Cryptosporidiosis in an Immunocompetent Individual

An unusual case with brief review of the literature

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Abstract

Cryptosporidiosis infection involves most commonly the small intestine but can occur in any part of the gastrointestinal (GI) tract. Typical infection by this parasitic organism occurs in immunocompromised individuals. However, rare cryptosporidiosis in immunocompetent individuals has been reported. Herein, we describe a case of cryptosporidiosis in an 85-year old woman who has hypertensive heart disease and diabetes, but is otherwise immunocompetent. This patient had protracted chronic diarrhea, however, medical workup failed to identify the etiology of this diarrhea. Awareness of the possibility that cryptosporidiosis can involve immunocompetent individuals should be kept in mind among healthcare professionals to avoid
misdiagnosis or lengthy delay in identifying the cause of the diarrhea or other GI illness. In particular, obtaining biopsy of the small or large intestines by the examining gastroenterologists in spite of normal endoscopy is very important to establish the diagnosis.

**Keywords:** cryptosporidiosis, immunocompetent, chronic, diarrhea

**Virtual Slides:** [http://www.diagnosticpathology.eu/vs/2015_1_10/](http://www.diagnosticpathology.eu/vs/2015_1_10/)

### Background

Immunocompromised individuals generally are susceptible to rare and uncommon infections by bacteria, viruses, protozoa and fungi. *Cryptosporidium parvum*, a genus of apicomplexan protozoans, is one of the frequent causes of waterborne diseases among humans in the United States. The organism infects and reproduces in the epithelial cells of the GI tract. Once infected, the main symptom is diarrhea but may also include nausea, vomiting, and abdominal pain. These symptoms are generally self-limiting in an immunocompetent patient, but tend to be chronic diarrhea in immunocompromised hosts.

*Cryptosporidium* was first identified in 1976 as a cause of GI disease in humans. The organism is generally seen in three main epidemiologic scenarios: sporadic outbreaks and self-limited diarrhea in immunocompetent hosts, chronic and life-threatening diarrhea in immunocompromised hosts, and diarrhea in young children of developing nations. The main risk factors are immunodeficiency: HIV/AIDS, organ transplant recipients, hypogammaglobulinemia or immunosuppressive therapy. Transmission of *cryptosporidium* is via the ingestion of oocytes in contaminated water, foodborne, person-to-person or respiratory route. These oocytes are immediately infectious once ingested and cause malabsorption with secretory diarrhea.

The pathogenesis is not well understood and no specific toxin has been identified. The life cycle of the organism is completed within a single host. Once ingested, the oocytes release motile sporozoites that attach to the epithelial cell wall, and then mature into meronts, which release merozoites intraluminally. The merozoites have the ability to reinvade the host cells leading to autoinfection, or can undergo sexual maturation to become new oocytes and remain within the host GI tract or pass into the environment and infect a new host.
The cryptosporidia attach to the epithelial cells of the intestinal wall and distort the villi. Inflammatory changes can be seen; however, the intensity of inflammation is not well correlated with the clinical disease. The cellular and humoral immune system plays a major role in controlling the spread of infection. The T-lymphocytes are particularly important, as evidenced by the severity of disease seen in HIV/AIDS patients\textsuperscript{6, 7}. Sporadic cases occurring in immunocompetent hosts are generally self-limited and resolves without therapy in 10-14 days\textsuperscript{8}, although it has been rarely reported to cause chronic diarrheal illness.

**Case Report:**

This is an 85-year-old Caucasian female with a history of hypertensive cardiovascular disease, diabetes, and cerebrovascular disease. She presented to the Detroit Medical Center outpatient GI clinic with acute worsening of chronic diarrhea. The patient reported having loose, watery stools for one month's duration, worse post-prandially, and associated with bloating and flatulence. She had mild generalized abdominal tenderness without rebound or guarding. Stool Guaiac test was negative. A colonoscopy carried out 5 years prior to the onset of the chronic diarrhea was significant for diverticulosis coli of the sigmoid colon, but was otherwise unremarkable. At this time, she was afebrile, had not travelled abroad, and denied the use of tobacco, alcohol or illicit drugs, and had no evidence of immunocompromised status. HIV antibody screen and *C. difficile* stool toxin tests were negative.

Initially the diarrhea was attributed to bacterial overgrowth due to her diabetes and was given Xifaxan, 200mg TID for 1 week. With failure of treatment the patient underwent a colonoscopy which revealed severe diverticulosis in the sigmoid area. A random biopsy was taken to rule out microscopic colitis. Surprisingly, histologic examination showed colonic mucosa with cryptosporidia present on the luminal border of the surface epithelium consistent with *Cryptosporidium parvum colitis*. These organisms were highlighted by Alcian Blue-Periodic acid Schiff (AB-PAS) special stain. CT of the abdomen and pelvis did not reveal any acute abnormalities.

The patient was started on nitazoxanide 500 mg q12h for 3 days. Within days the diarrhea had resolved. Stool studies performed later at a primary care office were negative for *Cryptosporidium*.

**Pathology:**
The specimen was received in 10% formalin and consisted of 2 tan small pieces of tissue measuring 0.3 cm each. Microscopic examination of routine Hematoxylin & Eosin (H&E) stained slides at low magnification showed colonic mucosa with normally shaped crypts with no distortion, ulceration or cryptitis (Figure 1). However, microscopic examination at high magnification revealed the presence of minute basophilic spherical structures about 3 micron adherent to the surface epithelium (Figure 2). Special Alcian blue/Periodic acid Schiff (AB/PAS) stain highlighted these structures bright eosinophilic and were morphologically consistent with Cryptosporidium organisms (Figure 3).

