CLINICAL VIGNETTE

Bloating, Malaise and Weight-loss in a Healthcare Provider: An Unexpected Case of Giardiasis

Spencer R. Adams, M.D.

Intestinal parasites cause significant morbidity and mortality throughout the world, particularly in underdeveloped countries, but are also prevalent in the United States (US). *Giardia lamblia* is a protozoan parasite that is spread by the fecal-oral route either through contaminated water or food or directly from person to person. Symptoms range from asymptomatic cyst shedding to severe gastrointestinal illness, diarrhea, malabsorption, and weight loss. Diagnosis relies on stool studies and metronidazole is typically the treatment of choice. Prevention relies on clean water supplies, hand washing, and education about modes of transmission and safe sexual practices. A high index of suspicion and thorough history are important to diagnose this ubiquitous disease.

Case Report

A 35-year-old healthcare worker with no chronic medical problems developed severe malaise associated with abdominal cramping, bloating, foul smelling stools, increased flatulence, intermittent nausea and vomiting, anorexia, and weight loss of ~10 pounds over a one-week period. Stools were occasionally described as loose, but frank diarrhea did not occur. The patient initially believed he had a viral gastroenteritis, but when symptoms persisted, he presented for evaluation after seven days of illness. He had taken ibuprofen and acetaminophen for malaise but had no other chronic medications. History was notable for recent travel within the US including day hiking trips in the mountains but no known exposure to mountain water. He also reported recently caring for a patient who worked in a daycare center who was hospitalized with a diarrheal illness. That patient was hydrated, treated empirically with ciprofloxacin and metronidazole, and discharged from the hospital after an overnight admission. Stool ova and parasite (O&P) testing was not performed. Past medical history was unremarkable for any gastrointestinal or other chronic diseases. Social history revealed the patient had no history of homosexual sexual activity or oral-anal sexual activity.

Physical examination revealed a fatigued appearing male in no acute distress. Vital signs showed a blood pressure of 116/80 mmHg, heart rate 76 beats/min, and temperature of 36.6°C. Cardiopulmonary exam was normal. Abdominal examination was within normal limits with no distension or tenderness. Laboratory testing revealed a normal complete blood count, basic metabolic panel, and liver function tests. HIV antibody testing was nonreactive. *Giardia* antigen in the stool was positive and studies for ova and parasites (O&P) showed *Giardia lamblia* cysts and trophozoites in three consecutive stools. Giardiasis was diagnosed, and the patient was treated with metronidazole 500 mg three times daily for seven days. After three days of treatment, malaise and fatigue started to resolve. Bloating and flatulence resolved within seven days, and the patient recovered with no further complications.

Discussion

Giardiasis is a small intestinal infection caused by the protozoan parasite *Giardia lamblia* (also known as *Giardia duodenalis* or *Giardia intestinalis*) and is a major cause worldwide of waterborne and foodborne illness. *Giardia* was first discovered in 1681 by van Leeuwenhoek, who found trophozoites in his own feces using a homemade lens. Professor A. Giard of Paris published the first report about the parasite in 1859 that included line drawings of the trophozoite and cyst forms and *Giardia* was later named in his honor in 1915.[1] Initially, *Giardia* was thought to be a commensal organism in humans, but the pathogenicity of the parasite was proven in 1915 when stool isolates from returning war veterans with diarrheal disease were shown to produce diarrhea in kittens.[2] *Giardia* is one of the most common parasitic infections worldwide and is reported to be the second most common parasitic infection in the US after pinworm with an estimated more than 2.5 million cases annually.[3] Transmission occurs by the fecal-oral route and animals serve as an endless reservoir of disease making prevention difficult. Despite many studies, it is unknown why *Giardia* causes such a wide range of disease.[2] Classic symptoms of the disease, often called 'giardiasis', are well described and treatment options are available.

