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A Case of Strongyloides Stercoralis Hyperinfection Syndrome

Pejman Soheili, Peter Papadakos, Daniel Cummings

Abstract

It is known that *Strongyloides stercoralis* can induce intestinal strongyloidiasis, hyperinfection syndrome or disseminated strongyloidiasis. Paralytic ileus and associated bacterial infections may be seen as complications of hyperinfection syndrome or disseminated disease. This report discusses a case of hyperinfection syndrome in a patient who was receiving chronic immunosuppressive treatment for rheumatoid arthritis. In spite of treatment for hyperinfection syndrome with oral albendazole and rectal ivermectin, the patient's condition worsened and he died of progressive respiratory failure. The limitations of treatment for hyperinfection syndrome will briefly be discussed.

Keywords: Strongyloides, hyperinfection syndrome, sepsis

Introduction

Infection with the helminth *Strongyloides stercoralis* is endemic in certain parts of the world. Sixty to one hundred million people are estimated to be infected worldwide, but infection is rare in Northeastern United States. *S. stercoralis* is a unique nematode since it completes its life cycle in humans. In an immunocompetent host, the infection is usually mild. People predisposed to severe infection include those who are immunosuppressed, especially through depletion of the TH-2 subset of T helper lymphocytes [1]. Complications from infection by *S. stercoralis* range from mild intestinal discomfort to severe intestinal and extraintestinal pathology. Intestinal manifestations include diarrhea, steatorrhea, ileus, small bowel obstruction, gastrointestinal bleeding, and colitis. Extraintestinal manifestations are closely associated with the autoinfection cycle within the host. These include cough, short-lived pulmonary infiltrates, bronchopneumonia, acute respiratory distress syndrome, abscess formation from secondary bacterial infection, pulmonary hemorrhage, and dissemination to other organs, including the central nervous system. The lung is the most frequent extraintestinal organ affected in the hyperinfection state [2]. Mortality of hyperinfection syndrome has been reported up to 80% [3-4]. We report of *Strongyloides* hyperinfection syndrome and attempted rectal treatment with ivermectin enema.

Clinical record

A 60-year-old retired die-caster was admitted to an outside hospital on September 12, 2005 with a two-day history of crampy lower abdominal pain, with intermittent nausea and emesis. He had a past history significant for a bleeding duodenal ulcer, rheumatoid arthritis, chronic hepatitis B infection, diet-controlled diabetes mellitus, thalassemia trait and *S. stercoralis* infection. He was born in Laos and moved with his family to the United States in 1980. After returning from visiting Thailand and Laos in May 2002, he developed abdominal pain and was diagnosed that June with intestinal strongyloidiasis. He received one dose of ivermectin. In September 2003, an esophagogastroduodenoscopy was performed for a possible malabsorptive syndrome and low carotene levels. Biopsies obtained from the duodenum exhibited helminths presumed by history to be *S. stercoralis*. In January 2004, the patient was treated for 14 days with thiabendazole, though follow-up stool samples were not obtained from him or from his wife. His medications included: prednisone (10mg a day), penicillamine (500mg twice

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daily), pantoprazole (40mg a day) and morphine sulfate sustained-release (30mg three times daily) for pain due to rheumatoid arthritis.

The abdominal exam at the outside hospital revealed guarding and diffuse tenderness. Abdominal roentgenogram showed dilated loops of small bowel (**Figure 1**). Exploratory laparotomy with intention to perform lyses of adhesions was performed that evening. A dilated small bowel and copious serous fluid in the abdominal cavity were observed; however, no adhesions were lysed. In the recovery room, the patient was re-intubated secondary to respiratory insufficiency and taken to the intensive care unit.

nin T level measured 3.63 and a limited-study transthoracic echocardiogram that night revealed a left ventricular ejection fraction of 25% with global dyskinesis. These results were interpreted as evidence for cardiogenic shock and a decision was made to transfer the patient to our institution with a diagnosis of cardiogenic shock and sepsis. The patient was given one dose of ampicillin/sulbactam and metronidazole prior to transfer for a presumed infection of unknown etiology.

