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Unrecognized *Strongyloides stercoralis* Infection in Hemodialysis Patient With Recurrent Diarrhea and Readmissions

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Abstract

Introduction: Strongyloidiasis can vary from asymptomatic infection to life-threatening multisystem disease especially in immunocompromised patients. Although strongyloidiasis is a rare diagnosis in USA, transmission through immigrants and refugees obscured the geographical boundary. The clinical presentations vary widely depending on underlying comorbidities and immunosuppression.
Case Presentation: Here we present a case of strongyloidiasis in hemodialysis patient requiring multiple admissions. Although the patient had high eosinophil count in previous admissions, eosinophil count was normal when the diagnosis was made.
Conclusions: Although strongyloidiasis is not endemic in USA, immigration obscured the geographical barrier of endemicity. The diagnosis can be difficult because of nonspecific symptoms and lack of sensitivity of microscopic diagnosis. Although eosinophilia is a common finding in patients with chronic strongyloidiasis, it is unreliable indicator of active infection, especially in immunosuppressed condition. Eosinophil count also may be falsely high in patients with hemodialysis. As Laboratory diagnosis is mainly based on microscopic identification of larvae in the stool, examination of multiple stool samples is warranted to increase the yield of diagnosis.

Keywords: Strongyloidiasis, Diarrhea, Hemodialysis, Immunocompromised, Renal Failure, Eosinophilia

1. Introduction

Strongyloides stercoralis is an intestinal nematode of humans. An estimated 30 - 100 million people worldwide are infected with *S. stercoralis* (1). Although most infected individuals are asymptomatic, the chronic infection reactivates and manifests as life-threatening multisystem disease in immunocompromized patients (2). The clinical manifestation of *S. stercoralis* hyperinfection vary widely. Healthy individuals are usually asymptomatic even if chronically infected. A number of conditions are known to predispose an individual to autoinfection or hyper infection including immunosuppressive therapy (glucocorticoids, chemotherapy), HIV/HTLV coinfection, malignancy, solid organ or bone marrow transplantation, diabetes mellitus, hypogammaglobulinemia and severe malnutrition (1). The diagnosis of strongyloidiasis is suspected in patients presented with gastrointestinal symptoms, maculopapular rash and with or without eosinophilia. In many instances, eosinophila is the only indication of presence of *S. stercoralis* infection. However in chronic strongyloidiasis, eosinophila may be intermittent and it can be even absent in immunocompromised patients (3). Direct microscopy and the culture have been gold standard for the diagnosis of strongyloidiasis. The low sensitivity of laboratory diagnosis makes the diagnosis further difficult. Here we present a case of strongyloidiasis in hemodialysis patient, who required multiple admissions for chronic diarrhea before the diagnosis could be made.

2. Case Presentation

This was a 58-year-old Hispanic lady, who was admitted with complaints of non-bloody, non-mucoid diarrhea for last 7 days. She had past medical history of end stage renal disease on hemodialysis for 4 years, hypertension, type 2 diabetes mellitus, and cirrhosis of liver with multiple paracentesis for intractable ascites. She reported 7-8 copious, watery bowel movements daily. Review of system was positive for postural lightheadedness. She also complained of burning, non-radiating epigastric pain and vomiting for last 4 days. She had one episode of coffee ground emesis in emergency department. She denied any fever, chill, abdominal pain, hematemesis, melena, dysuria, chest pain, palpitation and shortness of breath. She was on doxycycline and azithromycin for unknown reason for last 2

weeks as per records from dialysis center. On presentation, the vitals were stable without any fever. Physical examination was remarkable for mildly icteric sclera, epigastric tenderness and large ascites with shifting dullness.

Laboratory investigation showed normocytic anemia of hemoglobin 10.7, normal white count with 3.7% of eosinophil. The international normalized ratio (INR) was 4.19. Abdominal ultrasound showed marked abdominal ascites, fatty infiltration of liver, hepatosplenomegaly and atrophic pancreas and kidney. Intravenous fluid was started. Patient was admitted in Medicine floor and she was placed on contact isolation for possibility of *Clostridium difficile* colitis. First set of Stool sample was sent for leukocytes, ova, parasite, *Giardia* antigen and *C difficile* toxin. Patient had one episode of approximately 300 ml of coffee ground emesis in the night. Blood pressure was borderline low, 98/58 with heart rate 90 beats per minute. Hemoglobin was stable. Intravenous esomeprazole drip was started and the patient was transferred in intensive care unit (ICU). Two units of fresh frozen plasma were transfused. Ultrasound guided paracentesis was done with albumin support. Next day there was no further episode of vomiting, but she continued to have persistent diarrhea. computed tomography (CT) of abdomen and pelvis revealed diffusely thickened and edematous terminal ileal, cecal, ascending, transverse and proximal descending colonic wall suggestive of enteritis and colitis. Intravenous ciprofloxacin and metronidazole were started. First set of stool sample was negative for any infectious etiology. Stool was also negative for leukocytes and reducing substance but 2+ positive for fat. On 3rd day she deteriorated clinically. She had more frequent watery diarrhea with hypotension, orthostatic changes, dyselectrolytemia, leukocytosis and high anion gap acidosis with low bicarbonate. Urgent hemodialysis was done without fluid removal and bicarbonate replacement was started. Colonoscopy was on hold for profuse diarrhea and electrolyte imbalance. HIV test was negative. Diarrhea got worse on 4th day. Serum gliadin antibody and IgA against transglutamiase were negative. Second set of stool sample showed larvae suggestive of *Strongyloides stercoralis*. Patient was started on albendazole 400 mg daily as ivermectin was not available in our hospital. Ciprofloxacin and metronidazole were discontinued. On review of electronic medical record, it was found that patient was admitted twice in last 3 months with abdominal pain and diarrhea and the stool work up was unremarkable. Interestingly, it was also noticed that she had persistent eosinophilia ranging from 11% to 29% in last 2 years although all the stool workups were unremarkable for any infectious etiology. Next day diarrhea improved significantly. The patient was hemodynamically stable and transferred back to Medicine floor and subsequently discharged home to complete 5 days of albendazole.