The *Giardia* lifecycle consists of two stages: the cyst, which is transmitted by the fecal-oral route, and the trophozoite, which adheres to the intestinal wall and causes disease. In the first stage, cysts are passed in a host's feces and can remain viable in surface water or a moist environment for months and are responsible for transmission of *Giardia*.[2,4,5] The cyst wall is highly resistant to enzymatic digestion and resistant to chlorination procedures, which allow it to produce major water-borne outbreaks.[2] When cysts are ingested, excystation starts in the stomach when the cysts detect the acidic environment and is completed in the first part of the small intestine where it is believed to be aided by pancreatic enzymes. This process results in the release of the trophozoites in the proximal small intestine.[4,5]

The trophozoite comprises the second stage of the *Giardia* lifecycle. The trophozoite has two anteriorly placed nuclei and a flat ventral surface with an adhesive disk that allows it to attach to the brush border of intestinal epithelium and begin to replicate by binary fission. Trophozoites also have four flagella that aid in movement and attachment to enterocytes.[4] The trophozoite is responsible for clinical symptoms which are believed to result from both mucosal and luminal abnormalities. Mucosal changes such as damage to the intestinal brush border and mucosa, induction of a host response that causes an increase in chronic inflammatory cells and secretion of fluid and further damage, and reductions in disaccharidase activities have all been described. *Giardia* is not an invasive organism and it remains unclear why there is such an extensive variation in clinical disease. Along with mucosal factors, several luminal factors such as bacterial overgrowth and an alteration to the bile contents are also believed to contribute to clinical disease.[2] Like excystation, cyst formation requires environmental changes that occur as the parasite passes through the intestine. Specifically, cholesterol deprivation has been demonstrated to trigger differentiation of trophozoites into cysts. *Giardia* cannot synthesize its own cholesterol and due to intestinal absorption of this lipid, the cholesterol concentration is low below the jejunum. Thus, when *Giardia* travels down the intestine, it detects the low cholesterol levels and triggers the encystation process.[5] Subsequently, these cysts are then passed in the feces and the cycle begins again.

Giardia is ubiquitous and one of the most frequently diagnosed intestinal protozoa infections worldwide, mainly due to lack of adequate sanitation and hygiene.[6] Prevalence rates vary depending on location from 2-5% in the industrialized world to 20-30% in the developing world.[2] High-risk groups include infants and young children, travelers, and individuals with immunodeficiency. *Giardia* is typically considered in diarrhea in young children from developing countries and sporadic outbreaks of food related diarrhea in industrialized countries or in travelers returning from endemic areas.[6] Travel within a country such as the US can also lead to giardiasis, particularly in travelers who go from a low risk area like a large city to a high risk area such as a mountain resort or a National Park.[2] In the US, *Giardia* is found in around 5% of stool specimens from patients who have diarrheal illness that present to healthcare providers and is responsible for around 5000 hospitalizations per year and over 15,000 reported cases.[7] In the developing world, the burden of disease is much greater with an estimated 200 million people having symptomatic giardiasis, with around 500,000 new cases per year.[6]

Giardia is transmitted by the fecal-oral route either indirectly through contaminated water or food or directly from person to person. Prevalence is higher in populations with poor sanitation, close contact, and high-risk sexual behavior such as oral-anal sexual activity.[3] *Giardia* cysts survive in mountain streams and are resistant to chlorine levels in normal tap water leading to major water-born outbreaks involving domestic water supplies.[2] Children in day care and backpackers, campers, hunters, and travelers to disease-endemic areas are affected most frequently.[4] *Giardia* is a zoonosis and infected beaver, cattle, dogs, rodents, etc. serve as a constant reservoir of human infection as do other humans with asymptomatic disease.[3] In developing countries, *Giardia* commonly infects children with a prevalence rate of up to 30% in children younger than 10 years of age.[4] Poor fecal-oral hygiene places children and workers in day care centers at risk. Outbreaks have also occurred in commercial food establishments and corporate office settings.[4] Thus, some patients may not have classic historical risk factors and *Giardia* should be considered in outbreaks of gastrointestinal illness.

While protozoan infections are not commonly thought of as a sexually transmitted infection, it is well known that several intestinal protozoans including *Giardia* may be spread by sexual activity, specifically by oral-anal sexual contact. Sexually active gay men and those who engage in anal or anal-oral sexual practices have increased risk of disease. *Giardia* has been reported frequently among men who have sex with men including high rates in several studies in Los Angeles.[6] Performing a detailed sexual history is important to elicit risk factors for this mode of transmission. Furthermore, it is important that healthcare practitioners provide education on the modes of transmission and risks of different sexual practices so that patients make more informed choices.

