Clostridium Difficile Colitis: One Woman's Journey

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Abstract

Clostridium difficile (C. diff) associated diarrhea is an occasional complication that may result from the use of broad-spectrum antibiotics. This particular infection is a growing concern among medical professionals. Patients suffering with C. diff are generally treated with the oral medications metronidazole and/or vancomycin. Even with the use of metronidazole and vancomycin antibiotics, there is often a problem with recurrent episodes of diarrhea. Stool transplantation was successful in one woman’s bout with recurrent C. diff. This woman suffered with recurrent C. diff for several months using the standard treatment of metronidazole and vancomycin, with each round of antibiotic ending in failure. Stool transplantation was then recommended. The patient chose to proceed with the unconventional procedure. Stool transplantation is a procedure with minimal complications that disrupts the cycle of repeated antibiotic use. With the evolving prevalence and severity of C. diff, the need for improved treatment strategies is of utmost importance.
Clostridium Difficile Colitis: One Woman's Journey

_Clostridium difficile_ (C. _diff_\_) is an anaerobic, gram-positive, spore-forming bacillus and is the leading cause of antibiotic-associated diarrhea as well as pseudomembranous colitis (Aas, Gessert, & Bakken, 2003). Cases of _C. diff_\_ are commonly associated with the use of antimicrobial agents. The most frequent causative agents are fluoroquinolones, cephalosporins, and clindamycin (Bakken, 2009). Treatment protocol combines supportive measures and additional antibiotics that have been proven to be effective against _C. diff_\_. The purpose of this article is to present the journey of a woman with recurrent _C. diff_, following her story from beginning diagnosis and treatment, to resolution with fecal transplantation. The case study describes eight encounters over a 6-month period in the inpatient and outpatient setting.

_C. diff_\_ is a prevalent bacterium with malignity that is becoming more common and with increased severity, resulting in an infection that is more difficult to treat than ever. It is a cause of considerable increased mortality in the United States. _C. diff_\_ associated diarrhea was reported during 1999-2004 as the reason for death in 20,642 persons (Redelings, Sorvillo, & Mascola, 2007). The median age of death in this study was 82 years and it was found that mortality rates were greater in men than women and occurred more frequently in Caucasians than any other racial or ethnic group (Redelings et al., 2007). The majority of _C. diff_\_ associated deaths, approximately 80%, were discovered in hospitals, 8% in long-term care facilities, and 10% in home health (Redelings et al., 2007).

This anaerobic bacterium incites a range of problems, including diarrhea, colitis, pseudomembranous colitis, and toxic megacolon (Butler & Zips, 2010). It is spread by fecal-oral transmission. _C. diff_ was first noted to cause problems in the early 1970’s during the time when broad spectrum antibiotics were used liberally (Fekety, 1997). These particular antibiotics are most frequently implicated in the disruption of normal intestinal flora. The bacterium begins to
proliferate within the intestine and produces toxins that lead to inflammation and mucosal injury (Gould & McDonald, 2008).

There are predisposing conditions and risk factors correlated with C. diff associated diarrhea. Factors include severe underlying disease, persons older than 65 years of age, the presence of a nasogastric tube (NGT), receiving gastric acid suppression therapy, extended hospital stay, an extended length of antibiotic use, as well as receiving multiple antibiotics (Starr, 2005). Mortality rates are higher in Caucasians than any other racial or ethnic group and males more than females (Redelings et al., 2007). It is suggested by Redelings et al. (2007) that Caucasian elderly are more likely to receive antibiotics which then predispose them to C. diff. The key to prevention of the overgrowth of C. diff in the intestine is to refrain from the overuse of antimicrobials.

**Case Study**

**Hospitalization 1 (March 20)**

The patient is a 57 year-old white female with a three day history of abdominal pain, diarrhea, and fever up to 103.0 F. She has a history of diverticulitis requiring sigmoid colectomy 4 months prior to this admission. The patient completed several rounds of antibiotics and most recently was taking a flouroquinolone for “flu-like” symptoms. White blood cell count on admission was 7.2. She denies any sick contacts, foreign travel, suspicious foods, lake or stream contact. Stool for C. diff toxin was negative.

