An Unlikely Guest With an Overstayed Welcome: *Cyclospora*-Induced Postinfectious Irritable Bowel Syndrome

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ABSTRACT

Introduction: Postinfectious irritable bowel syndrome is a phenomenon that can occur following bouts of acute gastroenteritis. While bacterial pathogens are typically implicated in the development of postinfectious irritable bowel syndrome, viral and parasitic infections should also be considered as inciting pathogens.

Case Presentation: An immunocompetent, 65-year-old woman presented with several weeks of watery diarrhea, which polymerase chain reaction testing confirmed to be a *Cyclospora* infection. Resolution of diarrhea was achieved with antibiotic treatment, however, months later she presented to the gastroenterology service with persistence of loose stools and abdominal cramping consistent with a diagnosis of postinfectious irritable bowel syndrome.

Discussion: Postinfectious irritable bowel syndrome has a similar presentation to sporadic irritable bowel syndrome, with diagnosis aided by the identification of an inciting pathogen. To our knowledge, this is the first documented case of *Cyclospora*-induced postinfectious irritable bowel syndrome. While parasitic infections typically are not implicated in cases of postinfectious irritable bowel syndrome, this case highlights the value of considering this condition as a cause of protracted diarrhea in patients previously diagnosed with *Cyclospora*.

INTRODUCTION

Some patients may experience symptoms of irritable bowel syndrome (IBS) following an exposure to acute gastroenteritis. This phenomenon, known as postinfectious IBS (PI-IBS), is the persistence of diarrhea, abdominal discomfort, and bloating that can continue despite clearance of the inciting pathogen.[1] Risk factors for development of PI-IBS can include severity of enteric infection, host immunity factors, and identity of the infectious pathogen.[2] PI-IBS typically is associated with bacterial pathogens, with other studies showing a possible pathogenetic link between IBS and parasites.[2,3] However, there are no documented cases of *Cyclospora*-induced PI-IBS.[2,3]

CASE PRESENTATION

A 65-year-old woman with a history of fatty liver and Gilbert syndrome presented with 3 weeks of persistent, nonbloody, nonmucoid diarrhea. She denied recent travel, sick contacts, or changes in eating habits prior to the onset of her symptoms. Her illness began with a subjective fever followed by watery diarrhea, which prompted her to seek treatment twice in the emergency department. Workup at these encounters included testing for *Clostridium difficile*, SARS-CoV-2, and stool cultures, which were all negative. Computed tomography of the abdomen was also unremarkable. Symptomatic management with hydration and antidiarrheal medication was recommended before she was sent home.

Conservative treatments were ineffective, and the patient was admitted to the hospital with ongoing diarrhea 11 days after the initial onset of symptoms. Her vital signs were stable, physical exam was pertinent for diffuse abdominal tenderness, and her complete blood cell count did not show leukocytosis. Gastroenterology service was consulted and recommended repeat stool culture, fecal leukocytes, ova and parasites, *Clostridioides difficile* testing, fecal elastase, calprotectin, and celiac antibody testing, which were all negative. A colonoscopy was performed with no acute findings. She was discharged 5 days later on ciprofloxacin, which she discontinued due to myalgias.

Four days later, the patient was readmitted to the hospital with persistence of symptoms. The infectious disease service was con-

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sulted, and it was discovered she had eaten a bag of lettuce prior to the onset of her diarrhea, raising suspicion for *Cyclospora* infection. An acid-fast smear for *Cyclospora* was negative. Additional testing for HIV, norovirus, rotavirus, cryptosporidium, and giardia were negative. The clinical suspicion for *Cyclospora* remained high, so polymerase chain reaction (PCR) testing was sent out and she was started on trimethoprim-sulfamethoxazole empirically while results were pending. PCR testing confirmed *Cyclospora*. Given that her diarrhea had improved by the time she was discharged, it is highly unlikely that the PCR was falsely positive.[4]

During a virtual visit with gastroenterology 2 months later, the patient complained of an increase in the number of her daily bowel movements and reported that they were associated with abdominal cramping. The cramping was thought to be due to adhesions from a prior hysterectomy, so she was recommended a high-fiber diet and to follow up if symptoms persisted. Nearly 6 months later at a follow-up visit with gastroenterology, she reported ongoing soft stools, a frequent urge to defecate, and lower abdominal cramping sensations consistent with IBS. She was considered to have PI-IBS due to her *Cyclospora* infection and prescribed methyl cellulose for symptomatic management.

