Spontaneous perforation of the terminal ileum in an AIDS patient on highly active antiretroviral therapy with disseminated non-tuberculous mycobacterial infection

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Summary
Background: Despite the impact of highly active antiretroviral therapy (HAART), mycobacterial infections in patients with AIDS remain a frequent complication. In disseminated cases, both tuberculous and non-tuberculous mycobacterial infections may involve the gastrointestinal system and cause abdominal pain and diarrhea. While there have been cases of small bowel perforation in AIDS patients with Mycobacterium tuberculosis (MTB) infection, no case of bowel perforation in non-tuberculous mycobacterial (NTM) infection has been reported to date.
Case report: We report a case of spontaneous perforation of the terminal ileum in an AIDS patient with disseminated non-tuberculous mycobacterial infection who was responding to HAART.
Conclusions: Non-tuberculous mycobacteria can lead to spontaneous bowel perforation in patients with AIDS who are responding to HAART.

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Introduction

Patients infected with HIV are at high risk to develop active disease with both Mycobacterium tuberculosis (MTB) and non-tuberculcus mycobacteria (NTM).1 In disseminated cases, both species cause gastrointestinal involvement presenting with abdominal pain and diarrhea. Most NTM are found in wet soil, natural waters, and even in tap water.2,3 Of note, Mycobacterium avium complex (MAC) is known to be one of several common opportunistic infections in advanced AIDS patients when the CD4 count is less than 50 cells/mm3, and the gut is the portal of entry of the organisms in >90% of
the cases. Although the incidence of NTM such as MAC infection has been decreasing in the era of highly active antiretroviral therapy (HAART), it remains a major complication in patients who have difficulty adhering to the drug regimen, in those for whom the drug regimen has failed, and for those who are restoring their immune system with successful HAART.

We present herein a rare case of spontaneous perforation of the terminal ileum in an AIDS patient who had disseminated infection with NTM and had recently resumed HAART.

Case report

A 44-year-old woman with a 12-year history of HIV presented to The Miriam Hospital after returning from a 1.5-year stay in Puerto Rico with 70+ lbs (32+ kg) weight loss and generalized weakness. She had been followed by the Immunology Clinic but had difficulty with medication adherence. Reportedly, she did not take antiretrovirals while in Puerto Rico, and her viral load was greater than 500 000 with a CD4 count of 53. Upon initial presentation, the patient appeared cachectic and very weak. While in the hospital she was found to have multiple enlarged retroperitoneal lymph nodes. Biopsy of the lymph nodes was performed and preliminary results showed acid-fast bacilli (AFB) in a pattern most consistent with MAC. The patient was re-started on anti-retroviral therapy; the viral load initially decreased from >500 000 to 10 164 and the CD4 count increased to 63.

Because the AFB culture was not obtained during the first biopsy, the patient was readmitted for repeat biopsy. Upon admission, she had diffuse abdominal pain and diarrhea that was AFB positive. At this point the identification of the mycobacterial species was still pending, and the patient was started on a combination of isoniazid, pyrazinamide, ethambutol, and azithromycin in order to cover not only MAC but also MTB, given her potential exposures and immunosuppression. She was continued on her HAART regimen and her viral load was 186 copies/ml during this admission.

The patient complained of diffuse abdominal pain since admission, and morphine was given for pain control. The pain worsened on day 11 with decreased bowel sounds and a firm abdomen without rebound tenderness, but an abdominal CT scan showed no evidence of peritonitis or ileus, and no significant change in retroperitoneal adenopathy was noted. The patient was started on an active bowel regimen and adequate pain control with morphine was continued. On day 15, the patient was started on a prednisone taper because of a high clinical suspicion for immune reconstitution inflammatory syndrome (IRIS). Despite the diffuse abdominal pain and firm abdomen, the patient felt relatively well until day 19, when she developed severe abdominal pain with peritoneal signs. This time, a CT scan showed multiple enhancing loculated fluid collections in the peritoneal cavity of the abdomen and pelvis, suggesting peritonitis. Ileus was noted, likely secondary to the peritonitis, and she was emergently taken to the operating room. During the exploration of the lower gastrointestinal tract, there was evidence of a small bowel obstruction with spontaneous perforation of the terminal ileum. The appendix and transverse colon were intact. The abscesses were drained, and the terminal ileum and appendix were resected for histological examination. The patient tolerated the operation and recovered in the intensive care unit. She remained intubated and was on pressors initially, but was extubated uneventfully and transferred to the floor in a stable condition.