Past medical history included diverticular disease requiring sigmoid colectomy, gastroesophageal reflux disease, remote peptic ulcer disease, irritable bowel syndrome, migraine headaches, asthma, hypertension, mitral valve prolapse, hiatal hernia, and shingles. Past surgical history includes cholecystectomy, sinus surgery, bladder suspension, and bilateral ankle surgery.
CLOSTRIDIUM DIFFICILE COLITIS

Home medications include Protonix, Tenormin, Seroquel, Celexa, Astelin, and Advair Diskus, as needed.

Computed tomography (CT) scan showed diffuse thickening and inflammation of the colon. Flexible sigmoidoscopy revealed severe left-sided pseudomembranous colitis. Colon biopsy demonstrated moderately acute colitis with pseudomembrane formation suggestive for antibiotic associated colitis. She was treated with metronidazole and vancomycin.

**Symptoms of C. diff colitis.**

Symptoms of *C. diff* appear during or quickly after antibiotic therapy is initiated, however symptoms may be deferred for up to eight weeks (McQuaid, 2010). Patients generally report mild to moderate greenish, foul-smelling, watery diarrhea with lower abdominal discomfort. In mild disease, bleeding and fever are not present and the physical exam is relatively normal. Severe disease is described by a copious amount of diarrhea and abdominal pain with systemic features such as fever, nausea, anorexia, and dehydration (Diggs & Surawicz, 2009).

**Diagnosis of C. diff colitis.**

Early diagnosis of *C.diff* colitis is essential to preventing complications. The production of toxin A and B in the stool leads to the diagnosis of *C. diff* (McQuaid, 2010). Rapid enzyme immunoassays (EIA) for both toxins are commonly used. Cell cytotoxicity assays are more sensitive but are high maintenance, costly, and require 48 to 72 hours before any results are available (Butler & Zips, 2010). Despite these hurdles, cell cytotoxicity assay testing is considered the gold standard in *C. diff* colitis diagnosis. It is recommended that three specimens be sent on three consecutive days in order to yield better results of either test (Nazarko, 2007). It is important to remember that a negative test for *C. diff*, especially in moderately ill patients, should not deter one from initiating treatment. In addition to the stool studies, endoscopy can assist practitioners in identifying other causes of diarrhea, such as ischemic colitis, inflammatory
bowel disease, or irritable bowel syndrome (Diggs & Surawicz, 2009). Pseudomembranous colitis, which can also be identified through endoscopy, develops in response to the toxins produced by C. diff (Nazarko, 2007). Diagnosis of C. diff is established by both clinical and laboratory data.

Hospitalization 2 (April 14)

The patient returned to the hospital with complaints of diarrhea, right lower quadrant abdominal pain, and nausea that exacerbated yesterday morning. She completed her course of vancomycin one week earlier. She had up to twenty episodes of diarrhea without any gross gastrointestinal bleeding. White blood cell count was 16,000. Stool culture and C. diff toxin were negative. Stool for occult blood was positive and there were large numbers of white blood cells in the stool. She was treated with metronidazole and vancomycin 250 mg by mouth four times daily for 10 days.

Management of C. diff colitis.

Supportive therapy. Supportive therapy consists of fluid and electrolyte replacement and discontinuation of the offending agent, if possible. The patient may require intravenous fluids until the diarrhea resolves. Avoiding anti-peristaltic agents as well as narcotics is imperative as these medications may inhibit the body’s attempt to eliminate C. diff and may lead to toxic megacolon.

Pharmacological therapy. For nearly three decades metronidazole and oral vancomycin have been the mainstay therapy for C. diff colitis (Cohen et al., 2010). Practice guidelines supported by the American College of Gastroenterology (ACG) recommend metronidazole as first line therapy for the treatment of C. diff colitis (Fekety, 1997). When there is a high index of suspicion in the seriously ill patient, empiric treatment with metronidazole is advised. Oral vancomycin is recommended when the patient (a) fails metronidazole, (b) is unable to tolerate
metronidazole, (c) is pregnant, or (d) is critically ill due to *C. diff* colitis (Fekety, 1997). More recent clinical guidelines published by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Disease Society of America (IDSA) also supports metronidazole (500 mg three times daily for 10-14 days) for initial episodes described as "mild or moderate" which are clinically distinguished by mild leukocytosis (white blood cell count <15,000) and a serum creatinine level less than 1.5 times the pre-morbid level (Cohen et al., 2010).

