

A severe and complicated case of recurrent *Clostridium difficile* colitis in a 27-month-old boy: A rare entity in young children

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Abstract

We present a case of a 27-month-old boy with severe *Clostridium difficile* infection complicated by toxic megacolon, rectal prolapse, hypoalbuminemia, and ascites. The patient improved with antibiotics but later presented with recurrent *Clostridium difficile* colitis. Antibiotic therapy for recurrent *Clostridium difficile* infection was given and after recovery, fecal microbiota transplantation was performed to prevent further recurrence of disease. The patient did well on follow-up. Severe *Clostridium difficile* disease is rare in young children and colonization is common.

Case report

A 27-month-old male patient presented to the pediatric emergency department with complaints of diarrhea and vomiting for 4 days. He had large, watery, non-bloody, non-mucoid stools with a frequency of 10-12 episodes/day. The patient was reported to be febrile at home with a temperature of 102°F. His oral intake was significantly decreased, and he had minimal urine output. Past medical history included a recent hospitalization for respiratory syncytial virus bronchiolitis for 3 days and the use of antibiotics during this stay. On physical examination, the patient appeared ill and fussy with dry mucous membranes. He was tachycardiac on initial evaluation with a heart rate of 156 beats/min. His abdominal examination showed a distended but soft abdomen with mild diffuse tenderness to palpation. His initial laboratory studies were significant for a white blood count of 21.8 cells per microliter (μ L), sodium of 122 mEq/L, potassium of 5.2 mEq/L, and a chloride of 95 mEq/L. He was also hypoalbuminemic with an albumin of 2.6 gm/dL. The patient was admitted to the hospital for supportive care and correction of electrolyte imbalances.

Stool studies were positive for *Clostridium difficile* (*C. difficile*) via DNA amplification testing and the patient was started on oral metronidazole, which was later switched to the intravenous route due to vomiting. Oral vancomycin was later added due to persistent symptoms. The patient developed peripheral edema with pleural effusion and ascites. On repeat laboratory evaluation, his albumin and total protein both were low at 1.6 g/dl and 3.5 gm/dl respectively. The patient underwent therapeutic paracentesis along with an infusion of 25% albumin. His upper gastrointestinal endoscopy revealed esophagitis, gastritis and a duodenal ulcer. Flexible sigmoidoscopy showed bowel wall edema and pseudomembranous colitis (Figure 1). Colonic biopsies demonstrated fragments of edematous colonic mucosa and fragments of hyperplastic-appearing colonic mucosa with abundant associated mucin; negative for active inflammation or granuloma. An abdominal x-ray revealed dilated bowel loops concerning for toxic megacolon (Figure 2) which was confirmed on

subsequent CT scan of abdomen. Meanwhile, the patient developed rectal prolapse. Toxic megacolon was treated conservatively with nothing per oral, intravenous antibiotics and total parental nutrition. No surgical intervention was required. The patient was continued on antibiotics and total parenteral nutrition for 3 weeks. His condition improved gradually and he was discharged home after completion of antibiotics.

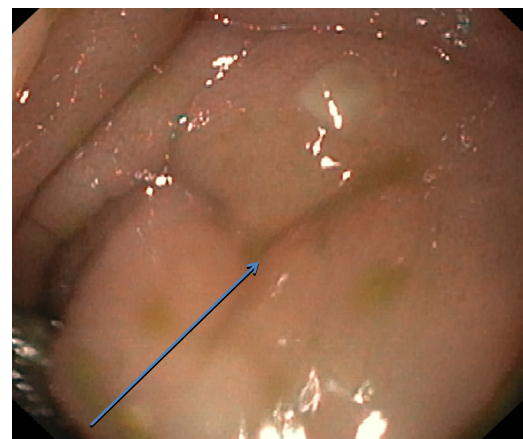


Figure 1. Endoscopic image of pseudo-membranes in colon.

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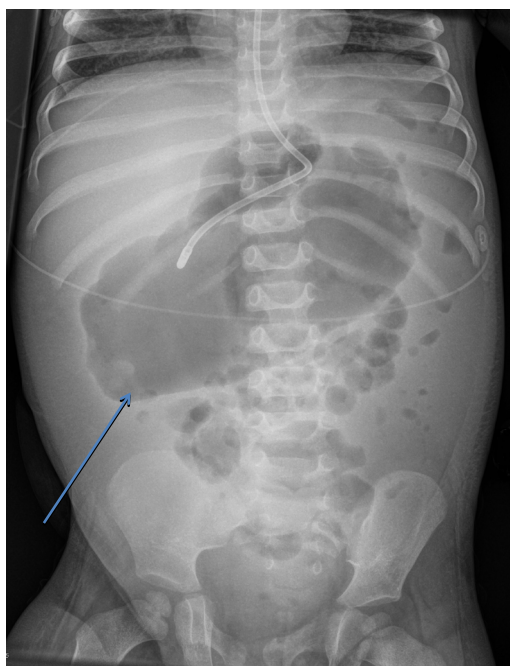


Figure 2. Abdominal radiograph with toxic megacolon.