DISCUSSION

Here we present a rare case of *Cyclospora*-induced PI-IBS in an immunocompetent host. The mechanisms of development of PI-IBS are thought to be multifactorial, although they are not fully understood. It is proposed that due to persistent subclinical inflammation from an infectious pathogen, alterations take place in intestinal permeability and gut flora.[1] Some studies also have indicated a possible genetic susceptibility, which causes decreased epithelial and mucosal barrier function exacerbated by acute bouts of gastroenteritis.[1] Incidence and prevalence of PI-IBS can be variable, with global numbers ranging from 5% to 32%, and no apparent endemic geographic or environmental predispositions.[1] Similar to cases of sporadic IBS, there appears to be a higher risk of developing PI-IBS in females than males.[1] The proposed explanation for a higher incidence of PI-IBS in females could be due to higher rates of psychological distress, as preexisting psychiatric diagnoses have been implicated as risk factors for PI-IBS. The severity of initial infection and duration of diarrhea also can be risk factors for the development and severity of PI-IBS.[1] Additional symptoms, such as abdominal cramping, bloody stools, and weight loss from the inciting gastroenteritis, can indicate higher risk for developing PI-IBS. There is limited evidence to link the severity of PI-IBS with the identity of infectious pathogens; however, bacteria remain the most common inciting factor.[2]

The diagnosis of PI-IBS remains a diagnosis of exclusion. As evidenced by our patient, the diagnosis can be aided by a clear onset of symptoms combined with positive identification of an infectious pathogen.[1] Diarrhea remains the predominant symptom in cases of PI-IBS. However, such as in this case, PI-IBS also can include abdominal discomfort and bloating. PI-IBS typically has a favorable prognosis, with resolution of symptoms occurring in up to 50% of patients at the 5- to 6-year mark after acute gastroenteritis.

Treatment of PI-IBS is similar to treatment of sporadic IBS, which typically is centered around nonspecific alleviation of symptoms.[1] Supplements, such as probiotics that have been shown to be effective in treating acute gastroenteritis, may be indicated, but no specific interventions for modulating gut flora have been studied for PI-IBS. Treatment with antimicrobials can be indicated when infectious pathogens have been identified.[1] Literature is limited regarding the incidence of viral and parasitic causes of PI-IBS, and there appears to be no documented cases of *Cyclospora*-induced PI-IBS.[2]

Cyclospora cayetanensis is a protozoan responsible for the diarrheal illness cyclosporiasis.[5] *Cyclospora* infection is usually self-limited in immunocompetent hosts, but it can be more severe in immunocompromised patients.[5] The presentation of illness is typically large-volume watery diarrhea with a variable duration. Additional presenting symptoms can include anorexia, nausea, flatulence, low-grade fever, and weight loss.[6] Less common complications of *Cyclospora* infection include cardiac arrest,[7] biliary disease and acalculous cholecystitis in AIDS patients,[8-10] Guillain-Barré syndrome,[11] and reactive arthritis syndrome.[12] Treatment usually consists of a 7- to 10-day course of trimethoprim-sulfamethoxazole, with longer treatments required in the setting of immunosuppression.[5]

Clinicians should have a higher clinical suspicion for *Cyclospora* infection in patients who have recently visited tropical and subtropical areas.[13] Most outbreaks of *Cyclospora cayetanensis* in nonendemic areas can be traced to consumption of contaminated produce, which is what appears to have occurred in this case.[5] Since oocysts that are shed in the feces of infected humans sporulate outside their host, direct person-to-person transmission is rare.[13] Diagnostic testing for *Cyclospora* is not routinely performed in the US and is not commonly included in PCR panels.[13] Patients also can shed an insufficient amount of oocysts in stool even when symptomatic, further making diagnosis more difficult.[13] When there is a high suspicion for *Cyclospora*, patients can be asked to provide multiple samples collected on different days to ensure adequate sampling.[13] When a diagnosis is confirmed, clinicians should be aware of their local guidelines for reporting purposes. The state of Wisconsin lists cyclosporiasis as a category 2 reportable communicable disease that requires reporting in writing within 72 hours upon recognition of a case or suspected case.[14] In some instances, clinicians also can enlist the help of infection preventionists to obtain the relevant history and information to prevent additional infections.

CONCLUSIONS

Here we present a rare and, to our knowledge, the first documented case of *Cyclospora*-induced PI-IBS. This case highlights the value of maintaining clinical suspicion for PI-IBS as a potential cause for protracted diarrhea. While bacterial infection is commonly considered to be the inciting factor for PI-IBS, viral and parasitic cases should also remain on the list of differential diagnoses. When clinical presentation is typical, such as in this case, *Cyclospora cayetanensis* can be considered as a potential cause of parasitic infection in patients with PI-IBS.

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