CASE REPORT

Strongyloides hyperinfection syndrome in an immunocompetent host resulting in bandemia and death

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SUMMARY

Strongyloides stercoralis infection is usually asymptomatic but can result in a hyperinfection syndrome, most commonly triggered by acquired or iatrogenic immunosuppression. Here, we present a case of a man aged 60 years originally from a strongyloides endemic area with a medical history of alcohol abuse who presents with strongyloides hyperinfection syndrome (SHS) complicated by partial small bowel obstruction, pulmonary haemorrhage, large bandemia without eosinophilia and cardiac arrest resulting in death. This case is notable for the presence of bandemia and absence of eosinophilia, lack of historical risk factors for hyperinfection, specifically corticosteroid immunosuppressants, and dramatic decline in clinical status which ultimately resulted in the patient's death. Clinicians should suspect SHS in immunocompetent patients who are from an endemic area and who have persistent gastrointestinal and/or pulmonary manifestations in the absence of a clear cause.

BACKGROUND

Strongyloidiasis is caused by the nematode parasite *Strongyloides stercoralis* which can cause a clinical spectrum of disease ranging from asymptomatic eosinophilia in immunocompetent patients to a life-threatening strongyloides hyperinfection syndrome (SHS) and disseminated infection in the immunosuppressed.¹ In the USA, uncomplicated strongyloidiasis is commonly reported in immigrants and refugees; however, SHS resulting in death is rarely reported and has not been described in the absence of immunosuppression.² South American publications³ have suggested that prior alcohol abuse is an independent risk factor for developing SHS; however, in this case, the patient had been abstinent from alcohol for the prior 8 months, and had no biochemical or imaging evidence of chronic liver disease. Therefore, we present an unusual case of SHS in an otherwise immunocompetent immigrant man, which resulted in massive bandemia and unexpected death.

CASE PRESENTATION

Our patient is a man aged 60 years with a medical history of hypertension, diabetes and obesity who initially presented with abdominal pain, poor oral intake, nausea and vomiting. He had been admitted to an outside hospital 1 week prior to admission to our hospital with similar symptoms. During that admission, the patient was treated for gastritis with

intravenous proton pump inhibitors and underwent an oesophagoduodenoscopy. The endoscopy report made mention of a 'parasitic infection' which was treated with one dose of albendazole without any further treatment or follow-up. The patient was discharged 3 days prior to admission to our hospital. On arrival to our hospital's emergency department, the patient expressed symptoms of severe abdominal pain, nausea and vomiting. He was haemodynamically stable. Laboratory tests as outlined in [table 1](#) were notable for leucocytosis as well as severe hyponatraemia, prompting admission to our intensive care unit for fluid and electrolytes management.

CT scan of the abdomen at the time of admission showed peripancreatic inflammatory changes and oedema consistent with acute pancreatitis. Also seen were prominent fluid-filled loops of small bowel with mild wall thickening and enhancement, thought to be secondary inflammation from acute pancreatitis.

Review of the patient's social history revealed that he was originally from a rural village in El Salvador and had immigrated to the USA 5 years prior to be closer to his family. He was a prior tobacco smoker but had quit smoking 10 years ago. He was previously a moderate to heavy alcohol drinker (between 12 and 24 12-ounce beers daily), but had stopped drinking alcohol 8 months prior to admission. He had no personal or family history of *S. stercoralis* or other parasitic infections. The patient had no known history of congenital or acquired immunodeficiency and had never been treated with immunosuppressants.

INVESTIGATIONS**Laboratory testing**

Haemogram on admission was significant for leucocytosis of 15 000 with 10% bands. Leucocytosis with bandemia persisted for the remainder of the hospitalisation (see [table 1](#)). Liver function panel, including alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase and bilirubin, were within normal limits. Serum albumin was depressed at 1.3 mg/dL and serum total protein was depressed at 3.3 mg/dL. Serum sodium was significantly low at 114 mmol/L, BUN was 10 mg/dL, creatinine was 0.5 mg/dL, calcium was 6.8 mg/dL (calcium corrected for hypalbuminaemia was normal). Lipase level was 20 units/L on admission and remained low on subsequent testing over the course of the hospitalisation. HIV ELISA

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Table 1 Laboratory results

	Day 0	Day 1	Day 2	Day 3
WCC	$15.99 \times 10^3/\mu\text{L}$	$14.86 \times 10^3/\mu\text{L}$	$19.94 \times 10^3/\mu\text{L}$	$16.83 \times 10^3/\mu\text{L}$
Bands	$1.5 \times 10^3/\mu\text{L}$	$6.98 \times 10^3/\mu\text{L}$	$8.57 \times 10^3/\mu\text{L}$	$7.24 \times 10^3/\mu\text{L}$
Eosinophils	$0.16 \times 10^3/\mu\text{L}$	$0.15 \times 10^3/\mu\text{L}$	$0.0 \times 10^3/\mu\text{L}$	$0.0 \times 10^3/\mu\text{L}$
Sodium	114 mmol/L	122 mmol/L	118 mmol/L	122 mmol/L

performed 1 week prior to admission at the outside hospital was negative. Fractionated immunoglobulin testing and testing for HTLV were not performed.