The patient arrived early on September 14, 2005, where a bedside transthoracic echocardiogram showed a left ventricular ejection fraction of 75%, a hyperdynamic heart and decreased central venous pressure. WBC count from that

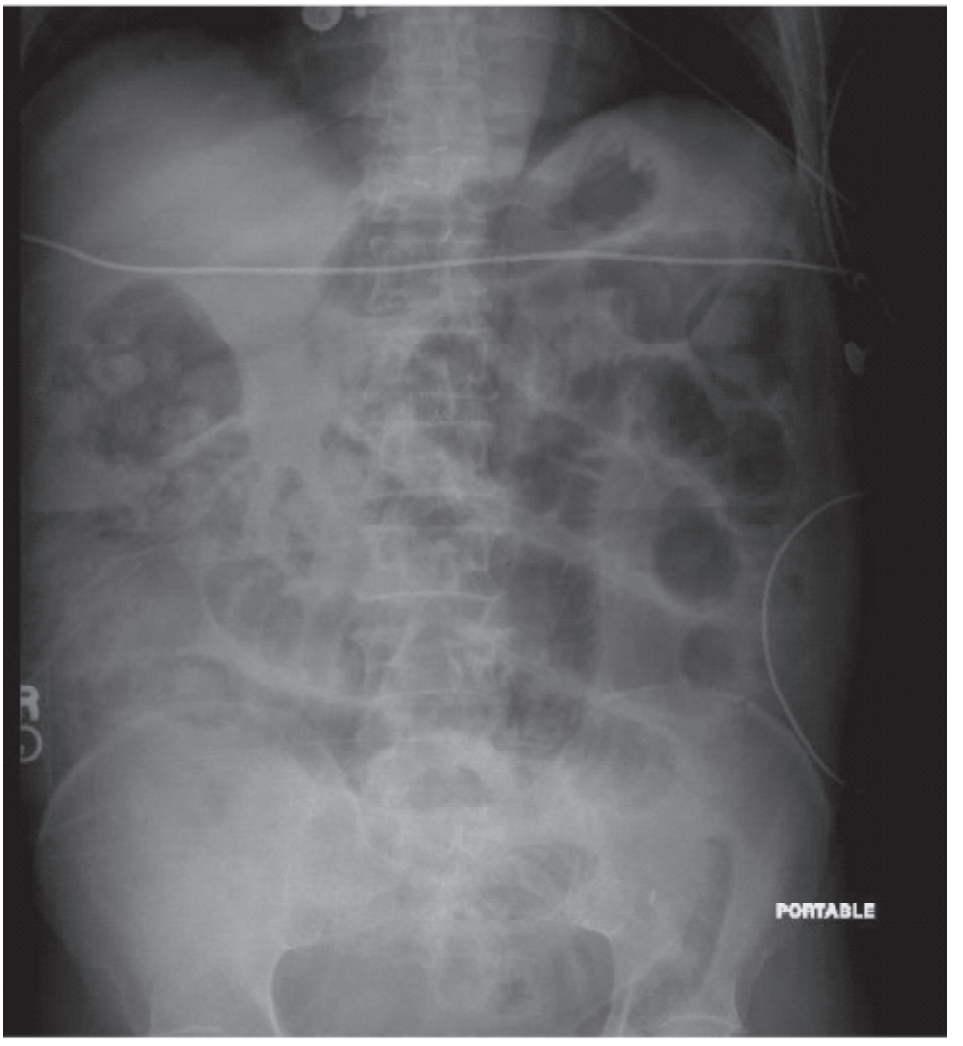

FIGURE 1. ABDOMINAL ROENTGENOGRAM

On September 13, the patient was noted to have persistent sinus tachycardia, a temperature of 40.7 degrees Celsius, and WBC count of 3,400/microliter, 46% segmented neutrophils and 28% band neutrophils. A tropo-

morning was 800/microliter. Blood, urine and sputum cultures were repeated, the patient's antibiotics were changed to vancomycin, tobramycin and piperacillin/tazobactam, and drotrecogin alfa treatment was started (APACHE score

of 25). Stress-dose steroids were started secondary to the patient's history of long-term steroid use. In addition norepinephrine and vasopressin were also immediately started due to refractory hypotension. As the day progressed, increased abdominal pressures (20 mmHg at 1200 to 36 mmHg at 1800) as well as high peak inspiratory pressures led the surgery team to perform another exploratory laparotomy at bedside. Diffuse bowel edema with dilatation and erythema of small bowel were observed without any other noted abnormalities.