Discussion:

Given the patient’s resolution of her gastrointestinal symptoms with nitazoxanide and the clearing of the parasitic oocytes from the stools post-treatment, a casual relationship between the patient’s symptoms and Cryptosporidiosis was made. The patient lacked any evidence or cause of being immunodeficient, and did not have any prior history of immunosuppressive therapy. Cryptosporidiosis typically generates a self-limiting diarrhea in immunocompetent patients, resolving in a few days or weeks, whereas chronic protracted diarrhea caused by
Figure 2. At high magnification, one can see clearly small tiny round structures adherent to the luminal surface of the colonic mucosa. (Hematoxylin and Eosin, X400).

Figure 3. Microscopic examination of AB/PAS special stain reveals these structures strongly positive with eosinophilic pink color, morphologically consistent with *cryptosporidium* organisms. (Alcian blue-Periodic Acid Schiff, X600).
Cryptosporidiosis is seen in patients with immunosuppression due to HIV, IgA deficiency, Hyperimmunoglobulin M syndromes, common variable immunodeficiency, or immunosuppressive therapy. Cryptosporidiosis can affect people of all age groups all over the United States. The number of reported cases continues to be substantial approximately 748,000 cases annually. The rate in the Midwest region was 1.8-4.6 times greater than that of other regions in 2010.

The prevalence of cryptosporidia in HIV patients in the United States and Europe is estimated to be 8-30%, whereas it is about 1-3% in the general population. There is increased risk to contract the disease from the use of water from wells, swimming pools, rivers, and streams. Individuals also have increased risk for infection from contact with livestock, or individuals who have traveled to endemic areas. These risk factors vary by geographic setting (e.g., rural or urban) and by the Cryptosporidium species.

Histologically, often no abnormalities are seen, but villous atrophy, crypt hyperplasia, mixed inflammation or crypt abscesses can be seen. Special stains such as Giemsa or AB/PAS stains or immunostains can help in the diagnosis. The 2-5 micron size of these spherical organisms, special stains and their unique apical location on the surface epithelium helps in distinguishing them from other structures.

As seen in this case report of an 85-year old female, cryptosporidium infected the epithelial cell lining of the GI tract causing secretory malabsorptive diarrhea. The AB/PAS stain highlighted the oocytes as bright eosinophilic round minute structures about 2-3 micron each. Base on this and the overall morphology of the colon biopsy, a conclusion was made that this individual was in fact infected with Cryptosporidium. This brings to question whether there are many more cases of unreported chronic diarrhea caused by Cryptosporidium in the general immunocompetent population.

Infection with cryptosporidium in immunocompetent patients has been rarely described. 12 cases of immunocompetent individuals with cryptosporidium were reported in which the individuals had direct contact with feces of infected calves. Nine out of the twelve individuals had diarrhea and abdominal cramps that lasted 1 to 10 days. The infections were detected and diagnosed via oocysts in the feces. The cryptosporidiosis oocysts were also obtained from the calves but not from other animals of which the patients were in contact with. The oocysts were also detected with repeated examination of feces from two immunodeficient patients with persistent cryptosporidiosis. This study indicates that cryptosporidiosis may produce a moderate self-limited illness in immunocompetent individuals, which contrasts sharply
with the prolonged severe diarrhea in immunocompromised patients. Hence, contact with such animals should be avoided in immunocompromised individuals.\textsuperscript{13}

In another study cryptosporidium was identified in the stools of 43 immunocompetent individuals, mostly in individuals under 4 years or 30-39 years of age. 15 of the 43 patients (35\%) were exposed to other gastrointestinal pathogens, of which only \textit{Giardia lamblia} was associated with \textit{cryptosporidiosis}. In 28 individuals where other gastrointestinal pathogens were not identified, clinical manifestations were predominantly watery, nonbloody diarrhea and less commonly, abdominal discomfort, fever, nausea, and weight loss. The infection was self-limited in all 43 patients. Clustering of cases occurred in a day-care center and in two families. These clinical findings suggest that \textit{cryptosporidiosis} is a relatively common non-viral cause of self-limited diarrhea in immunocompetent individuals in the northeastern United States.\textsuperscript{1}

\textbf{Conclusion:}

In summary, this case is of an immunocompetent patient who presents with a protracted chronic diarrhea attributed to \textit{Cryptosporidium parvum} infection. The patient responded to nitazoxanide, an anti-parasitic agent therapy, which effectively cleared the oocysts from her stools. This case highlights the possibility of rare occurrence of \textit{Cryptosporidiosis} in immunocompetent individuals who have no signs or evidence of immunosuppression or debilitating chronic disease.

Primary physicians and gastroenterologists should keep in mind this possibility in immunocompetent patients who present with protracted diarrhea and fail to demonstrate any specific cause of the diarrhea. It should also be considered when detailed work-up of the patients including all diagnostic tests fail to identify an etiology of the chronic diarrhea.

\textbf{References}


Consent:

A written informed consent was obtained from the patient for publication of this Case Report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

List of abbreviations used:

AB-PAS: Alcian Blue-Periodic acid Schiff

H& E: Hematoxylin and Eosin

HIV/AIDS: Human immune deficiency virus/ acquired immune deficiency syndrome

GI: Gastrointestinal

Competing interests.

All the authors verify and confirm that they have no competing interests. No financial or any other affiliation.
Authors contributions:

Drs. Bo Jin and Husain Saleh, main contribution in the discussion, pathology description and taking pictures.

Avneil Yashpal, Nisha Deol and Dr. Ahmed AbuRashed main contribution in writing the case report and the clinical history. Also, reviewing and editing the manuscript.