Microbiology testing

One out of two sets of blood cultures (aerobic and anaerobic) drawn on admission grew coagulase-negative staphylococcus species. Two sets of repeat blood cultures drawn on day 1 returned as no growth after 5 days of incubation. *Clostridium difficile* toxin and antigen from the stool as well as standard stool culture were negative. A stool sample sent on day 2 for ova and parasites returned on day 4 and demonstrated a high burden of *S. stercoralis*.

Imaging studies

The admission CT scan of the abdomen and pelvis is described above. Anterior–posterior chest X-ray performed on admission was unremarkable. On hospital day 3, upright and supine X-ray of the abdomen was suggestive of partial small-bowel obstruction.

DIFFERENTIAL DIAGNOSIS

The initial management for this patient was focused on managing electrolyte abnormalities, pancreatitis and partial small-bowel obstruction. Pancreatitis in the absence of elevated pancreatic enzymes was thought possibly secondary to active pancreatic inflammation in the setting of chronic pancreatitis and ‘burnt-out’ pancreas. When more history was obtained, including history suggestive of only moderate alcohol abuse, lack of prior episodes of pancreatitis as well as an unknown parasitic infection from the outside hospital, the differential diagnosis was expanded to include causes of duodenitis, which may cause local inflammation of the pancreas as well as possible protein-losing enteropathy manifesting as a very low serum albumin. Finally, the large bandemia prompted exploration of occult infection. When the ova and parasites study from the stool returned with high parasite burden, our attention turned to the possibility of SHS.

TREATMENT

Initially, the patient was admitted to the intensive care unit for aggressive volume resuscitation and monitoring of fluids and electrolytes. He was kept NPO given imaging findings and examination consistent with pancreatitis and was given intravenous fluids for hydration. Nasogastric intubation with suction was performed on day 3 for conservative management of partial small-bowel obstruction seen on imaging. The patient was also placed on a patient-controlled analgesia pump with morphine sulfate for pain control. On discovery of strongyloides infection in the stool, treatment with ivermectin was initiated; however, the patient’s clinical status deteriorated rapidly on hospital day 4 and thus definitive treatment was not initiated.

Figure 1 A strongyloides larvae (centre of the photograph) is seen crossing an alveolar septae. There is minimal surrounding inflammation (H&E $\times 400$ magnification).

OUTCOME AND FOLLOW-UP

As described, the patient was diagnosed with strongyloidiasis and scheduled to receive ivermectin. However, prior to the first dose, he developed asystolic cardiac arrest. Immediate resuscitation efforts were initiated; however, the patient did not regain a perfusing rhythm, and the patient was pronounced dead on hospital day 4. At the request of the patient’s family, an autopsy was performed which was consistent with the SHS.

The autopsy results were notable for several important findings. First, the patient had confirmed hyperinfection syndrome with *S. stercoralis* rhabditiform larvae present in the lung alveoli (figure 1) as well as invading the small bowel. Gross and microscopic examination of the lung was consistent with pulmonary oedema as well as pulmonary haemorrhage. Gross examination of the small bowel was consistent with ileus paralyticus resulting in partial small-bowel obstruction and twisting of the duodenum at the level of the head of the pancreas. Bone marrow biopsy revealed a high density of eosinophils (figure 2). There was no evidence of acute coronary syndrome, liver cirrhosis or aspiration pneumonia.

DISCUSSION

This case describes many important points pertaining to the diagnosis and treatment of strongyloides infections within countries where *S. stercoralis* is not considered endemic and therefore is less readily included in a practitioner’s differential diagnosis. While it is estimated that 30–100 million people are infected worldwide, strongyloidiasis is underdiagnosed in

Figure 2 Bone marrow biopsy shows typical marrow elements with numerous eosinophils. (H&E $\times 400$.)

nations where it is not endemic.⁴ The major diagnostic problem is that strongyloides infection often does not show distinctive features clinically and may also have non-specific laboratory and imaging findings.⁴

