



Treating *Cryptosporidium* with Immunoglobulin, an Alternative Approach

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Introduction

- Infection with the intracellular parasite *Cryptosporidium* causes self-limited diarrhea in immunocompetent hosts, but severe diarrhea resulting in weight loss and malabsorption in immunocompromised hosts
- Transmission occurs via infected person or animal, or from fecally contaminated food or water
- Causes secretory diarrhea associated with malabsorption
- Although it is typically treated with antibiotics and antiparasitics, a novel approach with oral immunoglobulin can be utilized

Case Description

- A 72-year-old man with a history of diffuse large B-cell lymphoma s/p recent BEAM chemotherapy was admitted for autologous stem cell transplant
- He developed neutropenic fever on HD4, started on meropenem and vancomycin, then changed to cefepime
 - Blood cultures grew *Escherichia coli* 4/4 bottles
- On HD 10, he developed persistent, non-bloody diarrhea with liquid stools and abdominal pain
 - Then had a hypotensive episode while going to the bathroom, systolic BP to 80-90s
 - Prompted transfer to the MICU...

Vitals: BP 101/53, HR 110, T 36.4, RR 18, PO2 100% on RA

Exam: well-appearing male in mild distress, severe abdominal distention with moderate tenderness to palpation b/l lower quadrants

Labs:

24.8	137	114	78	102
0.78	3.7	11	2.6	
8.4				

AST 24	Phos 5.6
ALT 30	T protein 4.6
T bdi 2.7	Lactate 0.9
ALP 54	Alb 1.5
Mg 2.8	

- UA: 8 RBC, 8 WBC, 22 granular casts
- Blood culture x2 negative

Imaging:

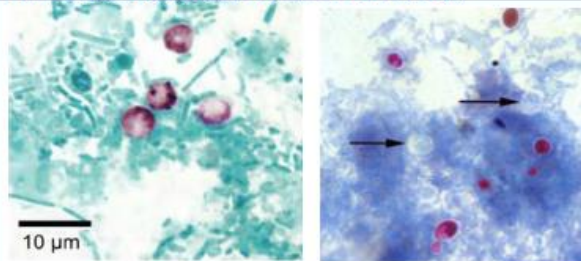
- Abdominal X-ray: consistent with ileus or low grade obstruction
- CT abdomen-pelvis: diffuse ileal and right colon bowel wall thickening and edema, with fat stranding around ascending colon

ICU Course

- Given fluids and vasopressors once in the MICU, after which his vitals stabilized
- Metronidazole added for anaerobic coverage, but he continued to have non-bloody diarrhea on metronidazole and cefepime
 - Was then changed back to just meropenem (ultimately completed 14 day course)
- Tests for *Clostridium difficile*, GI pathogen panel, and ova and parasites were all negative
- Stool *Cryptosporidium* immunoassay testing was positive!**
 - Nitazoxanide was started
 - It was later discovered that the patient had been drinking well water near his cabin for the past few months
- He then developed an ileus, and a nasogastric tube was placed
 - Oral nitazoxanide was temporarily held secondary to absorption concerns
 - Oral immunoglobulin was started**
- The patient completed 48 hours of oral immunoglobulin, the ileus resolved, and nitazoxanide was restarted
 - He improved clinically with this therapy and diarrhea resolved
- Six days later, the patient contracted a respiratory *Aspergillus* infection and died shortly thereafter

Modified acid-fast stain

Cryptosporidium oocysts often range from 4-6 um, have distinct oocyst walls, and typically stain from pink to bright red, as seen on the left. However, resolving infections can have colorless oocyst "ghosts," seen on the right (4).



CT abdomen-pelvis

This image demonstrates the ileal and ascending colon bowel wall thickening (arrow) and fat stranding (arrowheads), which is typically seen in *Cryptosporidium* enteritis. This infection can involve the small bowel, large bowel, or even the biliary tract!

Discussion

- This case demonstrates a typical transmission route for *Cryptosporidium*...
 - Fecally-contaminated well water!
 - Cryptosporidium* oocysts are present in 67 to 95% of raw surface waters
 - This patient's exposure to the well water near his cabin was most likely the infectious source (1)
- In immunocompromised patients, *Cryptosporidium* is treated with nitazoxanide for at least two weeks, adding an antibiotic such as azithromycin if initial treatment fails
 - Data on treatment in immunocompromised patients is largely from HIV-positive patients, with much less from HIV-negative patients (as was this patient)
 - A study of immunocompromised HIV-negative patients showed a 61% cure rate with nitazoxanide alone vs. a 95% cure rate with nitazoxanide combined with antibiotics (2)
 - Thus, nitazoxanide combined with antibiotics can be an effective therapy!
- Our patient's ileus decreased the efficacy of oral nitazoxanide
 - Prolonged ileus causes edematous sequestration of the gut walls, impairing drug diffusion and thus drug absorption
 - Oral immunoglobulin acts on microbes within the gastrointestinal tract itself, so an ileus does not affect its drug absorption
 - The powder form of immunoglobulin has demonstrated treatment promise in HIV-positive patients (3)
 - If a patient is not recovering with nitazoxanide +/- antibiotic therapy, oral immunoglobulin can be considered

Teaching Points

- This case demonstrates a classic source for a *Cryptosporidium* infection, via well water
- Nitazoxanide combined with antibiotics is an effective therapy for immunocompromised patients infected with *Cryptosporidium*
- Consider oral immunoglobulin if the patient is not recovering with nitazoxanide +/- antibiotics

References

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- Greenberg PD, Cello JP. Treatment of severe diarrhea caused by *Cryptosporidium parvum* with oral bovine immunoglobulin concentrate in patients with AIDS. *J Acquir Immune Defic Syndr Hum Retroviral*. 1996;13(4):e43-44.
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