

Twenty-Year History of Gastrointestinal Hemorrhage and Abdominal Pain

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Strongyloides stercoralis is a gastrointestinal parasite. It infects millions of people worldwide, and its unusual life cycle enables it to persist indefinitely in a human host. The parasite is difficult to isolate, and immunosuppression of the host can lead to hyperinfection, resulting in death. This case report describes the clinical course of a man who initially presented with gastrointestinal symptoms in 1972. The patient underwent extensive evaluations by multiple specialists, but no definitive diagnosis was made until autopsy 23 years later. The life cycle, clinical and laboratory features, and treatment of strongyloidiasis are discussed.

CASE PRESENTATION

September 1972

In September of 1972, a 56-year-old Hispanic man presented to the hospital with the chief complaints of diarrhea, fever, myalgia, and abdominal pain. Because of a language barrier, it was difficult to obtain a thorough history. The patient's medical history included peptic ulcer disease, which was diagnosed 1 year earlier. He was not taking any medication at this time. His surgical history included a peptic ulcer resection. His social history was positive for alcohol use; he drank approximately 1 case of beer per week. He denied smoking.

Upon further questioning and a review of systems, the patient stated he was having persistent dull abdominal pain, with periods of exacerbated pain. He denied any association of his symptoms with food, and he could not localize the pain to any specific abdominal region. The patient reported no blood in his stools, constipation, or relief of pain with a bowel movement. He also stated a recent history of cough. Physical examination revealed diffuse abdominal tenderness to palpation but no rebound, rigidity, or guarding. Bowel

sounds were present, and a stool sample was negative for occult blood. At this point, the patient was admitted with the chief diagnosis of abdominal pain of uncertain etiology.

Over the next 11 days, the patient underwent an extensive evaluation by multiple specialists. Results are shown in **Table 1**. The patient's inpatient treatment consisted of intravenous (IV) administration of ampicillin, IV hydration, oral administration of Lomotil (diphenoxylate hydrochloride with atropine sulfate), and generalized supportive care. The patient responded well to this treatment and was discharged with a diagnosis of hypereosinophilia of unknown etiology. The possibility of schistosomiasis was considered; however, the patient had not been outside the United States for several years, and therefore, if schistosomiasis was present, it was thought to be a long-standing infection.

Over the next 20 years, the patient was lost to follow-up care.

August 1992

In August of 1992, the patient visited his primary care physician's office for a routine physical examination and laboratory evaluation. The physical examination revealed diffuse abdominal tenderness and mid-epigastric pain consistent with gastroesophageal reflux.

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Table 1. Results of Case Patient's Diagnostic Evaluations, September 1972

Test	Result
Chest radiograph	Within normal limits
Abdominal obstruction radiographic series	Scattered collections of gas, dilatation of the small intestine, possible reactive ileus, evidence of a previous Billroth II resection
VDRL test	Nonreactive
PPD tuberculin test	Reactive
Urinalysis	Unremarkable
Stool occult blood test	Negative
CBC with differential	Eosinophilia (12% of leukocytes)
Stool culture	Positive for salmonella group D
Repeated stool occult blood test	Positive
Repeated CBC with differential	Eosinophilia (18% of leukocytes)
Repeated stool culture	Negative
Blood culture	Negative
Blood chemistry panels (6- + 12-channel)	Elevated serum uric acid level
Liver function tests	Within normal limits
Electrocardiogram	Within normal limits
Liver CT scan	Within normal limits
Spleen CT scan	Within normal limits
Rectal biopsy	Granulomatous tissue

CBC = complete blood count; CT = computed tomography; PPD = purified protein derivative.

A stool sample was negative for occult blood. His laboratory evaluation revealed eosinophilia (37% of leukocytes). An upper gastrointestinal radiographic series with small bowel follow-through revealed normal mucosa and no signs of ulceration. The patient was prescribed a proton pump inhibitor, which resulted in a marked improvement of his symptoms.