3. Discussion

Strongyloidiasis is distributed in tropical and subtropical areas. It is endemic in Sub-Saharan Africa, the West Indies, South America, Southeast Asia and in Eastern Europe (3). Soil transmitted helminths were historically considered endemic in several areas in United States, especially throughout the southeastern United States (4). Although *S. stercoralis* is a rare diagnosis in USA, change of US population as a result of immigration obscured the geographical barrier of endemicity. Transmission through immigrants and refugees to the USA has been well documented (5). Low socioeconomic status, alcoholism, white race and male gender have been associated with high prevalence of *S. stercoralis* stool positivity.

Humans acquire strongyloidiasis when filariform larvae in fecally contaminated soil penetrate the skin or mucous membranes. The larvae then travel through the bloodstream to lungs, where they break into alveolar spaces, ascend the bronchial tree, are swallowed and thereby reach the small intestine. There, the larvae mature into adult warms that penetrate the mucosa of proximal small bowel. The adult female worms reproduce by parthenogenesis. Eggs hatch in the intestinal mucosa releasing rhabditiform larva that migrate to the lumen and pass with the feces in soil. Alternatively, rhabditiform larvae in the bowel can develop directly into filariform larvae that penetrate the colonic wall or perianal skin and enter the circulation to repeat the migration that establishes ongoing internal reinfection. This autoinfection may explain the possibility of persistent infections for many years in persons, born and raised in endemic area, but residing in non-endemic area (6).

Although steroids and HTLV-1 infections are most common immunocompromizing conditions associated with strongyloidiasis, any condition that decreases Th-2 response can lead to these infections. Uremia is associated with a state of immune dysfunction characterized by immunodepression that likely contributes to high prevalence of infections. On one hand, hypercytokinemia is a typical feature of uremia, likely due to accumulation of pro-inflammatory cytokines as a consequence of decreased renal elimination, and/or increased generation following induction by uremic toxins, oxidative stress, and volume overload or dialysis procedure. On the other hand, uremia is also associated with immunosuppression due to impaired T cell function and increased Th1/Th2 ratio (7). A deregulation of host's immune response during the latent infection may be lethal because of multiple infective larvae

can develop and invade other organs leading to hyperinfection syndrome. Although there are several case reports of strongyloidiasis in Kidney transplant patients mostly secondary to immunosuppressive therapy, there are very few case reports of strongyloidisasis in hemodialysis patient available in the literature mostly from Southeast Asia, Africa and Europe (6). As per best of our knowledge this is first report of strongyloidiasis in hemodialysis patient from USA.

Blood eosinophilia is generally present during the acute and chronic stages but may be absent during a generalized hyperinfection (6). In chronic infection, a dynamic balance between host immune system and parasite may limit the infection and keep the patient asymptotic. The balance is lost after a certain limit in a patient with progressively decreasing immune function, which may lead to hyperinfection and disseminated strongyloidiasis. It may be possible in our patient that she had persistent eosinophilia for long time probably secondary to chronic infection. The stool test was persistently negative as the parasite load was probably below the detection limit. Although it is known that persistent eosinophilia in hemodialysis patient may be secondary to allergy to dialysis-material, our case emphasizes that it also warrants a detailed work up to rule out parasitic helminthiasis (8). It is also known that acute immunosuppression can suppress the eosinophilia as does steroid treatment. It can be hypothesized that our patient had persistent eosinophilia secondary to chronic strongyloidiasis for many years although she was asymptomatic and sporadic stool testing did not reveal any larva. Recent literature suggests that any defect in cellular immunity could tip the equilibrium of chronic strongyloidiasis to hyperinfection. As she was on dialysis and she had diabetes and other comorbidities, immune status was declining progressively to the point that she became symptomatic secondary to increased parasite load. At the time of diagnosis eosinophil count became normal probably secondary to profound immunosuppressive state and parasitic load was sufficient enough to be detected in microscopy.

Laboratory diagnosis is mainly based on microscopic identification of larvae in the stool although relying on stool studies alone for screening is inadequate. Usually testing of at least three consecutive samples is recommended as the sensitivity of single fecal sample examination is as low as 25% (6). In asymptomatic individual, stool examinations are probably even less sensitive. Serologic testing is now widely available and is sensitive although not specific. Although a single serological test does not reliably distinguish past from current infection, a positive serology test in a patient with compatible clinical history preparing to undergo steroid therapy may be sufficient ground for empirical treatment.

Footnotes

Authors' Contribution: All authors have equal contribution.

Conflicts of interests: None for all the authors.

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