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Case Report

Strongyloides stercoralis Hyperinfection Complicated by Secondary Infections in a Case of Transformed Diffuse Large B-Cell Lymphoma

Abstract

We report *Strongyloides stercoralis* hyperinfection complicated by secondary infections in a case of transformed diffuse large B-cell lymphoma. The hyperinfection was followed by a sequela of candidemia and infection of the peritoneal fluid that was associated with the leakage of gut flora from the bowel damaged by the migration of larvae. This phenomenon has seldom been reported in a case of hematolymphoid cancer such as transformed diffuse large B-cell lymphoma. The complications arising due to *S. stercoralis* hyperinfection are associated with a high fatality rate in immunocompromised patients, and this should be taken into account in the diagnosis and management of this condition.

Keywords: *B-cell lymphoma, hyperinfection, secondary infections, Strongyloides stercoralis*

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Introduction

Strongyloides stercoralis is an intestinal nematode that is the cause of strongyloidiasis and is found to infect at least 30 million people in 70 countries.[1] Nematodes such as *S. stercoralis* have the distinct ability to cause autoinfection, thereby enabling the parasite to live in the host body for many years and even decades. Immunocompromised patients are at risk of lethal infection as the larvae can develop and proliferate in the intestine, and also sometimes invade the bloodstream and other organs, causing complications such as sepsis and death (hyperinfection syndrome).[2] The most fatal *Strongyloides* infections are reported in patients suffering from autoimmune diseases and cancer.[3] In hyperinfection syndrome, disruption of the mucosal patterns, ulcerations, and paralytic ileus have been observed. Leakage of gut flora into the bloodstream from a damaged bowel due to moving *Strongyloides* larvae often predisposes to bacterial and fungal infections.[4] The enteric bacteria are carried by invasive larvae on their outer surfaces; blood and tissue invasion results in septicemia, pneumonia, meningitis, and disseminated bacterial or fungal infection.[5] Massive fungal infections are frequently the immediate cause of death in patients with hyperinfection syndrome.[6] Hereby, we report a case of a patient with transformed diffuse large B-cell lymphoma infected by *S. stercoralis* leading to hyperinfection syndrome with a subsequent sequela of secondary bloodstream infection, in addition to infection of the peritoneal cavity due to bowel leakage.

Case Report

A 66-year-old male patient with a history of follicular lymphoma (who had completed treatment in 2015) was admitted with complaints of abdominal pain, abdominal distension, fever, and diarrhea of 15 days' duration with a clinical suspicion of relapse. He was a known case of long-standing diabetes and hypertension. His clinical and radiological workup revealed ascites and bilateral pleural effusions along with supra- and infra-diaphragmatic lymphadenopathy. A diagnosis of transformed diffuse large B-cell lymphoma was made. Physical examination of the stool showed greenish, semiformed mucoid fecal matter, and the microscopy was positive for the presence of live, motile larvae of *S. stercoralis*. Antigen testing of the stool for enteric adenovirus, norovirus, astrovirus, and rotavirus was negative. Stool cultures were plated on bacteriological media to identify any bacterial pathogens. Coproculture on MacConkeys agar showed lactose-fermenting colonies of *Klebsiella pneumoniae* along with "tracks" of the creeping *Strongyloides* larvae growing

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minute colonies of bacteria that they carry with them as they move on the surface of the agar [Figure 1]. Pinpoint nonhemolytic colonies that grew on blood agar were identified as *Enterococcus* spp. Antibiotic susceptibility tests revealed it to be vancomycin resistant (VRE).

The patient was given antibiotic treatment with injection colistin, tigecycline, meropenem, and linezolid. Tablet ivermectin was added 12 mg, two doses, 14 days apart.[7] The patient developed acute abdomen during hospitalization. The liver and renal function tests were deranged with an increase in C-reactive protein to 64 mg/dl and procalcitonin >10 ng/ml. Total white cell count was normal, but the differential count showed increased neutrophils: 91.6% (40.0–80.0) with low lymphocytes: 4.8% (20.0–40.0) and eosinophils: 0.4% (1.0–6.0). Hemoglobin was low at 8.2 g/dL (12.0–15.0). Computed tomography abdomen showed intestinal perforation [Figure 2]. Exploratory laparotomy was performed which revealed gastric and jejunal perforations. The gastric perforation edge biopsy revealed yeast and pseudohyphal forms (likely *Candida* spp.). Jejunal perforation edge tissue biopsy showed fungal hyphae suspicious for mucormycosis. Peritoneal fluid sent for culture grew *Candida tropicalis* sensitive to amphotericin B, caspofungin, micafungin, fluconazole, and voriconazole with minimum inhibitory concentrations of ≤0.25, ≤0.25, ≤0.06, ≤1, and ≤0.12 μg/ml, respectively. Peritoneal fluid also grew VRE *Enterococcus faecium* sensitive only to linezolid. Five days later, blood culture grew *Candida glabrata* sensitive only to amphotericin B and micafungin. The patient was administered liposomal amphotericin B and caspofungin. However, the patient continued to deteriorate clinically and succumbed to the multiple infections 17 days after the perforation.

