Strongyloides stercoralis hyperinfection associated with impaired intestinal motility disorder

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ABSTRACT

Infection by Strongyloides stercoralis is a highly prevalent helminthiasis, which is mostly distributed in the tropical and subtropical regions of the world. Although a substantial number of cases are asymptomatic or paucisymtomatic, severe and life-threatening forms of this infection still occur and not infrequently is lately diagnosed. Gram-negative bacteria septicemia, which frequently accompanies the severe helminthiasis, contributes to the high mortality rate. Severe infection is invariably triggered by any imbalance in the host's immunity, favoring the auto-infective cycle, which increases the intraluminal parasite burden enormously. Clinical presentation of severe cases is varied, and diagnosis requires a high suspicion index. Acute abdomen has been reported in association with S. stercoralis infection, but intestinal necrosis is rarely found during the surgical approach. The authors report the case of a man who sought the emergency unit with recent onset abdominal pain. Clinical and imaging features were consistent with obstructive acute abdomen. Scattered adhesions and a necrotic ileal segment with a tiny perforation represented the surgical findings. The patient outcome was unfavorable and respiratory distress required an open lung biopsy. Both surgical specimens showed S. stercoralis infection. Unfortunately the patient underwent multiple organ failure and septicemia, and subsequently died. The authors call attention to the finding of intestinal necrosis and impaired intestinal motility disorder as possibilities for the diagnosis and risk factor, respectively, for a severe infection of S. stercoralis.

Keywords
Strongyloidiasis; Strongyloides stercoralis; Intestinal Diseases; Parasitic

INTRODUCTION

Intestinal strongyloidiasis still represents a marked cause of overwhelming helminthiasis in the tropical and subtropical regions, which is strongly associated with poor sanitation and hygiene. It is estimated that 100 million people are infected in these regions; among them, 50% are asymptomatic. However, when the equilibrium (maintained by the immune system) between the host and the parasite is impaired,
life-threatening infection ensues.\textsuperscript{1-3} This frequently severe complication may happen up to 40 years from the time the infection was first acquired.\textsuperscript{4}

Quite often, the diagnosis of strongyloidiasis is somewhat challenging or unnoticed due to some particularities of the worm’s biological cycle and the non-negligible number of the aforementioned symptomless cases.\textsuperscript{5,6} Although the infection occurs through the penetration of the infective filariform larvae into the skin, auto-infection does occur after the transformation of non-infective rhabditiform larvae into filariform inside the intestine, which invade the colonic mucosa or perianal skin (a process enhanced by corticosteroids). Therefore, in contrast to other nematodes species, the *Strongyloides stercoralis* may maintain its biological cycle without leaving the host.

The auto-infection phenomenon may explain the persistence of infection for a long time (even when the host is out of the endemic area) and the high-burden infections in the immunocompromised hosts.\textsuperscript{2,3,7} In this setting, hyperinfection syndrome comprises an increase in parasite burden due to acceleration of the auto-infection cycle restricted to the sites of the biological cycle; whereas the disseminated strongyloidiasis consists in a systemic spread of filariform larvae to sites outside their normal migration pattern. The hyperinfection is usually accompanied by Gram-negative septicemia somehow facilitated by the infective filariform larvae through the intestinal mucosa.\textsuperscript{8,9}

**CASE REPORT**

A 52-year-old Caucasian male sought the emergency facility complaining of a 1-week history of abdominal pain and distension followed by vomiting. His past medical history included hypertension, previous ischemic stroke, and a laparotomy for trauma 15 years ago. He denied tobacco smoking but drank alcoholic beverages.

Physical examination on admission revealed an afebrile, ill-looking patient, with tachypnea and tachycardia. Blood pressure was 100/60 mmHg and body mass index was 29. Pulmonary and cardiac examination was normal, but the abdomen was distended, with rebound tenderness. Bowel sounds were present and hypodynamic. The initial laboratory work-up is shown in Table 1.

The abdominal radiograph showed air-filled dilated bowel loops with fluid levels consistent with the diagnosis of small bowel obstruction. No sign of pneumoperitoneum was evidenced.

Facing the clinical features, laboratory results, and imaging data, the diagnosis of obstructive acute abdomen was made. Considering the previous laparotomy, abdominal adhesion was the main suspected etiology. The patient underwent an exploratory laparotomy that – besides multiple adhesions of the omentum to the visceral peritoneum, and adhesions between duodenal loops – showed a necrotic jejunal area measuring 25 cm at its longest axis with a tiny perforation (Figure 1) 20 cm from the Treitz angle. The adhesions were manually released and