April 1993

Eight months later, the patient again presented to his primary care physician, this time with nausea, vomiting, and severe abdominal pain. He was immediately referred for an urgent esophagogastroduodenoscopy (EGD). The findings on the EGD showed diffuse gastritis and gastric mucosal hypertrophy, but no evidence of active ulceration. Histologic evaluation of prepyloric and duodenal biopsies showed hyperplastic changes with no evidence of malignancy. Treatment consisted of reinitiation of proton pump inhibitors, which again resulted in significant improvement of symptoms.

May 1993 to May 1995

Over the course of the next 2 years, the patient

repeatedly presented to his primary care physician's office with recurrent complaints of abdominal pain, episodic diarrhea, and occasional bloody stools. During this time, the patient was admitted repeatedly to the hospital. Extensive diagnostic tests revealed no definitive diagnosis. The tests included an EGD, colonoscopy, abdominal and pelvic computed tomographic scans, urinalysis, chest radiograph, stool cultures, and skin, muscle, and bone marrow biopsies. Blood evaluations consisted of complete blood counts with differential, blood cultures, complete metabolic profiles, hormone levels, angiotensin-converting enzyme levels, and serologic testing for P-ANCA and C-ANCA (antineutrophil cytoplasmic antibodies). The results of this extensive evaluation revealed hyper-eosinophilia and gastritis. The patient was diagnosed with hypereosinophilia syndrome, peptic ulcer disease, and chronic obstructive pulmonary disease. His treatment consisted of proton pump inhibitors, prokinetic agents, and oral and inhaled corticosteroids. The patient's response to this treatment included transient resolution of both his hypereosinophilia and peptic ulcer disease.

June to August, 1995

In June of 1995, the patient presented to the emergency department with the chief complaints of a syncopal episode, abdominal pain, and bloody stools. Emergency department evaluation revealed a microcytic anemia, hyponatremia, and hypereosinophilia. These findings were thought to be consistent with gastrointestinal hemorrhage, corticosteroid use, and the previous diagnosis of hypereosinophilic syndrome. The patient was admitted to the hospital for further evaluation, which consisted of repeated laboratory and diagnostic evaluations, a tagged erythrocyte scan, an abdominal laparoscopic evaluation, and multiple computed tomographic scans. The results revealed no additional information. Despite this aggressive diagnostic work-up and symptomatic treatment, the patient's condition continued to decline. The patient suffered a significant deterioration of his health, including a thrombotic stroke, respiratory failure, congestive heart failure, and massive gastrointestinal and pulmonary hemorrhage leading to his demise. The patient died on August 16, 1995.

Autopsy Results

Anatomic diagnosis: Diffuse acute hemorrhage of the stomach, esophagus, and small intestines associated with severe parasitosis consistent with *S. stercoralis* infection. Tracheobronchial mucosa hemorrhage. Congestive heart failure with bilateral pulmonary edema. Pulmonary candidiasis. Chronic prostatitis. Moderate coronary atherosclerosis.

Cause of death: Massive acute gastrointestinal hemorrhage associated with strongyloidiasis.

DISCUSSION

S. stercoralis is a ubiquitous nematode infecting millions of people worldwide. It has the unusual capacity to replicate in the human host. This capacity to replicate allows for an ongoing cycle of autoinfection. *S. stercoralis* has the ability to persist for decades without further exposure, and difficulty isolating the parasite allows for long-term infestation without detection.^{1,2}

S. stercoralis tends to be distributed in the hot, tropical regions of the world, and infection is more common in these regions. However, owing to increased world travel, infection can be seen anywhere in the world. Strongyloidiasis should be considered in immigrants and military personnel from endemic regions presenting with symptoms suspicious for gastrointestinal parasitosis.^{3,4} Strongyloidiasis also occurs in residents of mental health institutions and other long-term residen-

tial care facilities because of poor hygiene practices.

