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Fatal *Strongyloides* Hyperinfection Syndrome in an Immunocompromised Patient

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Patient: Male, 76
Final Diagnosis: Strongyloides hyperinfection syndrome
Symptoms: Abdominal pain • diarrhea
Medication: Cyclophosphamide • Prednisone
Clinical Procedure: —
Specialty: Infectious Diseases

Objective: Rare disease

Background: Currently, it is normal to screen for *Strongyloides* as part of the workup in pre-transplant patients who have eosinophilia. Given the high mortality rates in *Strongyloides* hyperinfection, this article illustrates the need to screen all patients with eosinophilia who will be started on immunosuppression.

Case Report: We present here an interesting case of a 76-year-old man with membranous glomerulopathy who developed a severe *Strongyloides* hyperinfection that required an ICU stay and ultimately led to his death a few weeks after initiation of cyclophosphamide and steroids.

Conclusions: We recommend that a detailed workup to detect or rule out this parasitic infection be conducted prior to the initiation of immunosuppression in any patient with eosinophilia.

MeSH Keywords: Cyclophosphamide • Eosinophilia • Immunosuppression • Strongyloides

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/894110

Background

Manifestations of *Strongyloides stercoralis* infection in an immunocompromised host can range from asymptomatic eosinophilia to a life-threatening hyperinfection syndrome that includes cutaneous, gastrointestinal, and pulmonary symptoms. Therefore, *Strongyloides* hyperinfection should be suspected in any immunosuppressed patient with unexplained GI symptoms who has been exposed to the parasite or who has unexplained eosinophilia [1]. We present here a case report of *S. stercoralis* hyperinfection in a 76-year-old man with membranous glomerulopathy, who was receiving immunosuppression in the form of corticosteroids and cyclophosphamide.

Case Report

A 76-year-male patient from Guyana with membranous glomerulopathy secondary to chronic NSAID use came to the Emergency Department with diarrhea, diffuse abdominal pain, and tenesmus that had started 6 weeks after the initiation of oral cyclophosphamide [100-mg oral tablet twice a day] and prednisone [30-mg oral tablet daily]. He was diagnosed with membranous glomerulopathy 2 months prior to admission, proven by renal biopsy. Baseline creatinine was 1.14. Upon admission, his laboratory workup was as indicated in Table 1.

The patient had visited Guyana 10 years previously, but had no other significant travel history. He was admitted with the impression of gastroenteritis/colitis and intravenous hydration and antibiotics (ciprofloxacin and metronidazole) were administered. The suspicion of bacterial gastroenteritis was also entertained, as he was on immunosuppressive therapy. Stool cultures were taken on admission, and were negative. Gastroenterology was consulted because of a drop in hemoglobin, but the patient went into hypercapnic respiratory failure and required bilevel positive airway pressure [BiPAP] before endoscopy/colonoscopy could be performed. A CT chest scan was performed, which showed small bilateral pleural effusions, micronodules, ground glass opacities, and consolidations in both lungs. BiPAP improved the gas exchange but the patient's condition continued to deteriorate during his hospital stay, with persistent diarrhea and severe renal failure that eventually required hemodialysis. ELISA testing for HIV and hepatitis B and C panel was negative. HTLV testing was not performed. *Strongyloides stercoralis* larvae were seen on examination of the stool for ova and parasites. An infectious disease team was consulted, the determination of *Strongyloides* hyperinfection syndrome was made, and the patient was started on Ivermectin. The patient's respiratory status began to deteriorate, with desaturation even on BiPAP, and he finally required intubation. Antibiotic coverage was broadened to include Vancomycin, Imipenem, and Gentamicin. The patient did not improve and died a few days later with the diagnosis of *Strongyloides* hyperinfection syndrome complicated by bacterial septicemia. Later, on review of the patient's laboratory data, it was found that he had persistent eosinophilia [WBC 13 with 20% eosinophils] even prior to the beginning of Cyclophosphamide/steroids. The eosinophilia was attributed to chronic NSAID use [ibuprofen and naproxen] and no investigation had been conducted to assess any potential parasitic infestation before initiating immunosuppression.

Discussion

Strongyloides is unique among the commonly occurring helminths, as it can complete its life cycle within the human host,

Table 1. Laboratory data.

Hemoglobin/hematocrit	9.1 g/dL/26.7%
White blood cell count with differential	4.6 K/mcL [Neutrophils: 73.8%, Lymphocytes: 5.8%, Eosinophils: 11%, Monocytes 9.2%]
Basic metabolic panel	Sodium: 133 mEq/L, Potassium: 3.9 mEq/L, Chloride: 98 mEq/L, Bicarbonate: 98 mEq/L, Urea Nitrogen: 78 mg/dL, Creatinine: 2.81 mg/dL, Calcium: 7.2 mg/dL
Hepatic Panel	Alkaline phosphatase: 79 U/L, Aspartate transaminase: 42 U/L, Gamma glutamyl transferase: 40 U/L, Alkaline transaminase: 32 U/L, Lactate dehydrogenase: 308 U/L, Albumin: 1.5 g/dL, total protein: 4, Bilirubin [total/conjugated]: 0.39 mg/dL/0.1 mg/dL
Stool RBC	Positive
Urinalysis	Sp Gr: 1.030, Protein: 100, Leukocyte esterase: Small, Nitrite: Negative, Blood: Negative, Rare bacteria
Clostridium difficile GDH and toxin	Negative
Lipase	Normal levels
Magnesium, phosphate	2.25 mg/dL, 4.3 mg/dL