| Exam         | Result       | RV            | Exam         | Result    | RV            |
|--------------|--------------|---------------|--------------|-----------|---------------|
| Hemoglobin   | 16.3         | 12.3–15.3 g/dL| Potassium    | 3.7       | 3.5–5.0 mEq/L |
| Hematocrit   | 47.8         | 36.0–45.0%    | Sodium       | 140       | 136–146 mEq/L |
| Leukocytes   | 11.540       | 4.4–11.3 x 103/mm3 | Urea       | 134       | 5–25 mg/dL   |
| Segmented    | 47           | 45–70%        | Creatinine   | 1.41      | 0.4–1.3 mg/dL|
| Eosinophil   | 0            | 1–4%          | CRP          | 170       | < 5 mg/L     |
| Basophil     | 0            | 1–4%          | Lactate      | 15.3      | 4.5–19.8 mg/dL|
| Lymphocyte   | 8            | 18–40%        | Anti-HIV     | negative  |               |
| Monocytes    | 17           | 2–9%          |              |           |               |
| Platelets    | 339          | 150–400 x 10\(^3\)/mm\(^3\) |           |           |               |

CRP = C-reactive protein. RV = reference value.
the necrotic jejunal segment was resected followed by enteroanastomosis.

The post-operative follow-up was troublesome. Although the patient was prescribed a broad-spectrum antimicrobial regimen, he presented respiratory failure with disseminated rales and wheezing on the very first postoperative day, which required corticotherapy (hydrocortisone 100 mg/daily) and mechanical ventilatory support. The thoracic computed tomography (CT) showed cystic bronchiectasis in the upper right lobe, confluent cavitation centrilobular nodules, and ground glass opacity (Figures 2 and 3).

The bronchoscopy showed a huge amount of purulent secretion in both lungs, edematous and hyperemic respiratory tree mucosa. Bronchoalveolar lavage was undertaken, and the acid-fast bacilli research was negative, unfortunately *S. stercoralis* larvae was not researched because the lack of clinical suspicion. An open lung biopsy was performed; the histologic examination revealed diffuse alveolar damage with focal chronic inflammatory process characterized by eosinophil aggregates and epitheliod granulomas, and the presence of parasites consistent with filariform larvae of *S. stercoralis* (Figure 4). Acid-fast bacilli research by Ziehl-Neelsen staining was negative.

In the meantime, the histologic examination of the resected necrotic jejunal segment showed chronic inflammatory infiltration in the intestinal wall with marked eosinophilia, granulomas through the intestinal wall and serosa, rare giant multinucleated cells, with focal necrosis and ulceration and venous thrombosis, besides the presence of structures consistent with *S. stercoralis* (Figure 5). Perforation was focal, probably related to parasite migration, with concurrent serositis.

Although the patient was treated with ivermectin, albendazol, and a broad-spectrum antibiotic regimen, the outcome was unfavorable with multiple organ failure. He died on the thirty-second day of hospitalization.

**DISCUSSION**

Although half of the cases of *S. stercoralis* remain asymptomatic for a long time, mild or moderate gastrointestinal symptoms represent the majority of symptomatic cases. However, severe and life-threatening infection does occur and should always be included in the differential diagnosis of acute abdomen in the endemic areas. These cases occur when the auto-infective cycle takes place and the intraluminal burden of parasites increases. In this setting, hyperinfection syndrome or disseminated disease may occur, which is often accompanied by...
intestinal-bacteria septicemia. Respiratory symptoms also occur during the auto-infective cycle and may be represented by pneumonia or asthma-like features.\textsuperscript{10}

All these severe cases are invariably associated with a clear cause of immunosuppression, namely: corticotherapy\textsuperscript{5,6} and/or chemotherapeutic agents,\textsuperscript{1,11} chronic immunodeficiency,\textsuperscript{12} chronic renal failure,\textsuperscript{13} diabetes mellitus,\textsuperscript{14} burns,\textsuperscript{11,13} gut motility-impairing disorder,\textsuperscript{15} malnutrition,\textsuperscript{11,13} alcoholism,\textsuperscript{11} hypochloridria,\textsuperscript{16} malignancies,\textsuperscript{11,17} leprosy,\textsuperscript{13} post transplantation,\textsuperscript{18} and HTLV-1 infection.\textsuperscript{19} HIV infection also constitutes a risk factor for severe strongyloidiasis, but contrary to what one might expect, there are few case reports on this association.\textsuperscript{20-22}

Clinically, these severe forms of infection may be preceded by diarrhea, steatorrhea,\textsuperscript{4} and weight loss, which may be of indolent or of subtle onset. Hematemesis, partial small bowel obstruction,\textsuperscript{23-25} and adynamic ileus,\textsuperscript{26} have also been reported, but necrosis of the intestinal wall is rarely described. In 2006, Giavina-Bianchi et al.\textsuperscript{8} reported a case of hemorrhagic necrosis of the intestinal muscular layer in an immunodeficient patient, and prior to that, in 1975, Ali-Khan and Seemayer\textsuperscript{27} had reported a case with necrosis of the small bowel and right colon due to obliterative arteritis secondary to \textit{S. stercoralis} infection. In 2001, Rodrigues et al.\textsuperscript{9} described the case of an obstructive acute abdomen caused by a narrowed ileal segment in an old man taking corticosteroids for osteoarthritis who, despite surgical treatment, died because of Gram-negative septicemia. In our case report, the surgical finding was a necrotic segment of ileal loop with a tiny perforation, probably related to parasite migration and causing serositis. Adhesions did exist and a suspicion of internal hernia was

