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CASE REPORT | COLON

Coinfection of *Cytomegalovirus* and Cryptosporidiosis in a Patient With AIDS

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ABSTRACT

Patients with poorly controlled human immunodeficiency virus are subject to a wide range of opportunistic infections. *Cryptosporidium* is a parasitic gastrointestinal infection associated with chronic and life-threatening diarrhea in patients with acquired immunodeficiency syndrome. Cytomegalovirus colitis is a serious complication caused by reactivation of the virus, leading to viremia and end-organ disease by hematogenous spread. Both diseases can be fatal in less than 4 months. We present an example of a comprehensive investigation in a patient with symptoms that could not be explained in a single diagnosis.

INTRODUCTION

Cytomegalovirus (CMV) colitis and cryptosporidiosis infections are both potentially fatal diseases in immunocompromised hosts. This case emphasizes the importance of an in-depth workup in an immunocompromised patient with symptoms out of proportion to disease caused by a single infection. Continued evaluation of this patient led to the diagnosis of this rare coinfection.

CASE REPORT

A 47-year-old white man with human immunodeficiency virus (HIV)/AIDs noncompliant with combination antiretroviral therapy (cART) presented with 2 weeks of diarrhea described as 10 explosive watery bowel movements per day without visible blood. Associated symptoms included subjective fevers and a 20-lb weight loss. Physical examination revealed hypotension, cachexia, a mildly tender abdomen without distension or guarding, and anal ulcerations. Abnormal laboratory findings included a white blood cell count of 2.6×10^9/L, a CD4 of 42 cells/μL, and a positive fecal occult blood test (FOBT). Abdominal computed tomography demonstrated focal intussusception of the small bowel without obstruction and pancolonic distension with fluid, wall thickening, and mucosal enhancement (Figure 1).

Because of drug allergies, the patient received levofloxacin and doxycycline for empiric infectious diarrhea treatment. He was restarted on cART (darunavir, emtricitabine/tenofovir, and ritonavir) and prophylaxis for *Pneumocystis jirovecii* pneumonia with atovaquone and for *Mycobacterium avium* complex with azithromycin. Additional laboratory workup resulted in a positive *Cryptosporidium* antigen and fecal lactoferrin. All additional infectious disease testing was negative, including Shiga toxin, *Clostridium difficile*, *Giardia*, *Campylobacter*, ova, and parasites. Levofloxacin and doxycycline were subsequently discontinued, and the patient was started on nitazoxanide 500 mg by mouth 2 times a day for 2 weeks to treat the *Cryptosporidium* infection.

Of note, the patient was admitted 3 months before with similar complaints. At that time, infectious workup of the diarrhea was negative, including a negative *Cryptosporidium* stool antigen. No endoscopic abnormalities were visualized on colonoscopy, but random biopsies were consistent with lymphocytic colitis. Given the chronicity of the patient's explosive diarrhea and associated symptoms unexplained by *Cryptosporidium* alone, colonoscopy was performed again. Results included diffuse erythematous mucosa and ulcerations throughout the entire colon and deep, serpiginous rectal ulcerations (Figure 1). Random biopsies were taken of the colon and rectal ulcerations. The patient's diarrhea condition improved on nitazoxanide, and he was discharged before biopsy results. Pathology later

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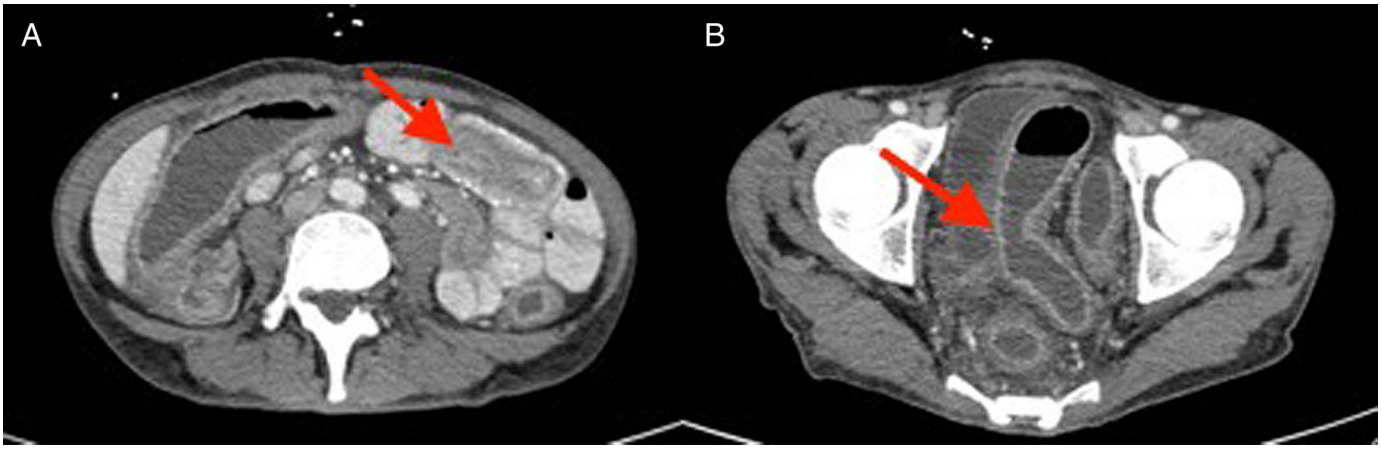

Figure 1. Computed tomography of the left mid-abdomen showing (A) a focal small bowel intussusception without obstruction and (B) diffuse dilation, fluid, wall thickening, and mucosal enhancement of the colon extending to the rectum.

resulted in CMV colitis showing intranuclear and intracytoplasmic inclusions. The plan was to initiate anti-CMV outpatient treatment with valganciclovir, but attempts to contact the patient were unsuccessful.