A wide range of clinical presentations can occur with giardiasis ranging from asymptomatic shedding of cysts, as well as mild self-limited diarrhea to severe symptomatic acute or chronic diarrhea.[2] Among those who ingest *Giardia* cysts, 5-15% pass cysts but have no symptoms, 25-50% develop acute but self-limiting diarrhea, and 35-70% have no evidence of infection at all. Cardinal complaints in symptomatic individuals with acute giardiasis include diarrhea (~90%), malaise (84%), flatulence with foul-smelling stools (~70%), abdominal cramping (~70%), nausea (68%), and anorexia and weight loss (~65%).[4] As *Giardia* is non-invasive, the white blood cell count is typically normal and eosinophilia does not occur. Although most symptomatic individuals have a self-limiting infection over 2-4 weeks, ~30% can have chronic diarrhea often with steatorrhea and profound weight loss.[2] Lactase deficiency can persist for several weeks after treatment and severe malabsorption, including fat and lactose malabsorption, chronic fatigue, depression, and an irritable bowel type syndrome have been described.[4,6] The major complication of giardiasis is malnutrition, which can cause nutrient deficiencies in adults that typically do not have severe long-term effects but can have profound effects on growth and development in infants and young children.[2]

Diagnosis of *Giardia* can be challenging as acute diarrhea in adults is common (~179 million cases/year in the US) and most frequently caused by viral gastroenteritis (mainly noroviruses).[8] Individuals with acute diarrhea often do not present for medical evaluation, but for those that do, a thorough history is important to determine which patients require further workup. Relevant historical information includes recent travel to a high-risk foreign country or an area in the US with higher risk, recent antibiotic treatment, high-risk sexual practices including oral-anal sexual contact, day care center exposure, and any immunosuppressive disorders. The character of the stool in terms of odor, whether it floats or not, and color (other than a

bloody) has not been shown to be helpful.[8] Routine stool studies are expensive and positive in only ~1.5% to 5.5% of patients and not recommended. Routine stool analysis for O&P is also not cost effective, especially in developed countries. However, O&P testing should be considered in cases of persistent diarrhea > 7 days and in those with high-risk activities such as day care exposure, foreign or mountain travel, or men who have sex with men.[9]

If the history suggests an increased risk of giardiasis or diarrhea is persistent, stool for O&P by light microscopy should be considered. Stool O&P examination is the primary diagnostic test, and sensitivity is improved significantly by sending multiple stool specimens (~50-70% for a single specimen, ~85% for three specimens).[2,3] As stated previously, *Giardia* is not invasive, so leukocytosis and eosinophilia are not expected. Enzyme linked immunoassays that detect fecal antigens to *Giardia* have higher sensitivity and specificity (>90%) than stool O&P and are becoming the standard diagnostic tests in the US.[4]

The first goal of treatment for all diarrheal illnesses is to correct dehydration and electrolyte abnormalities, which may be life saving for the elderly and infants.[8] The main treatments for Giardia are metronidazole, tinidazole, and nitazoxanide (**Table 1**). Alternative agents such as quinacrine, furazolidone, and albendazole are available but used less frequently. None of the treatment regimens are ideal because of the high incidence of side effects, the significant failure rate, and the contraindications in certain circumstances.[10] Metronidazole was discovered in the late 1950s and has been the mainstay of treatment for giardiasis for decades and is still widely used. Adverse side effects may occur (**Table 1**). Metronidazole treatment for 7 days in divided doses has an efficacy of 80-95%.[4] For patients who fail initial treatment, are pregnant, or are breastfeeding mothers, infectious disease consultation should be strongly considered to choose the appropriate treatment regimen. It is important to recognize that when symptoms continue after initial treatment several different scenarios are possible including drug resistance, cure followed by rapid reinfection, non-compliance with treatment, or co-infection with another disease producing organism.[10] Providing patient education about the modes of transmission and safe sexual practices is also key to avoid recurrences.

