly, the worms suck between 0.03-0.2 mL of blood per day. When a worm moves from one area of the intestine to another, it detaches its mouth from the intestinal lining, leaving an irritated area that may continue to bleed for some time. This results in even further blood loss. A single adult worm can live for up to 14 years in a patient’s intestine. Over time, the patient’s blood loss may be very significant. Anemia is the most serious complication of hookworm disease, progressing over months or years. Children are particularly harmed by such anemia, and can suffer from heart problems, mental retardation, slowed growth, and delayed sexual development. In infants, hookworm disease can be deadly.\(^{21,22}\)

Clinical manifestations mentioned above were also found in this case. The patient experienced chronic diarrhea, nausea and vomiting, abdominal pain, decreased appetite and weight loss; however, he didn’t feel itchy and fever, no cough, and no wheezing or pallor were found. Establishing the diagnosis of hookworm disease involves collecting a stool sample for examination under a microscope. Hookworm eggs have a characteristic appearance. Counting the eggs in a specific amount of feces allows the healthcare provider to estimate the severity of the infection.\(^{23,24}\)

In this patient, a full review of fecal analysis has been performed with no finding of the parasite. The colonoscopy finally revealed the colon along with many worms invading the mucosa, which subsequently identified as hookworm infection. Although the patient already had a complete review and fecal analysis, which showed negative results, but colonoscopy should be performed to evaluate whether there is any existence of worm infestations throughout the colon.

It could be explained since the literatures have mentioned that stool examinations for the eggs of *Necator americanus* or *Ancylostoma duodenale*, the diagnostic test for mature intestinal hookworm infections, are not helpful during early infections. Fecal egg excretion does not become detectable until about two months after dermal acquisition of *Necator americanus* infection and up to 38 weeks for *Ancylostoma duodenale*. Thus, negative stool examinations would be expected during early stages of dermal, pulmonary, or gastrointestinal involvement; positive tests at these times would reflect earlier, now fully established intestinal tract infections. Repeated stools may be needed to make the diagnosis.\(^{25,26}\)

In addition, adult worms can be detected at endoscopy in patient with abdominal pain or other gastrointestinal symptoms. Reliable serologic tests are not available. Similar situation was experienced by the patient as worm infestations were found during the colonoscopy.

Hookworm infections should be treated with mebendazole (100 mg orally twice daily for three days or single dose of 500 mg). Alternative agents include
pyrantel pamoate (11 mg/kg per day for three days, which should not exceed 1 g/day) or albendazole (single dose of 400 mg). Anemia is treated with iron supplements. In severe cases, blood transfusion may be necessary. Two medications, pyrantel pamoate and mebendazole, are frequently used with good results.

The patient was treated with albendazole 400 mg/day for three days and after one week later the stool sample was taken to see if the infection was still exist. The patient was not anemic; therefore, no treatment was given to overcome anemia.

The prognosis for patients with hookworm disease is generally good. However, reinfection rates are extremely high in countries with poor sanitation. Prevention of hookworm disease involves improving sanitation and avoiding contact with soil in areas with high rates of hookworm infection. Children should be required to wear shoes when playing outside in such areas, and people who are gardening should wear gloves.

REFERENCES