Strongyloides stercoralis is a roundworm endemic to tropical and subtropical areas (as in our patient from El Salvador) and is often contracted by humans walking in bare feet on soil contaminated with free-living larvae. The filariform (infectious) larvae penetrate the skin of the feet, migrate haematogenously to the lungs, climb to the trachea and are then swallowed. Adult worms burrow into the small intestine and shed rhabidiform (non-infectious) larvae which can mature into filariform larvae in the gastrointestinal (GI) tract. Its life cycle is notable for the cycle of autoinfection whereby larvae are excreted in the GI tract and reinfect the host via the GI mucosa or perianal skin. Commonly, strongyloides infection is asymptomatic, but when present, symptoms can involve the GI tract, skin and lungs in a waxing and waning pattern which can be undiagnosed for years. Laboratory tests are usually notable for eosinophilia and may be the only indication of strongyloides infection.^{5–6} Strongyloides infection is diagnosed by microscopic examination of the stool or by serological testing.⁷

Rarely, the cycle of autoinfection can escalate to a hyperinfection syndrome in which filariform larvae penetrate the GI tract, and enter the bloodstream. Known risk factors for converting into SHS include exogenous or acquired immunosuppression⁸ including steroid immunosuppressants,^{9–10} or the presence of human T-lymphotrophic virus type-1.¹¹ Although HIV was previously considered a risk factor for developing SHS, this has been under debate.^{12–13} South American studies have also demonstrated that infection rates are higher in alcoholics than in control groups. It has been hypothesised that regular ethanol intake might lead to an immune modulation or alteration in corticosteroid metabolism even in the absence of liver cirrhosis.³ In our case, our patient had been abstinent from alcohol for several months; however, his prior alcohol use may have predisposed acquisition of strongyloides as well as increased the parasite burden in the GI tract.

The hyperinfection syndrome may be manifested by a number of clinical findings, including shortness of breath, cough, abdominal pain, nausea, vomiting, diarrhoea and fever. Our case is unique in that there was no known triggering immunosuppression other than the history of moderate alcohol use, nor did the patient have eosinophilia during this hospitalisation or previously.

Eosinophilia is commonly absent during the hyperinfection syndrome because hyperinfection is often triggered by administration of glucocorticoids which suppress eosinophilia. Hence, relying on peripheral eosinophilia to diagnose strongyloides hyperinfection may limit the differential diagnosis and prevent an accurate diagnosis of this life-threatening condition. In our case, there was extensive eosinophil production within the bone marrow; however, in the peripheral smear, there were only extensive band forms. Some case reports have shown lack of eosinophilia in SHS when coupled with bacteraemia;¹⁴ however, our patient's blood cultures remained negative off of all antimicrobials and the autopsy did not discover an occult pyogenic source. To the best of our knowledge, there are no other literature reports of large peripheral bandemia in the SHS.

Typical treatment for uncomplicated strongyloidiasis is with ivermectin given orally in two separated doses.^{13–15} An alternative to ivermectin is albendazole; however, efficacy may be lower for this agent.¹⁶ In patients with disseminated infection, treatment guidelines recommend prolonged courses of

ivermectin alone¹⁷ or in conjunction with albendazole¹⁸ until symptoms resolve and serial stool examinations return negative. In immunocompromised hosts, treatment may require prolonged courses of ivermectin.^{12–19} In our case, treatment with ivermectin was prescribed as soon as microbiology data returned from the patient's stool sample; however, the patient died before the first dose could be administered.

Finally, there are several systems-based issues that may have contributed to the final outcome in this case. First, the clinical team relied heavily on the imaging studies showing pancreatitis despite a normal lipase level, which delayed the diagnosis of duodenitis and bowel obstruction. Second, records from the prior hospitalisation were slow to arrive and did not clearly describe the endoscopy findings nor the diagnosis and treatment of the incidentally mentioned 'parasite'. Finally, ova and parasite studies from the stool returned several days into the patient's hospitalisation at which point the patient's clinical status had already deteriorated. More rapid diagnosis of strongyloides infection may have prevented an escalating hyperinfection syndrome.

In summary, we believe that this patient's SHS manifested as partial bowel obstruction, pulmonary haemorrhage and peripheral blood bandemia. The inciting trigger leading to the autoinfective cycle and the SHS remains unknown, but the patient's prior alcohol abuse history may have been contributory.

Learning points

- ▶ Strongyloides hyperinfection syndrome (SHS), while uncommon in developed countries, should be considered in patients who are critically ill and who are originally from endemic countries.
- ▶ The SHS can uncommonly present with bandemia, and pulmonary and gastrointestinal symptoms, even in the absence of immunosuppression or concomitant septicemia.
- ▶ Treatment for strongyloides should be initiated as quickly as possible once the diagnosis has been made in order to prevent the high rates of mortality associated with the hyperinfection syndrome.
- ▶ Public health efforts may be considered to screen asymptomatic individuals who arrive in the USA from endemic areas.

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Competing interests None declared.

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