Proper sewage disposal and water treatment, proper and frequent hand washing and diaper disposal in day care centers, and consumption of only bottled water in endemic areas can be preventative. In endemic regions, uncooked foods that are prepared or washed with contaminated water should be avoided. For campers or hikers drinking mountain water, treating water by boiling for one minute, using iodine purification tablets for eight hours, or use of a proper water filter can reduce risk.[3] It is highly unlikely that giardiasis can be eliminated since other animals constitute a huge reservoir of infection.[2]

In conclusion, *Giardia* is a ubiquitous disease that should be considered in patients with gastrointestinal illness characterized by persistent gastrointestinal illnesses often with diarrhea, malaise, and weight loss. Diagnosis through stool O&P and antigen testing should be pursued in patients with risks of disease or those with persistent symptoms. First line treatment is metronidazole. Patient education about modes of transmission is key to avoiding recurrence. In the case reported, *Giardia* was diagnosed ten days after illness began when symptoms of severe bloating, cramping, malaise, and weight loss persisted. Metronidazole treatment for 7 days was curative and over the next month the patient's weight and activity level returned to baseline. The exact method of transmission was unclear in this patient although hiking and mountain travel and previous exposure to a day care worker with a diarrheal illness may have led to disease.

Table 1. **Selected Drug treatment of Giardiasis***

Metronidazole	Adult dose: 2 g daily for 3 days *OR* 250-750 mg TID for 5-7 days	Main adverse effects: nausea, vomiting, metallic taste, GI disturbances, rash, avoid in pregnancy
Tinidazole	Adult dose: 2 g single dose	Main adverse effects: same as metronidazole
Mepacrine	Adult dose: 100 mg TID for 5-7 days	Main adverse effects: GI disturbances, dizzy, headache, nausea, vomiting, psychosis rarely, avoid in pregnancy
Flurazalidone	Adult dose: 100 mg QID for 7-10 days	Main adverse effects: nausea, vomiting, hemolysis in G6PD deficiency

*****Adapted from Farthing MJ. Giardiasis. *Gastroenterology Clinics of North America*. 1996;25(3):493-515.

REFERENCES

1. **Dobell C**. The Discovery of the Intestinal Protozoa of Man. *Proc R Soc Med*. 1920;13(Sect Hist Med):1-15. PubMed PMID: 19981292; PubMed Central PMCID:PMC2151982.
2. **Farthing MJ**. Giardiasis. *Gastroenterol Clin North Am*. 1996 Sep;25(3):493-515. Review. PubMed PMID: 8863037.
3. **Kucik CJ, Martin GL, Sortor BV**. Common intestinal parasites. *Am Fam Physician*. 2004 Mar 1;69(5):1161-8. Review. PubMed PMID: 15023017.
4. **Huang DB, White AC.** An updated review on Cryptosporidium and Giardia. *Gastroenterol Clin North*

Am. 2006 Jun;35(2):291-314, viii. Review. PubMed PMID:16880067.

5. **Carranza PG, Lujan HD**. New insights regarding the biology of Giardia lamblia. *Microbes Infect*. 2010 Jan;12(1):71-80. doi: 10.1016/j.micinf.2009.09.008. Review. PubMed PMID: 19772929.
6. **Escobedo AA, Almirall P, Alfonso M, Cimerman S, Chacín-Bonilla L**. Sexual transmission of giardiasis: a neglected route of spread? *Acta Trop*. 2014 Apr;132:106-11. doi: 10.1016/j.actatropica.2013.12.025. Review. PubMed PMID: 24434784.
7. **Centers for Disease Control and Prevention, 2006**. Notifiable diseases/deaths in selected cities weekly information. *Morbidity and Mortality Weekly Report*. CDC Surveillance Summary; 55:1156-67.
8. **DuPont HL**. Acute infectious diarrhea in immunocompetent adults. *N Engl J Med*. 2014 Apr 17;370(16):1532-40. doi: 10.1056/NEJMra1301069. Review. PubMed PMID:24738670.
9. **Barr W, Smith A**. Acute diarrhea. Am Fam Physician. 2014 Feb 1;89(3):180-9. PubMed PMID: 24506120.
10. **Escobedo AA, Cimerman S**. Giardiasis: a pharmacotherapy review. *Expert Opin Pharmacother*. 2007 Aug;8(12):1885-902. Review. PubMed PMID: 17696791.

Submitted September 9, 2016