**INTRODUCTION**

*Clostridium difficile* (C. difficile) is associated with a broad spectrum of clinical expressions. It is established as the causative agent of pseudomembranous colitis (PMC) in 1978. Patients infected with a toxin-producing strain of *C. difficile* generally suffer with diarrhea though the severity can range from mild to life-threatening, and may be accompanied by abdominal pain and cramping, fever, malaise, nausea and leukocytosis. More severe manifestations include toxic megacolon, sepsis, perforation and even death.

Patients with Inflammatory Bowel Disease (IBD) are also at an increased risk of acquiring *C. difficile* infection, and generally have worse outcomes when associated with *C. difficile* infection.

**DISCUSSION**

Reports published in the 1980s did not support *C. difficile* infection as an important factor in IBD. Recent reports however have shown *C. difficile* infection to have a contributory role in IBD and for IBD to be a risk factor for the development of *C. difficile* infection. An evaluation of IBD patients who underwent stool analysis for PMC between 2000-2001 reported 20% of the patients to have been positive for *C. difficile*.

The epidemiology of *C. difficile* infection has changed over the past decade. IBD is now emerging as an important and previously unrecognized risk factor, as patients with IBD share many of the clinical risk factors for the development of *C. difficile* infection.

Disruption of the intestinal flora diminishes the ability of the microflora to control acquisition of *C. difficile* by means of colonization resistance. *C. difficile* infection is thus predominantly a result of broad-spectrum antibiotic use and fluoroquinolone resistance is a characteristic of the epidemic BI/NAP1 strains. Ciprofloxacin is commonly used in the treatment of IBD.

Corticosteroids are used in the treatment of IBD due to their inhibitory effect on the host’s immune system and were used by all 5 patients. It has been shown that infection with *C. difficile* is dependent on the host’s immune response to toxin A. As IBD exacerbation is routinely treated with high-dose corticosteroids, these patients may not be able to mount an effective immune response to *C. difficile*, rendering them highly susceptible to infection.

Moreover, immunosuppression as a result of chemotherapy or in organ transplantation is a known risk factor. Immunomodulators used in the treatment of IBD, including azathioprine, 6-mercaptopurine, and methotrexate, induce a similar state of suppression. All patients in our study had been exposed to immunomodulators, predominantly azathioprine, and one patient undertook a course of anti-TNF-α therapy.

Treatment of *C. difficile* infection is known to be problematic with approximately 15-30% patients experiencing an initial relapse and up to 65% of these patients suffering multiple relapses despite maximal antibiotic therapy. The use of antibiotics in the treatment of *C. difficile* infection may predispose patients to further relapses through the maintenance of a disturbed intestinal flora and may also contribute to the emerging problem of *C. difficile* resistance. Fecal Bacteriotherapy (FB), an extension of probiotic therapy, is the administration of healthy human fecal flora via enemas, colonoscopies or into the bowel of the patient. FB restores the colonic microflora of the patient, enabling the eradication of *C. difficile* and the re-establishment of ‘colonization resistance’ preventing further relapse.

**METHODS**

Patients

Five patients (4M, 1F; aged 11-59yr) presented to the Centre for Digestive Diseases between 2002 and 2006 with refractory IBD (see Table 1). All patients were diagnosed with ulcerative colitis (UC) and 2 with Crohn’s disease (CD), had been failing to respond to anti-IBD therapies for 4-10 years. Therapies included corticosteroids, 5-aminosalicylates, immunomodulatory agents, anti-tumor necrosis factor-α (TNF-α) therapy, and antibiotics. Patients presented with longstanding and worsening symptoms of abdominal pain (5/5), diarrhea (4/5), blood (4/5), mucus (4/5), urgency (4/5), weight loss (3/5), flatulence (3/5), abdominal cramps (3/5), and fatigue (1/5).

All 5 patients were found to be co-infected with *C. difficile*, confirmed by either a positive culture result (Patient 1), or a positive culture and antibiotic-induced toilet secession (Patients 2, 3 and 4). All patients subsequently failed anti-*C. difficile* therapies, including metronidazole, vancomycin, rifampicin, Lactobacillus acidophilus, Bacteroides species, and hyperimmune egg powder.

**RESULTS**

All 5 patients had confirmed *C. difficile* eradication by negative culture and toxin A + B results 8 weeks post treatment with FB. Follow-up stool tests for Patients 1, 2 and 3 over 12 months post FB revealed negative results for both endotoxin and *C. difficile* as per our study analysis was conducted .

**CONCLUSION**

IBD has emerged as an important and previously unrecognized risk factor for the development of *C. difficile* infection, an infection which can contribute to exacerbations of IBD. *C. difficile* must now be considered in IBD patients experiencing a flare even when no recent hospitalization or antimicrobial use can be identified. Vigilance is also important as *C. difficile* infection is notoriously difficult to isolate and multiple stool tests are often necessary to detect infection. Whilst standard treatments for *C. difficile* infection are incapable of reliably eradicating the bacterium, FB has shown great efficacy. Patients can experience marked symptom improvement after FB and thereafter exhibit better response to IBD therapies.

**REFERENCES**


**NOTES**

1 Abstract title originally “Clostridium difficile Complicating Inflammatory Bowel Disease: Cure after Fecal Bacteriotherapy”.
2 Abstract reported 6 patients hereunder, one patient was removed as further investigation could not confirm pre-treatment status.