Case Report: *Strongyloides stercoralis* Hyperinfection in a Patient with Chronic Lymphocytic Leukemia

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Abstract. *Strongyloides stercoralis* is an intestinal nematode that can cause disseminated infection in an immunocompromised host. It is most commonly acquired in developing countries. It was previously a common infection in many parts of the United States, particularly in the Appalachian region, but is rarely identified currently. Here, we describe a patient born and raised in Appalachia, with no history of travel outside the United States, who presented with chronic lymphocytic leukemia and *S. stercoralis* hyperinfection characterized by acute respiratory failure, altered mental status, and extended-spectrum-beta-lactamase *Klebsiella pneumoniae* bacteremia. Despite prompt identification of the parasite on sputum microscopy and initiation of therapy with oral ivermectin and meropenem, the patient subsequently died. This case highlights the continued possibility of *S. stercoralis* infection in patients from Appalachia.

CASE REPORT

A 64-year-old male presented at an outside facility with complaints of shortness of breath starting earlier that day, bilateral lower extremity swelling, poor oral intake, and was noted by the family to be nonverbal for 2 days before admission. He had a history of chronic lymphocytic leukemia (CLL) for which he had completed chemotherapy with bendamustine and rituximab 2 months earlier, chronic obstructive pulmonary disease (COPD) for which he received intermittent corticosteroids during exacerbations, and hypertension. On examination, the patient was obtunded and unable to participate in providing history. The family provided history that he was born near Bluefield, West Virginia, and lived between Benton and Mount Airy, NC, for the rest of his life. He never traveled outside of the United States. He worked in the textile industry and may have worked in the coalmines of West Virginia when he was young. He was otherwise disabled for the past 6–8 years due to unknown reasons.

Upon presentation, his initial vitals were blood pressure 97/60, heart rate 111, oxygen saturation 93% on BiPAP with 35% FiO₂, and respiratory rate 27. Initial laboratories included white blood cells 14,200/uL³ (6,600 neutrophils; 200 lymphocytes; 0 eosinophils), hemoglobin 10.7 G/dL, platelets 219,000/uL,³ creatinine 3.25 mg/dL (baseline 0.53 mg/dL), alanine aminotransferase 65 IU/L, aspartate aminotransferase 95 IU/L, alkaline phosphatase 201 IU/L, and total bilirubin 3.5 mg/dL. He was admitted for suspected COPD exacerbation versus acute pulmonary embolus and started on bronchodilators and intravenous (IV) steroids. A ventilation/perfusion scan and bilateral lower extremity ultrasound were obtained and were negative for pulmonary embolus or deep venous thrombosis. Over the next 24 hours, the patient continued to decompensate with tachycardia, hypotension, and hypoxia. His initial blood culture revealed gram-negative rods on gram stain, and he was empirically started on IV meropenem and levofloxacin. Given his declining status, he was intubated and transferred to a tertiary medical center for further care.

Upon transfer, the patient remained febrile and hemodynamically unstable on ventilator support. Positive findings on examination consisted of scattered bilateral small conjunctival hemorrhages, constricted pupils that were minimally responsive, thick bloody secretions from the endotracheal tube, diffuse coarse rhonchi in bilateral lung fields, hyperactive bowel sounds, and bilateral lower extremity pitting edema. All other examination findings were negative. Further examinations included computed tomography (CT) of the chest, abdomen, and pelvis that noted multilobar pneumonia most confluent in the bilateral lower lobes with a background of pulmonary edema, dilated and fluid-filled cecum, ascending, transverse and descending colon, and tiny locules of gas in the splenic flexure and descending colon (Figure 1). CT of his head was negative for acute pathology. His antibiotics were converted to IV piperacillin/tazobactam and vancomycin empirically. A tracheal aspirate was sent for assessment for eosinophils, and upon microscopic evaluation parasites were identified (Figures 2 and 3). He was empirically started on albendazole 400 mg via nasogastric (NG) tube. The next day, infectious diseases consult was placed and transitioned the patient from albendazole to ivermectin 200 mcg/kg/day via NG tube as the microbiology laboratory confirmed the presence of *Strongyloides stercoralis*. The outside hospital

FIGURE 1. Computed tomography of the chest with bilateral lower lobe consolidation and edema.

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FIGURE 2. Wet mount of material obtained from a tracheal aspirate showing larval forms consistent with the filariform stage of *Strongyloides stercoralis* (original magnification, $\times 40$). This figure appears in color at www.ajtmh.org.

blood cultures were finalized during this time with extended-spectrum-beta-lactamase positive *Klebsiella pneumoniae*. Given the concern for meningitis in the setting of his altered mental status, the patient was transitioned from piperacillin/tazobactam to meropenem 2 gm IV every 8 hours and vancomycin was discontinued. Lumbar puncture was recommended; however, later that day, while the patient was undergoing CT of the brain, his oxygen requirement and respiratory status continued to decline and lumbar puncture was unable to be performed. A do not resuscitate status was requested by the patient's family without any escalation in care. The patient became pulseless overnight and expired.