One week later, the patient again presented with watery, non-bloody diarrhea, accompanied by vomiting, fever and loss of appetite. His stool studies were positive for *C.difficile* and he was found to have hypoalbuminemia (2.5 g/dl) and mild ascites. He was started on intravenous metronidazole and oral Vancomycin to which he responded. As the patient presented with recurrent and complicated CDI, fecal microbial transplantation (FMT) was discussed with his family and was performed when a healthy related donor was identified. The donor was screened for transmissible infections per guidelines [1]. Antibiotics were held approximately 24 hours prior to the procedure. FMT was performed with 50g of donor stool homogenized with 100cc of normal saline and instilled via nasoduodenal tube. The procedure was well tolerated without complication. Post-transplantation, the patient did well with complete resolution of symptoms and no further recurrences on follow-up 2 months post-procedure.

Discussion

We present a unique case of a young, otherwise healthy child, with severe and recurrent *C. difficile* infection (CDI). The patient had significant morbidity related to CDI and required invasive diagnostic and therapeutic measures. Although symptoms initially responded to supportive measures and oral and IV antibiotics, CDI recurred within a week of hospital discharge. The second episode was also severe and required IV and oral antibiotics. Further recurrence was successfully prevented by FMT.

Severe CDI is rare in infants and young children and asymptomatic carriage is common, with carriage rates as high as 60-70% [2]. Due to these findings, the American Academy of Pediatrics has recommended limited testing in these young children [3]. In addition, CDI-related complications such as toxic megacolon, sepsis, and colectomy are very rare in young children [4], and there are few reported cases [5,6]. Recent analyses of hospital data from two different centers reported less than a 2% incidence of toxic megacolon and sepsis [4].

The treatment of CDI includes the discontinuation of the potentially

causative agent, supportive care such as hydration and if necessary, the use of pharmacological agents against CD [7,8]. The choice of the pharmacological agent depends on the severity of the disease [9]. Conventional pharmacotherapy includes metronidazole as a first choice drug, but if symptoms persist, tapered or pulsed oral vancomycin can be added [7]. A relatively new drug option include fidaxomicin which is a macrolide antibiotic and works by inhibiting RNA synthesis through its inhibitory effect on DNA-dependent RNA polymerase [10]. This drug has been approved for use in the adult population in the USA. However, its role in treating pediatric CDI is still under investigation [8]. A multicenter open-label, phase 2 clinical trial investigating the safety, efficacy, and pharmacokinetics of fidaxomicin in the pediatrics population (age 6 months to 18 years) has been recently completed [11]. (NCT01591863) Another ongoing multicenter, randomized, single-blind, phase 3 clinical trial is comparing the safety and efficacy of fidaxomicin and vancomycin for the treatment of CDI in the pediatric population (SUNSHINE) [12]. (NCT02218372) Nitazoxanide and rifaximin also contain antimicrobial activity against CD but sufficient data is lacking in children [8].

Only recently have we begun to understand the risk of recurrent CDI in children with reported recurrence rates of 20-31% [13-16]. The risk factors for recurrence of CDI in children include recent hospitalization, malignancy, and recent surgery, the use of the acid blocking and immunosuppressant agents and antibiotic use [7,13]. Recurrent CDI can also be treated with supportive care and pharmacotherapy such as metronidazole and vancomycin [9]. The efficacy of medical therapy to prevent further recurrence of CDI is limited and most of the data is from adult studies. The concept of restoration of colonic microbiota and improvement in 'colonization resistance' through probiotic treatment and FMT has shown promising results in some case reports in children [17,18]. Immunotherapy with monoclonal antibodies against CD toxin has also shown positive results in adults [19]. Very rarely, colectomy is used as a treatment for the complicated and life-threatening cases of CDI [7].

FMT has been used in the adult population to prevent the recurrence of CDI and is reported to be effective in up to 90% of patients [1]. Walia *et al.* reported two pediatric cases successfully treated with FMT for recurrent CDI [20]. A recent case series reported 10 pediatric cases that were successfully treated with FMT. Median age of the treated patients was 5.4 years and four of the patients were < 3 years of age [18]. The selection of the recipient for FMT is based on clinical judgment, while the donor is selected after extensive screening for communicable diseases [21]. The preparation for transplantation includes dilution via water or normal saline to create a stool suspension [21,22]. Selection of the methods for administration depends on clinical scenario, available resources, and patient preference and commonly used routes include nasogastric and nasoduodenal or nasojejunal tubes, gastroscopy, enemas and colonoscopic administration [17,21]. Resolution of CDI symptoms and absence of recurrence within 8 weeks is considered as successful FMT [21]. All reported data and our case, where FMT was used to prevent the recurrence of CDI in a complicated CDI, further authenticate the safety and effectiveness of FMT use in children.

Our patient was treated with FMT based on his severe and recurrent disease and had a successful response. The patient has done well since the transplant and no side effects have been reported on 2-month follow-up. This case illustrates that severe and recurrent CDI may occur in young children; a group classically felt to be without severe manifestations, and further recurrence can be safely and effectively prevented with FMT.

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