Upon gross examination of the surgical pathology samples, there was a portion of the terminal ileum that was dilated and paper-thin, with an irregular defect measuring 2.0 × 0.8 cm, and the remainder of the small bowel showed thickening of the wall with slight narrowing of the lumen. Focal hemorrhage was noted in the serosa and mucosa, and no obvious lymph nodes were identified. Microscopic examination of the small bowel site of defect revealed an area of almost transmural necrosis with granulation tissue and acute inflammatory infiltrate, consistent with focal spontaneous perforation (Figure 1). While granulomas were not identified in any of the sections examined, the Kinyoun stain highlighted focally increased numbers of AFB, in a pattern most consistent with MAC (Figure 2). A nucleic acid amplification test was negative for MTB, and further speciation of this NTM was attempted at both the Rhode Island Department of Health and Centers for Disease Control and Prevention.
organisms and their components tend to persist in host tissues or are shed in the form of antigens. The immune system of the host has a dual defense mechanism for mycobacteria that relies heavily on phagocytosis and intracellular digestion of the organisms in macrophages as well as cell-mediated killing by NK cells.

In advanced AIDS patients, not only do they have impaired cell-mediated defense mechanisms, but also the intracellular killing ability is impaired mainly due to insufficient cytokine production to activate macrophages. In patients with HIV, MAC organisms are noted in both intracellular and extracellular locations. This is why even the appropriate antibiotic regimen takes 2—4 weeks to reduce the quantity of organisms. In our case, the patient already had a severe symptomatic infection on presentation and empiric treatment was started for both tuberculosis and non-tuberculous mycobacteriosis.

Despite the continuous HAART and anti-mycobacterial treatment, the patient continued to be unstable, with abdominal pain, cycles of constipation and diarrhea, fever, and weight loss. At this point IRIS was suspected in the presence of active mycobacterial infection. IRIS is a clinical diagnosis characterized by a reactivation of subclinical/pre-existing opportunistic infections in HIV-infected patients as a direct result of the enhancement of immune responses to those pathogens during HAART. The temporal association between commencement of HAART and reduction in peripheral viral load supports a diagnosis of IRIS. By definition, hosts that have successfully restored their immune system introduce inflammatory responses to the infected sites. Philips et al. reported a variety of symptoms in NTM-IRIS, including 13 cases of abdominal involvement. All of the cases had intrabdominal nodal involvement, and while four cases had clinical peritonitis, no case of intestinal perforation was reported.

Antigens that trigger IRIS may be in the form of viable organisms, dead organisms, or shed antigen. Mycobacterial organisms and their components tend to persist in host tissues for weeks after initiation of treatment, which favors the high frequency of IRIS in this particular opportunistic infection. It is also notable that a lack of a rise in blood CD4 lymphocyte count does not indicate that there has been no restoration of T-lymphocyte responses, and therefore is not essential for the diagnosis of IRIS. Rather, a positive response reflected by a falling viral load is invariably seen and is probably a better indicator.

Currently there are no guidelines for the treatment of IRIS due to the lack of a clear-cut case definition and its self-limited natural history. In the present case, with the worsening symptoms, prednisone treatment was initiated. The viral load decreased from 10164 to 186, which further confirmed the highly effective HAART regimen and gave us the basis for initiation of prednisone. The patient eventually had the acute abdominal emergency on day 2 of 30-mg prednisone treatment. The perforation of terminal ileum was caused by an inflammatory response to the bowel wall by the host (Figure 1) due to NTM. Diagnosis is often delayed because symptoms of peritonitis are often muted by steroids and therefore close attention must be given to immunocompromised patients.

In summary, we have presented a rare case of spontaneous perforation of the terminal ileum in an advanced AIDS patient with non-tuberculous mycobacterial infection who had been responding to the HAART regimen. The diagnosis and etiology of the perforation was caused by the NTM in the gut wall, steroid use, and possible IRIS.

Conflict of interest: No conflict of interest to declare.

References