Life Cycle of *Strongyloides stercoralis*

Humans become infected with *S. stercoralis* when filariform larvae in fecally contaminated soil penetrate the skin or mucous membranes, travel through the blood stream to the lungs, ascend the bronchial tree, are swallowed, and then reach the small intestine (**Figure 1**). Adult female larvae then penetrate the intestinal mucosa and reproduce by parthenogenesis. Eggs then hatch in the intestinal mucosa and migrate back into the intestinal lumen to repeat the migration and autoinfection cycle (**Figure 2**).^{1,2}

S. stercoralis can survive a free-living cycle in addition to a parasitic life cycle. This adaptability facilitates the parasite's survival. Parasitic forms deposit ova as they burrow into the intestinal mucosa (**Figure 3**). Larvae then hatch in the intestinal mucosa, bore through the epithelium to the intestinal lumen, and are passed in the feces. The free-living larvae can either continue their life cycle in the soil or metamorphose into the filariform infectious form. The life cycle of *S. stercoralis* is depicted in **Figure 4**.

S. stercoralis are controlled by unknown host defenses that allow humans to live with the infection for several decades. If the human host becomes immunocompromised, either by disease or by immunosuppressive therapy, the autoinfection process leads to overwhelming larvae transformation and mucosal invasion, and hyperinfection develops. The massive larval load leads to rapid deterioration and a markedly increased likelihood of death of the human host.^{2,5,6} In the case presented, it is the authors' opinion that the combination of corticosteroid therapy and the patient's comorbid conditions (eg, heart failure, chronic obstructive pulmonary disease) and age contributed to his hyperinfection and subsequent death.

Clinical Features of Strongyloidiasis

A high clinical suspicion for strongyloidiasis and recognition of patients at high risk for the disease are important in arriving at a correct diagnosis. One third of people infected with *S. stercoralis* are asymptomatic; the remainder have symptoms related to the stage of migration and severity of infection in the host. Gastrointestinal symptoms of *S. stercoralis* include epigastric pain, nausea, diarrhea, and melena. Pulmonary symptoms include fever, cough, dyspnea, hemoptysis, chest pain, and pleural effusion. Cutaneous manifestations include a pruritic, raised, erythematous lesion often involving the wrist or buttock. A pathognomonic ser-piginous eruption known as *larva currens* may advance



Figure 1. *Strongyloides stercoralis*. Formed larva in egg. Magnification $\times 250$. Reproduced with permission from Zaiman H, Cain G. A pictorial presentation of parasites. Slide 1890. Available at <http://parasitepics.biosci.uga.edu>. Accessed April 28, 2001. Photograph courtesy of R. Hiss.



Figure 2. *Strongyloides stercoralis*. Rhabditiform larva in stool. Magnification $\times 250$. Reproduced with permission from Zaiman H, Cain G. A pictorial presentation of parasites. Slide 933. Available at <http://parasitepics.biosci.uga.edu>. Accessed April 28, 2001. Photograph courtesy of R. Hiss.

subcutaneously at a rate of 10 cm per hour. In chronic carriers, cutaneous manifestations are present in 84% of patients, whereas gastrointestinal symptoms are present in only 5%.^{7,8}

Laboratory Evaluation

Eosinophilia is a common finding, occurring in two thirds of patients with strongyloidiasis. Eosinophilia tends to fluctuate with the degree of infestation.^{7,9} Identification of larvae or ova in the gastrointestinal tract has the highest diagnostic yield; however, there is no gold standard for the diagnosis.^{7,10} The finding of larvae in the stool is diagnostic; however, eggs are rarely present in the stool because they hatch in the intestines and burrow into the mucosal lining.^{5,11,12} Serial stool examinations may increase the diagnostic yield. Examination of sputum, feces, bronchoalveolar lavage samples, and surgical drainage fluid for ova and larvae has a high diagnostic yield.

Although there was no serologic test for the diagnosis of strongyloides in 1972 (when the case patient initially presented with gastrointestinal symptoms), an enzyme-linked immunosorbent assay (ELISA) test is now available, which detects IgG to *S. stercoralis* antigen.^{12,13} This test, which has an 80% to 90% sensitivity,¹⁰ became commercially available in 1998.