Vancomycin, at starting doses of 125 mg four times daily, is recommended for the treatment of "severe" initial episodes with leukocytosis (white blood cell count > 15,000) or a serum creatinine level greater than or equal to 1.5 times the pre-morbid level. Higher doses of oral vancomycin, up to 500 mg four times daily, plus metronidazole, 500 mg every eight hours intravenously, are suggested for cases complicated by hypotension, shock, ileus, or toxic megacolon (Cohen et al., 2010). The main outcome should be symptomatic resolution which is defined by Nelson (2007) as the ending of symptoms during treatment and 30 to 60 days afterwards.

Approximately 20% of patients have a relapse of diarrhea associated with *C. diff* within 1 to 2 weeks after the completion of antibiotic therapy (McQuaid, 2010). Failure to eliminate, or re-infection with the organism, may be reasons for the relapse. These relapses may be difficult to treat. One’s own immunity plays a significant role in recurrent disease. The SHEA and IDSA advocate treating the first recurrence of *C. diff* colitis similarly to the initial episodes. Metronidazole, however, is not advised after the first recurrence or for long term therapy due to the risk of neurotoxicity. Tapered and/or pulsed regimens of oral vancomycin are recommended for further recurrences, which aids in controlling the vegetative form of *C. diff* while normal intestinal flora is restored (Cohen et al., 2010).
Probiotics (*Saccharomyces* and *lactobacillus* species) are used as adjunct therapies with antibiotics in an effort to restore normal intestinal flora (Gould & McDonald, 2008). Probiotics are not, however, recommended to be used to prevent *C. diff* infection as there is insufficient evidence to support this practice (Cohen et al., 2010). It is recommended that larger clinical trials with probiotics should be performed before they are routinely used as a preventative agent in the treatment of *C. diff* associated diarrhea.

**Preventative Measures.**

Infection control and prevention efforts are fundamental in controlling *C. diff*. Hand hygiene with soap and water is paramount for the prevention of *C. diff* infections in that *C. diff* spores are not eliminated by alcohol-based hand sanitizers (Diggs & Surawicz, 2009). It is vital to educate family members about good hand hygiene in order to control environmental contamination. A chlorine-containing cleaning product is the only effective bactericidal agent against *C. diff* spores (Gould & McDonald, 2008). These particular products should be used when cleaning equipment used by persons with *C. diff*. Caretakers should also be instructed on the use of bleach products in the home.

Barrier methods, such as gloves and gowns, should be enforced at all times by healthcare workers well as placing the patient diagnosed with *C. diff* in contact isolation. Placing patients known to have *C. diff* in contact isolation, the use of protective barriers, and the strict adherence to washing with soap and water after caring for a *C. diff* patient are just a few responsibilities nurses should incorporate into their practice.

**Clinic Visit 1 (June 1)**

The patient has been on vancomycin 250 mg by mouth three times daily for the past 5 weeks and is currently asymptomatic. Vancomycin was decreased to once daily for two weeks, then discontinued.
Hospitalization 3 (July 29)

The patient completed her tapering regimen of vancomycin three weeks ago. Diarrhea returned three days later. White blood cell count was 10.1. Stool studies, including culture and C. diff, was negative. CT scan showed inflammation of the sigmoid and recto-sigmoid colon. Vancomycin was restarted in addition to metronidazole.

Clinic Visit 2 (August 6)

The patient continued to take vancomycin 250 mg by mouth three times daily, as well as probiotics, and denies any abdominal pain, diarrhea, nausea, vomiting, or fever. To that date, all stools submitted for C. diff toxin had been negative. The patient was feeling better, but was concerned about further relapse once stopping vancomycin. Stool transplant was recommended.