On the morning of September 15, sputum and nasogastric drainage sent from the day before showed many polymorphonucleocytes, *S. stercoralis larvae* (**Figure 2**), also *S. marcescens, E. coli,* and *P. aeruginosa*. Vancomycin was discontinued, and the anti-helminthics albendazole (400mg daily through the nasogastric tube) and ivermectin enema (200mcg/kg) were started on September 15, as described in Tarr PE, *et al*. Subsequent sputum stains were negative for *S. stercoralis,* and though leukopenia improved, the patient's condition worsened. Progressively increase in serum lactate levels, persistent lymphopenia with thrombocytopenia requiring platelet transfusions, bandemia and lack of eosinophilia was noted. Norepinephrine and vasopressin, which were begun on September 14, and dobutamine therapy started on September 17, were increased in addition to fluid resuscitation. In spite of increased vasopressor therapy, difficulty with oxygenation persisted and on the night of September 18, 2005, the decision was made with the family to withdraw care. [Stool was not positive for *S. stercoralis* and remained negative during hospital course].

Discussion

This case emphasizes the limitations of anti-helminthic treatment in the setting of severe hyperinfection syndrome. Patients usually succumb to the sequelae of bowel obstruction, Gram-negative septicemia and the spread of filariform larvae, such as what happened to this patient.

Given the setting of small bowel obstruction or adynamic ileus, the patient was mistakenly thought to have adhesions that needed to be lysed. A high index of suspicion from the patient's history aided the team to suspect hyperinfection syndrome. In addition, a blind bronchoalveolar lavage helped establish the diagnosis

