Multiorganism HIV-associated diarrhea and telescoping bowel

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ABSTRACT

Diarrhea in individuals with human immunodeficiency virus (HIV) remains a diagnostic challenge. We treated a 53-year-old woman from Africa who presented with acute diarrhea, which yielded a diagnosis of HIV and severe immune deficiency. The patient's diarrhea resulted in hypovolemic shock and acute abdominal pain. Evaluation revealed an intestinal intussusception. Pathology findings were consistent with *Cryptosporidium*, *Entamoeba*, *Giardia*, and cytomegalovirus infections. The actual prevalence of multiple microorganisms causing HIV-associated diarrhea is unknown. A nonmalignant-related adult intussusception in this context is exceedingly rare and of noteworthy significance.

KEYWORDS AIDS; cytomegalovirus; *Cryptosporidium*; gastroenterology; HIV; infectious diarrhea; infectious disease

Diarrhea in the context of human immunodeficiency virus (HIV) infection is associated with poor quality of life and increased mortality.¹ Fortunately, since the advent of potent antiretroviral therapy, the incidence of infectious causes of diarrhea in HIV has declined.² Despite advances in treating HIV, clinicians continue to encounter immigrants and travelers who represent an at-risk population. In its worst form, HIV-associated diarrhea may lead to severe volume and electrolyte deficiencies and marked malnutrition. Complications leading to surgical management have been rarely reported. We document a rare complication of intestinal intussusception from multiorganism diarrhea in severe immunodeficiency.

CASE DISCUSSION

A 53-year-old black woman presented with complaints of nausea, diarrhea, and failure to thrive. She was healthy 1 month prior to presentation and had no chronic medical conditions. She was born and raised in Nigeria and was visiting her daughter who resided in the area. A laboratory workup revealed acute kidney injury. She was treated with volume resuscitation.

Diarrhea returned on a follow-up clinic visit 1 week after discharge. Stool studies returned positive for *Cryptosporidium* and *Giardia*, and the patient was started

on nitazoxanide. The HIV test was positive. She was referred to outpatient infectious disease, although due to ongoing diarrhea and failure to thrive she returned to the hospital for her second admission 1 week later. Her serum creatinine was 7.07 mg/dL (reference range 0.50–1.17), blood urea nitrogen, 100 mg/dL (reference range 6–24), and carbon dioxide 12 mMol/L (reference range 21–32). Her serum sodium level was 131 mMol/L (reference range 136–145), and other electrolytes were normal, as were liver function tests. A complete blood count revealed a hemoglobin of 9.1 g/dL (reference range 12.3–15.5), platelets of 139,000/L (reference range 150,000–450,000), and a white blood cell count of 8000/L (reference range 4.0–11.3). A coagulation panel was within normal limits. The HIV viral load was 318,924 copies/mL (reference range <1). The total helper CD4 cells were 7 cells/mm (reference range 441–2156).

The patient was admitted to the medical service. Comprehensive ova and parasites and *Clostridium difficile* stool toxin were negative. She was placed on an antiretroviral therapy regimen including dolutegravir, tenofovir alafenamide, and emtricitabine. A feeding tube was placed for malnutrition. Her renal function did not improve and dialysis was started for uremia. A second round of stool culture and ova and parasites was drawn but again returned negative. A

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Figure 1. Right hemicolectomy with intussusception of cecum. The colonic wall in the area of intussusception (arrow) is thickened. Mucosa in this area shows granularity and loss of normal folds.

gastroenterology consultation was obtained and a colonoscopy was scheduled.

On the morning of the procedure, the patient developed acute abdominal pain, which prompted a computed tomography scan of the torso. The scan revealed a large intussusception. At emergent exploratory laparotomy, the terminal ileum was intussuscepted and a right hemicolectomy was performed (*Figure 1*). Numerous organisms consistent with *Entamoeba histolytica* involving the intussuscepted segment of cecum with associated ulceration and necrosis were found (*Figure 2*). The remaining colon had scattered mucosal ulcerations with *Entamoeba* seen at the ulcer base. The terminal ileum demonstrated evidence of *Cryptosporidium* and *Giardia*. Immunohistochemical stains for cytomegalovirus were positive. She completed a course of metronidazole, ganciclovir, and paromomycin. The diarrhea resolved after several days. The patient improved clinically and was discharged home.

DISCUSSION

Diarrhea in the context of HIV infection is broadly categorized into infectious etiologies and noninfectious causes. The most important tool to construct a differential diagnosis is the patient's immune status. Our patient's severe immunodeficiency characterized by a total CD4 cell count of 7 cells/mm suggested both opportunistic and nonopportunistic pathologies were possible. In the evaluation of diarrheal illness in HIV, stool studies play a central role. A stool culture, ova and parasites, and specific stool antigen testing should be obtained in all HIV patients presenting with diarrhea. On the first outpatient visit, *Cryptosporidium* and *Giardia* were appropriately identified. While antimicrobial therapy is suggested, the mainstay of treatment is immune recovery. Following the patient's second hospital admission, intractable diarrhea was thought to be due to the aforementioned organisms anticipating immune recovery. Given the persistence of diarrhea, an alternative mechanism was

Figure 2. Infectious agents identified in the right hemicolectomy. **(a)** Numerous *Entamoeba histolytica* organisms (arrows), some with engulfed red blood cells in a background of extensive necrosis in colonic mucosa (hematoxylin and eosin stain, 400 $\times$). **(b)** Periodic acid-Schiff stain highlighting the *Entamoeba histolytica* organisms with engulfed red blood cells (arrows) (400 $\times$). **(c)** Cytomegalovirus immunohistochemistry stain showing strong nuclear positivity in an infected endothelial cell (200 $\times$). **(d)** Pear-shaped *Giardia* (circle) and numerous *cryptosporidia* (box) adherent to surface epithelial cells identified in ileal mucosa. *Cryptosporidium* organisms are round-shaped, gray, and discrete (400 $\times$).

investigated. The differential was expanded to include cytomegalovirus infection, immune reconstitution inflammatory syndrome, and infiltrative diseases, specifically *Mycobacterium avium* and lymphoma.

Endoscopy carries advantages over traditional stool testing. It provides direct visualization of mucosa and an opportunity for tissue sampling. The yield of colonoscopy in HIV-infected patients presenting with chronic diarrhea ranges from 27% to 37%.³ Stool testing obtained on two occasions was false-negative, failing to identify *Entamoeba*. Endoscopy is superior and the preferred modality when identifying a precise etiology. Endoscopic evaluation should be pursued early when there is doubt, especially in cases of severe immune deficiency.

Intussusception is a well-known abdominal emergency in the pediatric population. It is caused by telescoping of the bowel from one segment into another, leading to ischemia and necrosis. In children, most cases are idiopathic. Adult intussusception is uncommon, representing 5% of all cases of intussusception and only 1% to 5% of all intestinal obstruction in adults.⁴ Intussusception develops from a pathologic lead point, with more than 50% being malignant lesions in adults.⁵ We suspect that mucosal ulceration from *Entamoeba* infection was the source of this process, although the multiorganism infection or a combination of factors may have played a role in this surgical emergency.

Diarrhea in HIV is a leading cause of morbidity in untreated disease. Despite less familiarity with it in the Western world, clinicians should be mindful of the spectrum of etiologies. In the cases of severe immune

deficiency, avoiding anchor diagnosis is key as multiple offending pathologies are possible. Early endoscopic evaluation should be pursued in this evaluation to prevent a rare surgical emergency.

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