DISCUSSION

Coinfection with *Cryptosporidium* and CMV is rare and produces symptoms out of proportion to a single diagnosis. The incidence of cryptosporidiosis infections alone in patients with HIV is less than 1 per 1,000 person-years and only causes 3.8% of acquired immunodeficiency syndrome (AIDS)-related chronic diarrhea.[1,2] On the other hand, CMV is the most common opportunistic infection of the colon and is positive in 37.3% of patients with AIDS.[2] Although no studies have measured the incidence of patients with this combined infection, Viriyavejakul et al reported the severity of this coinfection in a patient with AIDS and Mohanlal and Karstaedt found *Cryptosporidium* to be one the of the most common copathogens in CMV colitis.[3]

Cryptosporidium is an intracellular parasite that causes secretory diarrhea, interfering with intestinal absorption. Clinical symptoms of infection include mild diarrhea, anorexia, malaise, crampy abdominal pain, and a low-grade fever. Fecal leukocytes and blood are a rare presentation of a cryptosporidiosis infection unless the patient has a coinfection with another enteric organism. Stool sample polymerase chain reaction (PCR) is the method of choice for diagnosis. It is more sensitive than microscopy and allows for differentiation of genotypes.[4,5] Biopsies with hematoxylin & eosin staining are less sensitive than those with PCR because the infection is typically patchy. *Cryptosporidium* cannot be grown in-vitro, and it is not typically included in ova and parasite stool testing.[6] Given the parasite's irregular shedding in stool, the CDC recommends collecting samples from 3 different days.[7] This could possibly explain the false-negative result during this patient's first hospitalization.

Cryptosporidium treatment involves supportive measures such as antidiarrheal agents and volume repletion. The most important therapy is restoring immune function with cART.[8] If a patient continues to experience severe diarrhea or has a slow return of immune function, nitazoxanide should be initiated.[9] If symptoms continue, azithromycin can be added. Given that most patients with chronic infections and a CD4 $<$50 survive less than 20 weeks, the patient would likely have benefited from treatment with nitazoxanide and azithromycin.

CMV typically presents in patients with HIV/AIDS with a CD4 $<$50 and can infect anywhere along the GI tract. CMV colitis is associated with explosive diarrhea, abdominal pain, anorexia, and low-grade fevers.[10] Diagnosis includes clinical symptoms, visualization of the characteristic lesions on endoscopy, and classic histopathology on biopsies. Endoscopy commonly

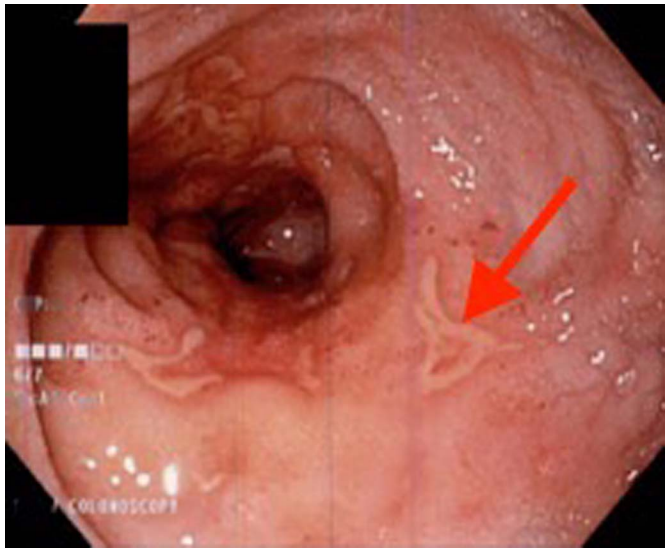

Figure 2. Colonoscopy showing diffuse erythematous mucosa and ulcerations.

shows large shallow ulcers or erosions and possibly necrotizing colitis.[11] Definitive diagnosis is done by performing biopsy and will show characteristic intranuclear or intracytoplasmic inclusions (Figure 2). Cultures, PCR, or CMV antibody testing should not be used to confirm the diagnosis, given that 50% of asymptomatic patients may test positive yet not reveal symptoms of end-organ disease.[8]

Similar to *Cryptosporidium*, the most important initial treatment for CMV colitis is cART. All symptomatic CMV-infected patients should be treated with either intravenous ganciclovir or oral valganciclovir.[12] Once the infection has cleared, no maintenance therapy is necessary.

In patients with AIDS with chronic diarrhea, proper testing for both CMV and *Cryptosporidium* infections is vital. Without immune restoration by cART and proper antimicrobial treatment, these infections can lead to death in less than 4 months.[6,13] Most importantly, a thorough evaluation of patients with poorly controlled HIV is necessary to diagnose all potentially fatal complications.

DISCLOSURES

Author contributions: M. Conner and T. Joshi wrote the manuscript and interpreted the data. SS Veerisetty and J. Hutchings interpreted the data and provided the images. J. Hutchings is the article guarantor.

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Informed consent could not be obtained. All identifying information has been removed to protect patient privacy.

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