DISCUSSION

Strongyloides stercoralis is a soil-transmitted intestinal nematode that infects humans, dogs, cats, and monkeys. Its distribution is worldwide; however, it is mainly found in

FIGURE 3. Wright's stain on material obtained from a tracheal aspirate highlighting larval forms consistent with *Strongyloides stercoralis* (original magnification, $\times 40$). This figure appears in color at www.ajtmh.org.

tropical and subtropical environments.¹ Historically, infection in the US with *S. stercoralis* was endemic throughout Appalachia, a 205,000 square mile region that follows the spine of the Appalachian Mountains from southern New York to northern Mississippi (Figure 4).²⁻⁴ The prevalence of *S. stercoralis* transmission in the Appalachian region has been reported to range from 0% to 3.8%.^{3,5} A study in 2013 conducted through Remote Area Medical clinics in Kentucky showed a 1.9% prevalence of seropositive patients, with only one patient having traveled to a foreign country known to be endemic for *S. stercoralis*.⁵

Socioeconomic status and environmental conditions, such as lack of indoor plumbing have been associated with infection.^{3,4} Between 2009 and 2013, the poverty rate in the US was 15.4%, whereas in Appalachia it was 17%, or more than 10% of the US average.⁴ Based on data from the 1970 Census, 13.6% of households in Appalachia were without complete plumbing facilities versus 6.9% in the US.⁴ As recent as 2000, a reported 169,000 housing units in the US were without indoor plumbing.³ While infection transmission has likely decreased in the US with improvement in sanitation, most studies reporting on the status of infection transmission were published before 1980s.⁵ Since then, most reported cases are related to imported cases. In a recent study evaluating the impact of screening and treatment options for intestinal helminth infection in Asian refugees, a > 20% seroprevalence of *S. stercoralis* was noted.⁶ Unfortunately, the current transmission status of *S. stercoralis* and other soil-transmitted intestinal nematodes in the US, including Appalachia remains unclear.³

Infection with *S. stercoralis* occurs via penetration of the filariform larvae through the skin that directly comes in contact with infested soil.⁷ Autoinfection, which occurs when rhabditiform larvae transform into invasive filariform larvae and are capable of reinfecting the host via invasion of the intestinal wall or the perianal skin, can then ensue and result in low level chronic infection for decades.^{1,5,7,8} Infection is mostly

FIGURE 4. The Appalachian region. This figure appears in color at www.ajtmh.org.

asymptomatic in the immunocompetent host. When symptoms do occur, it is mainly gastrointestinal (GI). In the immunocompromised host, however, the organism may migrate through the GI mucosa and into the bloodstream. It is during this time where it can infect the lungs and the central nervous system (CNS), potentially resulting in dissemination and fatal hyperinfection.^{1,7}

Hyperinfection with *S. stercoralis* occurs in immunocompromised hosts with impaired T-cell immunity, such as lymphoma, corticosteroid use, acquired immunodeficiency syndrome, human T-cell lymphotropic virus type-1 infection, and transplant recipients.^{1,7,9} Geri et al. describe 83.5% of patients with hyperinfection syndrome were receiving treatment with corticosteroids, with a median of 42 days of therapy before symptom onset.¹⁰ This form of infection can cause disruption of the GI mucosa resulting in paralytic ileus and bowel obstruction. Pulmonary involvement can also occur and can be characterized by shortness of breath, cough, bilateral patchy, rapidly changing infiltrates, and edema. As the larvae migrate through the disrupted GI mucosa into the bloodstream, they carry gut flora on their outer surface causing a septicemia. This septicemia can in turn result in disseminated bacterial or fungal infection in the lungs and the CNS.^{7,9} Peripheral eosinophilia is seen in about 70% of patients; however, it is present in about only 20% of patients with hyperinfection.¹⁰ Mortality has been reported to up to 87% in patients with *S. stercoralis* hyperinfection.¹¹

The American Society of Transplantation recommends screening for patients with epidemiologic risk factors or unexplained eosinophilia with combination serology and stool examination.¹² Screening patients from an endemic area who are at risk for disseminated disease because of immunosuppression should be considered.¹³ The treatment of choice for *S. stercoralis* is ivermectin 200 µg/kg orally daily until clearance of the parasite from the sputum and stool samples for 2 weeks. Ivermectin has been shown to be well tolerated and more effective in treating *S. stercoralis* than albendazole.¹⁴

Our patient highlights the continued risk for transmission of *S. stercoralis* and other soil-transmitted infections in the US and particularly in Appalachia. He was born and lived in the Appalachian region his entire life and never traveled to another country known to be endemic for *S. stercoralis*. It remains unclear as to when our patient was infected because the infection can last decades; however, it is clear that he was infected in the Appalachian region of the US. He had multiple risk factors for developing hyperinfection syndrome, including CLL, COPD requiring treatment with steroids, and chemotherapy; thus, screening before immunosuppressive therapy should have been considered. Screening and treatment of *S. stercoralis* should be considered in high-risk patients starting on immunosuppressive therapy. In conclusion, this case confirms that *S. stercoralis* infection can be acquired in the Appalachian region, and hyperinfection syndrome should be included in the differential diagnosis of immunocompromised patients presenting with sepsis syndrome, enteric flora septicemia, pulmonary or CNS involvement, and with or without eosinophilia.

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