Discussion

Strongyloidiasis is a disease of tropical and subtropical regions, and the prevalence as per community-based reports in India is 6.6%.[8] Gastrointestinal and pulmonary symptoms are predominant in hyperinfection syndrome attributed to increased migration of larva;[9] dermatologic, renal, and central nervous system manifestations can also occur. Immunocompromised patients are at a greater risk of disseminated *Strongyloides* infection. Cancer patients are generally immunocompromised due to disease or immunosuppressive chemotherapeutic drug regimens. The patient in our case presented with gastrointestinal complaints of abdominal bloating along with diarrhea, abdominal discomfort, fever, and nausea, which are known features of this condition. This was followed by a sequela of bacteremia and infection of the peritoneal fluid corresponding to signs of hyperinfection syndrome subsequent to the migration of the larvae of *S. stercoralis*. Although we could easily reveal the motile larval forms of *Strongyloides* in the patient's stool, it may sometimes be difficult to diagnose, particularly when the larval burden is low. The low eosinophil count seen in this patient corroborates with other reports of immunocompromised patients with disseminated strongyloidosis.[1] Exploratory laparotomy was performed which revealed a gastric perforation indicating disruption of mucosal patterns of the gut by the migrating larvae. Bacterial and fungal infections often occur in cases of hyperinfection syndrome due to the leakage of gut flora from a bowel damaged by the moving larvae. Due to this leakage, bacteremia due to Gram-negative enteric organisms (i.e., *Escherichia coli*, *K. pneumoniae* etc.) is a frequent complication.[10] Izquierdo *et al*. have reported a similar case of fatal *Strongyloides* hyperinfection complicated with a Gram-negative sepsis after an allogeneic stem cell transplantation.[4] Ivermectin is generally the treatment of choice because it is well tolerated and is preferred over thiabendazole, albendazole, and mebendazole.[9] Other gut organisms may also be involved. There have been reports of VRE *Enterococcus faecium* as a cause of secondary infection complicating hyperinfections due to *S. stercoralis*,[5,11,12] treated with linezolid. The VRE in our patient was also

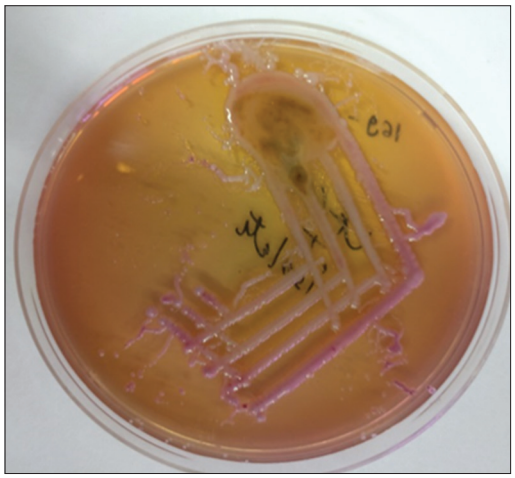

Figure 1: Creeping of *Strongyloides stercoralis* larvae at the surface of MacConkey agar plate

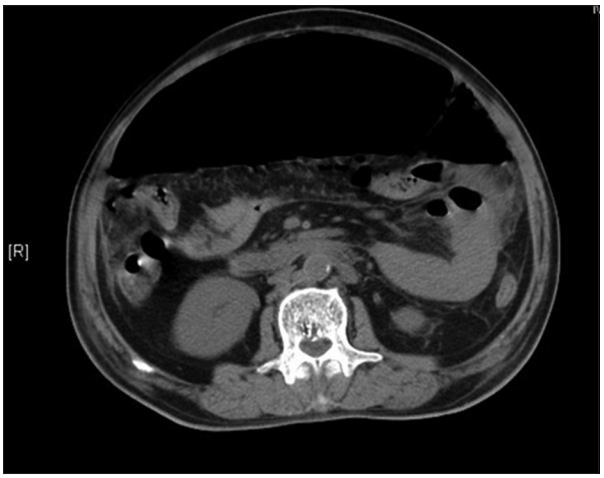

Figure 2: Computed tomography abdomen of the patient showing pneumoperitoneum

treated with linezolid as per the susceptibility pattern. Small numbers of candidal organisms may be normally present in the gastrointestinal tract. In the present case, *Candida glabrata* was also isolated from the blood culture subsequently; yeast organisms were also detected in the gastric perforation edge biopsy, and mycelial fungal forms were seen in the jejunal perforation edge biopsy. The recovery of multiple organisms from different sites (blood and peritoneal fluid) including Gram-negative and Gram-positive bacteria and fungi points to the role of the migrating larvae in the disruption of the mucosal barrier and translocating the gut microbiota to other sites along their migration journey. Although our patient was treated aggressively with multiple antibiotics and antifungals, he succumbed to the condition, due to the disseminated and widespread nature of the infection.

Conclusion

Strongyloidiasis should be considered as a differential diagnosis in immunosuppressed patients with gastrointestinal and respiratory symptoms in the cancer setting as early diagnosis and treatment may reduce the mortality and morbidity associated with disseminated infection. Given the complications of disseminated *S. stercoralis* infection, particularly in immunocompromised patients in endemic areas and the associated high mortality rate with hyperinfection syndrome, clinicians should be aware of and vigilant about this condition.

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Conflicts of interest

There are no conflicts of interest.

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