Clinic Visit 3 (August 14)

The patient continued to take vancomycin and reported improvement in her diarrhea. She was currently having two loose stools daily. The patient did report significant right-sided abdominal pain and rectal bleeding. There had been no fever. She had been advised to continue vancomycin and was to add metronidazole 500 mg three times daily. The patient was to be scheduled for fecal transplant once her symptoms became stable.

Stool Transplantation for C. diff colitis.

Stool transplantation, also known as fecal bacteriotherapy, is the transfer of stool from a healthy donor into the gastrointestinal tract of the patient experiencing recurrent C. diff. Stool transplantation has been performed since the 1950’s and has been shown to have great success (Bakken, 2009; Yoon & Brandt, 2010). Aas et al. (2003) performed a retrospective study that examined 18 patients who received donor stool by NGT. All cases were treated with stool transplantation for recurrent C. diff by a single clinician during a 9-year period. Ninety-four percent of patients reported their bowel patterns had returned to their normal state. Yoon &
Brant (2010) conducted a more recent retrospective study of 12 consecutive patients with recurrent *C. diff* colitis that were treated with fecal transplant administered via colonoscopy. The patients exhibited an immediate response and a 100% cure rate was demonstrated with the stool transplant. There were no adverse events documented in either of these studies.

**Stool donor.** Specific criteria must be met prior to stool transplantation. A suitable donor must be available. Generally this person is an individual that has intimate physical contact with the recipient, such as a spouse. Bakken (2009) suggests a screening protocol for donors, evaluating for infectious diseases, including viral hepatitis, human immunodeficiency virus, and syphilis. In addition, stool cultures and studies for *C. diff* and ova and parasites should be obtained. It is also recommended that the donor not have received antibiotic therapy for six weeks to three months prior to stool donation (Bakken, 2009).

**Stool preparation.** The timing of the stool collection from the donor should be as close to the administration time as possible. Once the stool is collected it is then mixed with 0.9 NaCl via a blender followed by filtering the suspension using a coffee filter in order to remove large particles (Bakken, 2009). Once the stool transplant specimen is prepared, it can be used immediately or frozen for later use (Bakken, 2009).

**Stool instillation.** Administration of donor stool can be achieved rectally via colonoscopy or enema or through the upper gastrointestinal tract by the use of a NGT (Bakken, 2009). NGT administration poses less risk and is a more cost-effective method of installation when compared to instillation via colonoscopy (Bakken, 2009). For those that receive stool instillation via NGT, Aas et al. (2003) recommend a proton pump inhibitor (PPI) the evening prior and morning before to decrease acid production and thereby create an optimal intestinal environment. The recipient should be treated with oral vancomycin for four days prior to the procedure; the vancomycin is
then discontinued the night before the procedure to decrease vegetative *C. diff* colony load (Bakken, 2009). No additional antibiotics or probiotics are needed after the procedure.

**Stool Transplant Procedure (September 1)**

The stool transplant was performed at an outpatient endoscopy center. Reglan, 10 mg, was administered to the patient 20 minutes prior to the procedure. She was sedated with Versed 5 mg IV and the oropharynx and right nare are sprayed with benzocaine. Subsequently, a 16-French NGT was inserted into the right nare and passes easily into the stomach. Placement is verified. A total of 50 ml of filtered stool, donated from her spouse, was flushed through the NGT followed by 50 ml of nonbacteriostatic 0.9% saline. She was instructed to discontinue all antibiotics including, probiotics.

**Clinic visit 4 (September 18)**

The patient presented to the clinic 18 days following fecal transplant. She had been feeling well until the development of a perianal abscess one week earlier that required incision and drainage. Since the development of the abscess she had experienced some loose stools, fatigue, and fever. Sedate flexible sigmoidoscopy was performed. Findings included healthy appearing mucosa to the descending colon, evidence of colo-colo anastomosis, and non-bleeding internal hemorrhoids. Random biopsies were consistent with the resolving stage of colitis.

**Conclusion**

The lack of aesthetic appeal of stool transplantation has not deterred patients from receiving this mode of treatment. Patients with recurrent diarrhea are either very ill or their quality of life is so negatively impacted, that they will do whatever assures relief (Yoon & Brandt, 2010). The long term effects of stool transplantation are not known. Further studies are needed to establish the most effective standardized regimen.
References


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