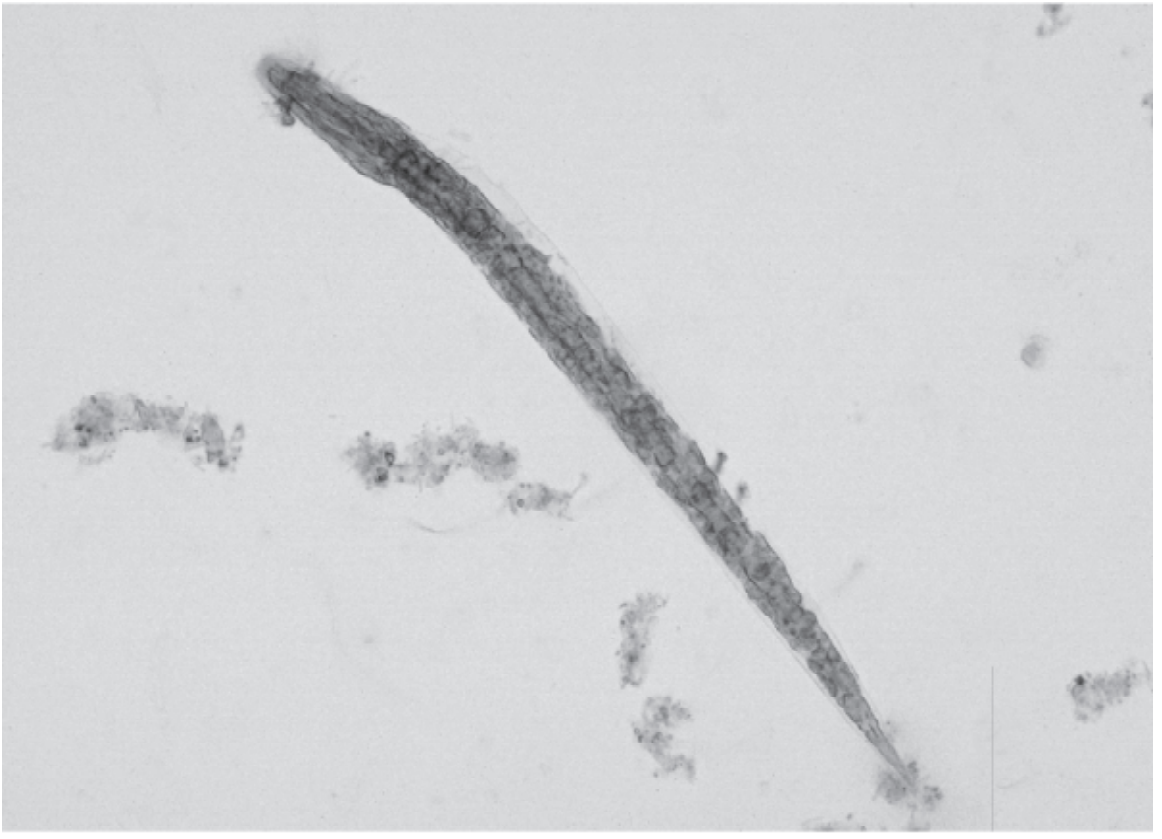

FIGURE 2. BAL ASPIRATE STAINED WITH IODINE (FORMULA OF DOBELL & O'CONNOR) SHOWING STRONGYLOIDES LARVAE.

when the patient was brought to our institution. The known medications to treat strongyloidiasis are not available in parenteral form [5,6], which has led others to attempt other means of administration in the setting of bowel obstruction or ileus [3,7].

Since approval in 1996 for use in human beings, ivermectin has been used most notably for treatment of onchocerciasis, lymphatic filariasis and strongyloidiasis. It is a semi-synthetic compound derived from a soil actinomycete. It induces tonic paralysis in the muscles of affected organisms, probably at nerve- or muscle-type glutamate-receptor Cl- channels expressed only in invertebrates [1,8]. The parasite is then paralyzed by hyperpolarization of the cell membranes and the influx of chloride. These ivermectin receptors have been hypothesized to be sites of resistance, where binding affinity may be altered or weakened. It is most effective given in a concentration-dependent manner. Ivermectin appears to be more efficacious than albendazole or thiabendazole in several small randomized studies for treating strongyloidiasis. Although it is predominantly used in an oral tablet form for uncomplicated intestinal strongyloidiasis, it has also been described to be delivered in the form of enemas and subcutaneous suspension [3,7,9].

Albendazole belongs to the benzimidazole group of antihelminthic drugs. The benzimidazoles are useful against gastrointestinal nematodes, where they have relatively little systemic absorption. It has broad anti-helminthic properties. Its killing mechanisms include inhibition of microtubule polymerization through binding to β-tubulin, inhibition of glucose transport, disruption of oxidative phosphorylation and blocking mitochondrial fumarate reductase [8]. Resistance develops from trading susceptible β-tubulin gene isotypes for resistant mutations (Tyr instead of Phe at position 200). It is variably absorbed after oral administration, and enhanced by presence of fatty foods as well as bile salts. This is different from thiabendazole, which is the best systemically absorbed drug of the benzimidazoles. The use of albendazole was justified in our patient for two reasons: one was that the patient had already failed a 14-day course of thiabendazole, so the benefit of treatment again with this drug was thought to be small compared to attempting a new drug; additionally, the patient's feculent and bilious gastrointestinal material that was suctioned out suggested that albendazole may have reasonable absorption; however, given that the drug was suctioned out even after 4 hours of clamping the nasogastric tube, this drug was probably not absorbed to any significant degree.

A challenge that these drugs face in the setting of strongyloidiasis is when the bowel is non-functioning, such as with ileus or mechanical obstruction. Others have attempted, with reported success, to administer ivermectin rectally as well as subcutaneously [7,9]. In spite of rectal administration in this case, the patient did not survive. Given the patient's background of rheumatoid arthritis and immunosuppression with prednisone therapy, this is no surprise. For one, corticosteroids reduce the absolute count of circulating eosinophils, basophils and monocytes. Moreover, corticosteroids are now thought to assist in the formation of infective larvae by female nematodes. This is posited to occur because the worm itself produces ecdyosone, a steroid that may transmit molting signals [1,10]. Exogenous steroids thus may cross-cover as it were, to increase molting signals for formation of larvae, which then perpetuate auto-infection.

In patients who are unable to absorb oral anti-helminthic therapy secondary to their gastrointestinal complications, other methods of drug delivery must be attempted. Further study is needed to assess the best means of drug delivery in such settings.

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