Strongyloidiasis hyperinfection after renal transplant presenting as diffuse alveolar hemorrhage with respiratory failure

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ABSTRACT

Strongyloides stercoralis is a helminthic enteric parasite estimated to infect at least 30 to 100 million people globally. It is transmitted via contaminated soil with a unique ability to complete its entire life cycle in the human host. It is common in humid, tropical, and subtropical regions of the world and is endemic in the Southeastern United States. Strongyloidiasis hyperinfection has been described in a variety of conditions that impair host immunity, including immunosuppression after transplantation. The syndrome has a high mortality rate but may initially present with nonspecific symptoms. A high degree of clinical suspicion coupled with early detection and aggressive therapeutic measures is paramount to a successful outcome.

KEYWORDS Filariform larvae; hyperinfection; larva currens; pulmonary hemorrhage; strongyloidiasis

S *strongyloides stercoralis* is an intestinal nematode that can remain dormant for decades in immunocompetent hosts, progressing to fulminant hyperinfection syndrome in immunocompromised hosts.¹ It is endemic in the Southeastern United States, where most cases occur in immigrants and military veterans.^{1,2} The life cycle of *Strongyloides* is composed of a free-living cycle outside of the host as rhabditiform larvae and a parasitic life cycle as infective filariform larvae (*Figure 1*). In hyperinfection syndrome, this classic life cycle is accelerated, and rhabditiform larvae may develop into infectious filariform larvae within the intestine, capable of causing disseminated strongyloidiasis.^{3,4} During this process, they induce alveolar capillary bleeding and potent eosinophilic inflammation.³ The adult female worms embed themselves in the small intestinal mucosa and produce eggs, which are excreted with stool. Lack of early recognition and aggressive therapy of hyperinfection can result in mortality rates as high as 87%.^{3–5} Our case highlights the specific vulnerability of transplant recipients, the atypical presentation with high mortality, and the diagnostic challenges associated with this syndrome.

CASE REPORT

A 60-year-old black male army veteran with end-stage renal disease on hemodialysis was admitted for deceased-donor kidney transplantation. He was born and lived in Central Texas for most of his life except for travel to Europe while in the military and to Mexico and Florida for vacations. There was no prior history of eosinophilia or chronic viral infections.

Following induction therapy with basiliximab and corticosteroid taper, maintenance immunosuppression consisted of tacrolimus, mycophenolate sodium, and prednisone. Tacrolimus levels were maintained between 8 and 10 ng/dL.

Posttransplant, he reported a 13-kg weight loss and irregular bowel movements even though oral intake was reasonable. At 2 months, he developed severe fatigue, cough productive of rusty sputum, dyspnea, and increasing anemia necessitating hospitalization. Physical exam was significant for an ill-appearing, cachectic, and fatigued man with diffuse bilateral rhonchi and a purpuric skin rash over the anterior abdominal wall. Initial laboratory results are listed in *Table 1*.

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Figure 1. Life cycle of *Strongyloides*. Used with permission from the Centers for Disease Control and Prevention, Division of Parasitic Diseases.

Chest x-ray/computed tomography showed bilateral infiltrates/ground glass appearance with worsening respiratory status requiring endotracheal intubation. Bronchoscopy with bronchoalveolar lavage showed diffuse alveolar hemorrhage, for which pulse steroids and plasmapheresis were initiated. Serologic evaluation and renal allograft biopsy were negative for vasculitis/lupus and rejection, respectively. A repeat bronchoalveolar lavage returned positive for the larval forms of *Strongyloides* (Figure 2). Due to concern that the purpuric skin rash may represent “larva currens,” a punch biopsy was done that revealed *Strongyloides* larvae in the skin (Figure 3). Blood cultures grew *Enterococcus faecium*. Stool for ova and parasites was positive for *Strongyloides*. Enzyme-linked immunosorbent assay for *Strongyloides* was equivocal to low.

The patient was started on albendazole and ivermectin subcutaneously and as retention enema in view of ileus/vomiting with discontinuation of immunosuppressant medications and initiation of dialytic support. His overall status continued to deteriorate, leading to irreversible septic shock and ultimate demise.

Postmortem biopsy of the liver and lung tissues showed filariform larvae with absence in the native and transplanted kidneys. Because testing for *Strongyloides* serology in the pre-transplant serum was negative in our patient and positive in the donor, this information was shared with the United Network for Organ Sharing. Despite negative testing of all other organ recipients from the same donor, they were treated empirically for the disease in light of our patient’s case.

Table 1. The patient’s initial laboratory results

Test	Result
Blood urea nitrogen (mg/dL)	36
Creatinine (mg/dL)	2.46
Sodium (mEq/L)	122
Potassium (mEq/L)	5.0
Chloride (mEq/L)	97
Carbon dioxide (mEq/L)	14
Anion gap (mEq/L)	11
Calcium (mg/dL)	8.3
Phosphorus (mg/dL)	3.6
Magnesium (mg/dL)	1.8
Tacrolimus (ng/mL)	10.6
Hemoglobin (g/dL)	7.2
Hematocrit (%)	21.0%
Platelets ($10 \times 9/L$)	265
White blood cell ($10 \times 9/L$)	5.4
Granulocytes (%)	73%
Lymphocytes (%)	10%
Eosinophils (%)	13%
Band (%)	1%
Monocytes (%)	1%
Metamyelocytes (%)	2%

DISCUSSION

S. stercoralis is capable of causing a fulminant illness that is often fatal in conditions associated with a decrease in host immunity.^{6–8} The true incidence of hyperinfection following renal transplantation is unknown but is believed to be uncommon.¹ The American Society for Transplantation guidelines recommend screening for *Toxoplasma* and *Trypanosoma cruzi* prior to organ transplantation in donors and recipients but only recommend screening for *Strongyloides* in at-risk recipients, living donors, and, where feasible, deceased donors.^{8–11} These guidelines are not policy; thus, there is varied practice among transplant centers and organ procurement organizations.

The infection source for solid organ transplant recipients is not always apparent and may result from reactivation of latent infection following initiation of immunosuppressive therapy or donor organ transmission. Donor-derived infection is rare and difficult to prove,^{12,13} especially if the infected recipient is from a region in which *Strongyloides* is endemic, as in our patient.

S. stercoralis commonly causes nonspecific gastrointestinal symptoms,^{14,15} as seen in our patient, except for the profound weight loss, which should have triggered an endoscopic evaluation. A delay in diagnosis and initiation of

Strongyloides-specific therapy in our patient led to complications of disseminated *Strongyloides* with enterococcal bacteremia and severe septic shock. Additionally, because the donor in our case was of Mexican origin, a pretransplant parasitic assessment would have been helpful. The definitive diagnosis of *S. stercoralis* infection depends on the demonstration of larvae in the feces or duodenal fluid. A single coprological examination fails to detect larvae in up to 70% of cases.^{14,15}

More sensitive and specific serologic tests are available at specific laboratories. The advantage of these tests is that there is typically a significant drop in titer by 6 months after parasite eradication, which may make it possible to use them as a “test of cure.”^{15–17}

Any immunosuppressed patient with eosinophilia who even briefly visits or lives in tropical or subtropical areas of the world or areas of the USA where *Strongyloides* is endemic should garner suspicion for possible strongyloidiasis.

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Figure 2. Bronchoalveolar lavage revealing *Strongyloides* larvae.

Figure 3. (a) Skin rash (larva currens) due to cutaneous migration of *Strongyloides* larvae, with (b) skin biopsy showing *Strongyloides* larvae at the dermoepidermal junction.

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