Treatment

Strongyloides infection should always be treated—even in the asymptomatic patient—because of the



Figure 3. *Strongyloides stercoralis*. Adult female in the duodenal mucosa. Magnification $\times 250$. Reproduced with permission from Zaiman H, Cain G. A pictorial presentation of parasites. Slide 1729. Available at <http://parasitepics.biosci.uga.edu>. Accessed April 28, 2001. Photograph courtesy of J.D. Harper.

possibility of hyperinfection.⁸ Until recently, the standard therapy for strongyloides infection was thiabendazole; however, thiabendazole has potential teratogenicity, questionable efficacy, and significant side effects.¹⁴ More recent therapies include albendazole (an off-label usage in the United States) and ivermectin, anthelmintic agents for oral administration.¹⁴

Albendazole and ivermectin have markedly improved efficacy of treatment and significantly fewer side effects.^{9,15} They are active against a broad spectrum of parasites. They are both well tolerated with few

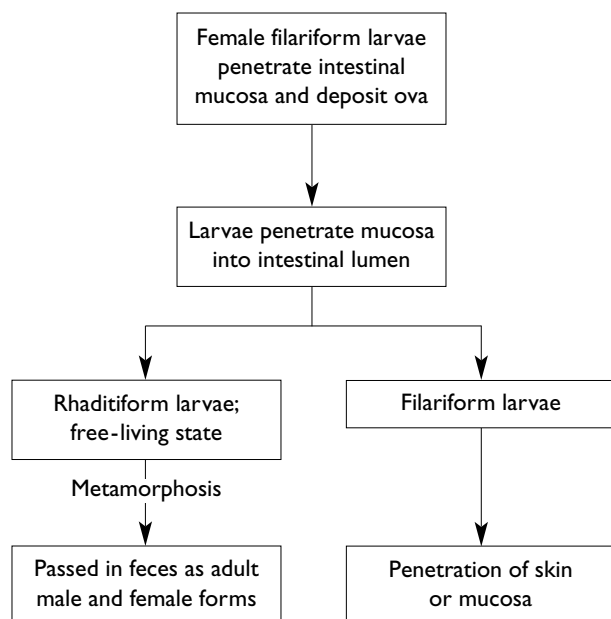


Figure 4. Diagram depicting the life cycle of *Strongyloides stercoralis*.

adverse effects. Liver enzyme levels and complete blood counts should be monitored because leukopenia and elevated liver enzymes occur in 2% to 3% of patients treated with either medication.¹⁶

Ivermectin activity against *S. stercoralis* is limited to the intestinal stages. Recommended dosing of ivermectin is 170 to 200 µg/kg body weight as a single dose. Patients should take ivermectin with water and should be reminded of the need for serial stool examinations to verify eradication of the parasite. At least 3 stool examinations should be conducted over 3 months following treatment. If a patient is still infected after treatment with ivermectin, a re-treatment with the same dose is recommended.

In 2 controlled clinical trials of ivermectin, in which albendazole was used as the comparative agent, ivermectin was found to be curative in 24 of 26 patients and in 126 of 152 patients (92% and 83%, respectively), whereas albendazole was curative in 12 of 22 patients and in 67 of 149 patients (55% and 45%, respectively).¹⁶ Cure rates were documented by serial stool cultures. The recommended dose of albendazole is 200 mg twice daily for 3 days.¹⁴

Corticosteroids should never be administered to a patient with known strongyloides infection, as this can lead to immunosuppression, hyperinfection, and fatal dissemination of the parasite throughout the host.⁸ If

there is a high clinical suspicion for strongyloides infection, an ELISA test should be performed.

CONCLUSION

The case of strongyloides infection presented here shows how difficult making the diagnosis is, even with a high degree of suspicion and modern laboratory and diagnostic procedures. Ancillary laboratory, radiographic, and endoscopic examinations often yield nonspecific or confounding data. Although this patient did initially have respiratory and gastrointestinal symptoms and laboratory results suggesting strongyloides infection, no definitive diagnosis was ever established because of the inability to localize the parasite. **HP**

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