thereby allowing it to persist and replicate indefinitely. In the life cycle of other helminths, such as hookworms and roundworms, 1 larva gives rise to only 1 adult worm. *Strongyloides* infection, in contrast, can lead to autoinfection in which rhabditiform larvae can re-penetrate the gastrointestinal mucosa or the perianal skin [2,3]. Hyperinfection syndrome exacerbates the gastrointestinal and pulmonary symptoms and increased numbers of larvae may be detected in stool and/or sputum [4]. This commonly establishes a latency that results in asymptomatic, chronic autoinfection of the gut, where it can remain undetected for years (the longest latency recorded is approximately 65 years) [5]. The autoinfection, which is reactivated during immunosuppression, can result in a life-threatening *Strongyloides* hyperinfection syndrome that is characterized by increased numbers of filariform larvae in the stool and sputum. Clinical manifestations of the increased parasite burden and migration are gastrointestinal bleeding and respiratory distress with high mortality rates (up to 87%) [6]. Inherently, patients with the nephrotic syndrome in membranous glomerulopathy are susceptible to infection [7] due to the impairment of normal defense mechanisms. Several hypotheses for this susceptibility have been advanced, including urinary loss of protein [8] leading to decreased immune globulin G, immunologic defect [9], decreased serum factor B [10], or lymphocytotoxins associated with certain renal diseases [11]. Inhibition of Th2 cell-mediated, humoral, or mucosal immunity with corticosteroid use is the most frequent risk factor for hyperinfection syndrome [12]. There is no definitive criterion standard for diagnosing *Strongyloides stercoralis* infection. Stool examination is the primary technique used for the detection of strongyloides larva, with a sensitivity of 50% if 3 consecutive daily samples are examined, and sensitivity reaching 100% if 7 consecutive daily stool specimens are examined in a specialized laboratory [13]. Serological testing for *Strongyloides,* like ELISA IgG antibody tests, has an approximate sensitivity of 90% for patients from non-endemic areas, but has potential false-positive results [14]. Agar plate culture method is a newer method, with infection detection rates 2-3 times higher than those estimated by the other methods [15].

Conclusions

Most of the deaths from helminthic infections in United States result from *S. stercoralis* hyperinfection [16]. Although pretransplant patients are evaluated routinely for infection, thorough assessment for parasitic infections is not conducted in non-transplant patients. Even though it is endemic primarily to tropical and subtropical regions, it is still prevalent in the Unites States due to its long latency periods and the large immigrant population. Given the high mortality rates [17] of hyperinfection syndrome, as well as the preventable nature of the condition, it is vital that a detailed workup for this parasitic infection is conducted before initiating immunosuppression in any patient with eosinophilia.

References:

1. Potter A, Stephens D, De Keulenaer B: Strongyloides hyper-infection: A case for awareness. Ann Trop Med Parasitol, 2003; 97(8): 855–60
2. Grove DI: Strongyloidiasis: A conundrum for gastroenterologists. Gut, 1994; 35(4): 437–40
3. Berk SL, Verghese A, Alvarez S et al: Clinical and epidemiologic features of strongyloidiasis: A prospective study in rural tennessee. Arch Intern Med, 1987; 147(7): 1257–61
4. Keiser PB, Nutman TB: Strongyloides stercoralis in the immunocompromised population. Clin Microbiol Rev, 2004; 17(1): 208–17
5. Leighton PM, MacSween HM: Strongyloides stercoralis. the cause of an urticarial-like eruption of 65 years' duration. Arch Intern Med, 1990; 150(8): 1747–48
6. Siddiqui AA, Berk SL: Diagnosis of strongyloides stercoralis infection. Clin Infect Dis, 2001; 33(7): 1040–47
7. Arneil G: 164 children with nephrosis. Lancet, 1961; 2(7212): 1103–10
8. Peterson PA, Berggard I: Urinary immunoglobulin components in normal, tubular, and glomerular proteinuria: Quantities and characteristics of free light chains, IgG, igA, and fc-gamma fragment. Eur J Clin Invest, 1971; 1(4): 255–64
9. Giangiacomo J, Cleary TG, Cole BR et al: Serum immunoglobulins in the nephrotic syndrome: A possible cause of minimal-change nephrotic syndrome. N Engl J Med, 1975; 293(1): 8–12
10. McLean RH, Forsgren A, Björkstén B et al: Decreased serum factor B concentration associated with decreased opsonization of escherichia coli in the idiopathic nephrotic syndrome. Pediatr Res, 1977; 11(8): 910–16
11. Ooi B, Orlina A, Masaitis L: Lymphocytotoxins in primary renal disease. Lancet, 1974; 304(7893): 1348–50
12. Marcos LA, Terashima A, Dupont HL, Gotuzzo E: Strongyloides hyperinfection syndrome: An emerging global infectious disease. Trans R Soc Trop Med Hyg, 2008; 102(4): 314–18
13. Siddiqui AA, Berk SL: Diagnosis of strongyloides stercoralis infection. Clin Infect Dis, 2001; 33(7): 1040–47
14. Roxby AC, Gottlieb GS, Limaye AP: Strongyloidiasis in transplant patients. Clin Infect Dis, 2009; 49(9): 1411–23
15. Sato Y, Kobayashi J, Toma H, Shiroma Y: Efficacy of stool examination for detection of strongyloides infection. Am J Trop Med Hyg, 1995; 53(3): 248–50
16. Muennig P, Pallin D, Sell RL, Chan M: The cost effectiveness of strategies for the treatment of intestinal parasites in immigrants. N Engl J Med, 1999; 340(10): 773–79
17. Link K, Orenstein R: Bacterial complications of strongyloidiasis: *Streptococcus bovis* meningitis. South Med J, 1999; 92(7): 728–31