Figure 4. Photomicrography of the lung showing in A – diffuse alveolar damage (100x). B – Subpleural well-formed granuloma (200x) and in C and D well-formed granulomas with eosinophils and \textit{S. stercoralis} larvae (arrows) (400x).
also suspected during surgery, and could justify the intestinal vascular suffering. However, we dare to consider that the intestinal necrosis due to the internal hernia was corroborated by the *S. stercoralis* infection as well. The presence of adhesions and the subtle impaired intestinal motility derangement could explain a prone situation for the development of the parasite’s auto-infective cycle. In 1996, Gutierrez et al., described six cases of *Strongyloides stercoralis* eosinophilic granulomatous enterocolitis, which presents similar histological findings found in this case report. However in our case diarrhea did not take part of the clinical features neither the colonic involvement was present. Moreover in our case the pulmonary involvement was outstanding, a different feature of the cases described by Gutierrez. Indeed, the histological findings of *Strongyloides stercoralis* hyperinfection in non immunocompromised patients are represented by intestinal wall (small intestine and colon) penetration of the filariform larvae accompanied by inflammatory response that varies from mild to marked infiltration of lymphocytes, plasma cells, histiocytes, neutrophils, and giant cells. Intestinal obstruction caused by paralytic ileus or mechanical obstruction is well known complications of *Strongyloides stercoralis* hyperinfection. Respiratory complaints are present in up to 68% of cases of hyperinfection syndrome and are represented by bronchitis, asthma, bronchopneumonia, and adult respiratory distress syndrome. Pulmonary

Figure 5. Photomicrography of the jejunum showing in A – chronic inflammatory infiltration with eosinophils and congestion in submucosa (100x); B – detail of penetrating filariform larva of *S. stercoralis* surrounded by eosinophils (400x). C – Eosinophilic infiltration of muscular layer with a giant cell (400x), and D – Serosal granuloma with focal central necrosis and transversal section of larvae. Serosa is inflamed (400x).
imaging studies may reveal the presence of fine mililiary nodules, interstitial infiltrates, pleural effusion, and lung cavitiation (secondary to bacteria septicemia). Our patient presented respiratory symptoms, and the pulmonary CT findings were typical.

The high index of suspicion is of paramount importance for the diagnosis of severe strongyloidiasis. Unfortunately, the severe cases are not accompanied by eosinophilia, which, indeed, may be normal or decreased, in some cases due to corticotherapy. In these cases, serologic tests are not as useful as they are in asymptomatic cases where eosinophilia is present. Therefore, diagnosis of strongyloidiasis is based on the finding of larvae in the stools, sputum, bronchial, gastric or duodenal aspirates, or gastric and/or duodenal or pulmonary biopsy.

Regardless of the type of infection, every patient diagnosed with S. stercoralis should be treated to prevent severe forms of the disease. Currently, the treatment of choice is made with ivermectin,30 although thiabendazol has been used for years with the cure ratio of 67–91%.31

Interestingly, the patient presented herein did not present any known cause of immunosuppression, but he presented abdominal adhesions and an internal hernia suspicion, which could favor the development of the severe infective form of S. stercoralis. A corticosteroid was used during the patient’s respiratory failure, which most probably was due to the worm pulmonary cycle and the Gram-negative bronchopneumonic foci.32

Our patient presented a recent history of symptoms consistent with acute obstructive abdomen diagnosis, which became more evident with the imaging studies. Abdominal adhesion was the preoperative diagnosis, since he’d had a previous laparotomy. The diagnosis of strongyloidiasis was made only with the histological examination. We can only consider this case as a S. stercoralis hyperinfection since the parasite was not found in any other site outside its biological cycle.

The diagnosis of severe forms of S. stercoralis infection is challenging and therefore a high level of suspicion is required. Imaging studies are non-specific and eosinophilia is an exceptional finding. In our case, the 6% of eosinophils in the initial blood cell count was helpless.

Quite often, incidental diagnoses through surgical specimens are done.33 In our case it was a surprise when in both surgical specimens S. stercoralis was the causative agent.

The treatment of choice for S. stercoralis infection is ivermectin 20 mcg/kg for 2 or 3 days and may be repeated after 14 days, and this should always be prescribed when, for any reason, the immune system is jeopardized, since disseminated strongyloidiasis has a mortality rate of 85–100%.7,34

Some investigators advocate the use of ivermectin combined with albendazol, but this concept requires more controlled studies. Other routes of administration, rather than the oral one, may be used for these drugs.35

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