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Cryptosporidial infection in children with inflammatory bowel disease

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Abstract

Background and aims: Cryptosporidiosis is usually a self-limiting illness in healthy patients. However, it can cause severe life threatening complications in immunocompromised patients. The effect of cryptosporidial infection on inflammatory bowel disease (IBD) has not been well studied and available literature is largely restricted to adult case reports. The purpose of this study is to describe the clinical characteristics of cryptosporidial infection in children with IBD.
Methods: Stool studies from children with IBD presenting with presumed relapse during the period 2005–2011 were reviewed retrospectively. Cryptosporidial infection was diagnosed by stool enzyme immunoassay. An age matched control group of IBD patients without cryptosporidial infection was used for comparison.
Results: Medical records of 170 IBD patients were reviewed and a total of 149 presumed relapses were identified. Cryptosporidial infection was found in seven of the 39 patients with positive stool studies (four ulcerative colitis/three Crohn's disease) presenting with relapse. The median age was 13 years (range: 3–17) and five patients were female. The median duration of the IBD was 18 months (range 2–48 months). All but one patient had stable disease prior to acquiring infection. Five patients required hospitalization due to significant dehydration. Three of the five patients treated with nitazoxanide had significant clinical improvement in 3 days. All patients had complete resolution of symptoms by three weeks and no infection related complications were noted. In comparison to patients with cryptosporidial infection, the control group required an increased need for escalation of therapy (71% vs. 0.0%, p=001) and higher re-hospitalization rates (24% Vs.0.0%, p=0.54) within 6 months following indexed relapse.
Conclusion: In IBD patients, cryptosporidiosis can cause significant illness leading to increased need for hospitalization. In the absence of appropriate stool studies, cryptosporidiosis can be

Abbreviations: CD, Crohn's disease; IBD, Inflammatory bowel disease; UC, Ulcerative colitis; 5-ASA, 5-Amino-salicylic acid; aTNFα, Anti-tumor necrosis factor alpha.

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misdiagnosed as disease relapse and lead to inappropriate therapy. Nitazoxanide appears to be effective along with supportive therapy.

1. Introduction

Cryptosporidium is an intracellular protozoan parasite that has been well recognized to cause diarrheal disease in humans. Since first described in 1976, it has been reported to cause major health problems worldwide.[1–4] In developing countries, cryptosporidiosis has been shown to be associated with chronic diarrhea leading to impaired growth, weight loss and physical and cognitive impairment in children.[5] The mean prevalence rate for *Cryptosporidium* infections in the general population is between 1 and 3% in North America but is considerably higher in underdeveloped countries (5–10%). In the United States, it is one of the most common causes of waterborne diseases (recreational water and drinking water) with an estimate of 750,000 cases occurring each year.[6] Several outbreaks of cryptosporidial infections have been reported and the most remarkable one was the waterborne outbreak from contamination of a water-treatment plant in Milwaukee in 1993, affecting more than 400,000 people.[7] *Cryptosporidium* is transmitted by ingestion of oocysts through contaminated food or water. The incubation period is about 2–10 days and most common symptoms include watery diarrhea, abdominal pain and dehydration. It is usually a self-limiting illness that lasts about 1–2 weeks in persons with healthy immune system.[3]

Cryptosporidiosis has been implicated as one of the more important opportunistic infections in patients with acquired immunodeficiency syndrome (AIDS) and transplant recipients[8–11]; however, there is very little data available about cryptosporidial infection in patients with pre-existing inflammatory bowel disease.

Patients with IBD often present with worsening diarrhea, which is attributable to their underlying disease relapse. With the increasing use of immunosuppressive agents, patients are at increased risk for opportunistic infections. Several enteric pathogenic organisms including bacteria, viruses, fungi and parasitic agents have been reported to cause acute worsening of symptoms in IBD patients and it is often difficult to differentiate enteric infection from a true disease relapse. In the absence of appropriate stool studies, these patients can be inappropriately diagnosed and treated as a relapse. *Cryptosporidium* has been reported to be associated with IBD relapses in adult IBD patients. However, the data is scarce in pediatric patients.

We retrospectively reviewed diarrheal episodes in our cohort consisting of 170 pediatric IBD patients over a seven year period and identified seven cases of cryptosporidial infection. We describe the clinical course and outcomes of these seven patients and discuss the role of specific antimicrobial therapy.

2. Patients and methods

This is a retrospective, observational case control study of pediatric IBD patients with disease relapse attributed to cryptosporidial infection. Following institutional review board approval, medical records of 170 pediatric IBD patients treated at our hospital during the period July 2005–June 2011 were reviewed. We analyzed symptomatic flares attributed to infections and identified those patients who were infected by *Cryptosporidium*.

It has been a routine practice in our hospital to send stool samples for culture, ova, parasites, *Giardia*, *Cryptosporidium*, *Clostridium difficile* and electron microscopy (if watery diarrhea) in all IBD patients presenting with diarrheal relapse. The clinical and the lab data of all patients were entered into a common electronic medical record system. We have therefore been able to review and collect that data by searching individual patient's medical charts.

2.1. Outcome measurements

The primary aim of this study was to evaluate whether infection with *Cryptosporidium* resulted in a more severe course of IBD. This was defined by escalation of medical treatment defined as addition of immunomodulator therapy or biologic therapy to anti-inflammatory treatment, or the addition of biologic therapy to immunomodulator treatment or increase in the dose of immunomodulator or biologic therapy. The secondary aim was to compare the long term outcomes, defined as the need for surgery within 6 months following index relapse.

The diagnosis of cryptosporidiosis was confirmed by stool rapid immunoassay test with ImmunoCard STAT!® (Meridian Bioscience, Inc.). To evaluate the impact of cryptosporidial infection, for each case with positive cryptosporidial infection, three control cases with IBD flare without co-existing cryptosporidial infection, matched by age were randomly selected and were used for comparison. One of the patients with cryptosporidial infection had no matches due to young age (3 years); as a result, this patient was dropped from the analysis.

Patient's records were reviewed for demographic information, including age, gender, extent of the disease, severity, clinical symptoms, IBD medications (5-aminosalicylic acid [5-ASA], immunomodulators [azathioprine, 6-mercaptopurine, and methotrexate]), anti-tumor necrosis factor therapy, antibiotics, and corticosteroids. The following clinical outcomes were analyzed: duration of illness, hospitalizations, re-admissions within 6 months following index relapse, escalation of therapy within 6 months following index relapse and need for surgery within 6 months following index relapse.

A flare was defined as an increase in the number of stools from the individual patient's baseline. In those patients with a positive stool study who received antimicrobials, we defined treatment success as a documented resolution of clinical symptoms or negative stool studies after treatment. Treatment failure was defined as persistence of clinical symptoms and or positive stool test while on treatment.