


Combination of oral vancomycin and intra-colonic vancomycin: Successful treatment of complicated pseudomembranous colitis in a child patient

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Abstract

The *Clostridium difficile* infection-related disease varies from mild diarrhoea to pseudomembranous colitis. Although *C. difficile* infection is commonly considered to be a hospital-acquired infection, a significant number of cases are community acquired. Community-acquired *C. difficile* infection can exhibit itself as ileus or toxic megacolon. Severe *C. difficile* infection that is unresponsive to intravenous metronidazole therapy requires more aggressive medical management and even surgical intervention. We present our case results for which vancomycin was administered both orally and intra-colonically. With this method, we treated the community acquired *C. difficile* infection patient who was presented as ileus.

Keywords

Pseudomembranous colitis, ileus, intracolonic vancomycin

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Introduction

Clostridium difficile causes diarrhea and intestinal infection in individuals taking antibiotics.^{1,2} Severe *C. difficile* infection (CDI) that is unresponsive to intravenous (IV) metronidazole therapy requires more aggressive medical management and even surgical intervention.³ In all, 87% of pediatric CDI cases have only diarrhea, 9% have severe CDI, and 4% have complicated CDI (i.e. with toxic megacolon, ileus, intestinal perforation).⁴ Current practice guidelines recommend classification of CDI patients as mild, moderate, or severe for initial management.⁵

Case

Herein, we report the case of a 5-year-old boy who had non-bloody diarrhea unresponsive to oral and IV metronidazole treatment with *S. boulardii* probiotic supportment for 10 days before hospitalization. The stool CDI toxin antigen assay was negative for pre- and post-treatment with metronidazole. The patient had not used any antibiotic within the first 6 weeks of the diarrhea. After hospitalization, abdominal pain, fever, leukocytosis (white blood cell (WBC) count >15,000/nL) with ileus occurred (Figure 1). Urgent

decompressive colonoscopy revealed inflamed mucosa and deep yellow plaque like lesions in sigmoid and descending colon (Figure 2). Biopsy could not be obtained due to the risk of perforation. Stool cultures and analysis for rotavirus, *Staphylococcus*, *Shigella*, *Salmonella* and candida were negative. Intraluminal single dose vancomycin was sprinkled on colon wall during colonoscopy. The dose was adjusted according to the patient's weight: 1 g in 250 mL serum physiologic, single dose. Oral vancomycin 500 mg four times in a day was also started after the procedure. The patient did not need any additional post-procedure doses via rectal tube. The patient's clinical symptoms improved after oral and intracolonic vancomycin treatment on the procedure day, and 3 days later soft diet was started (Figure 3). Since it is not available in our country, preventive oral fidaxomicin

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Figure 1. Ileus with excessive colonic dilatation.

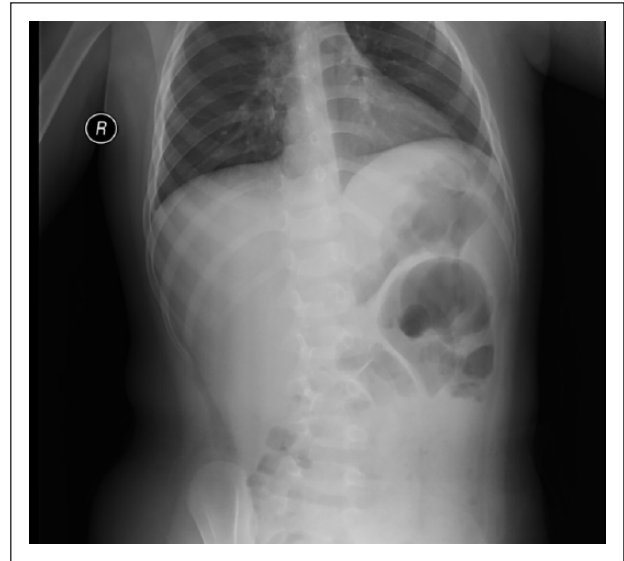


Figure 3. Ileus was improved after oral and intracolonic vancomycin treatment.

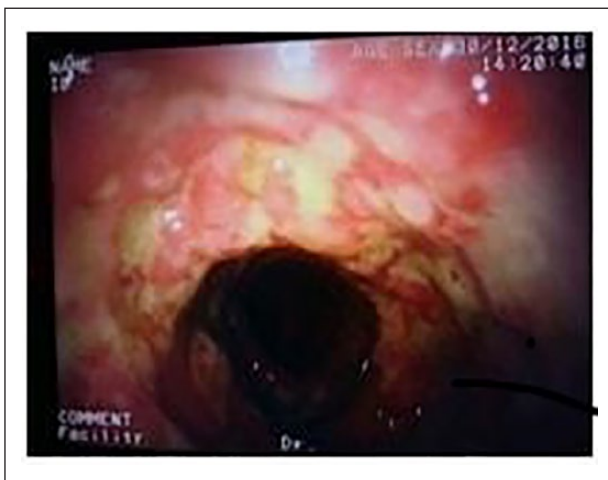


Figure 2. Inflamed mucosa and yellow plaque like lesions in flexible sigmoidoscopy.

could not be given, but CDI recurrence was not observed at 3-month follow-up.

Discussion

Frequency of CDI disease varies in pediatric patients.⁶⁻⁹ Although the correlation of CDI is highest with antibiotic usage, in one study, 24% of patients with CDI had no antibiotic exposure.¹⁰ Among these patients without any antibiotic exposure, 75% were either hospitalized or had close contact with a person with diarrheal illness. According to his history, the possible etiology of our patient's CDI was accepted as community-acquired. In the present studies, the sensitivity and specificity of CDI cytotoxin assay vary between 40%

and 100%.¹¹ Endoscopic diagnosis of CDI is usually preferred in special cases. The guidelines recommend endoscopy in the following situations: for rapid diagnosis, when the test result of toxin assay is delayed, or there is a negative toxin assay but CDI is suspected.¹² In cytotoxin negative CDI patients, multiple typical yellowish-white plaques (pseudomembranes) elevated above the surrounding mucosa are often detected at colonoscopic examination.^{12,13} Classification of pseudomembranous lesions can be made based on the degree and depth of inflammatory changes, with grading of lesions from focal surface epithelial inflammation to complete mucosal necrosis and significant inflammatory debris.¹⁴ Although CDI is the cause of most cases for pseudomembranous colitis, clinicians should also consider less common causes, especially if pseudomembranes are seen on endoscopy but testing remains negative for *C. difficile* or if presumed CDI does not respond to treatment. Histological review of colonic mucosal biopsy specimens can provide valuable signs to the underlying cause. However, in 22% of cases, pseudomembranes were visualized on endoscopy, but not assisted with histological and cytotoxin assays.¹² Urgent decompressive colonoscopy can provide a chance for diagnosis and treatment in severe CDI with pseudomembranous colitis (PMC).^{15,16} Gastroenterology guidelines¹⁷ recommend the option of oral and per rectum vancomycin plus IV metronidazole treatment for complicated CDI patients with ileus, toxic colon and significant abdominal distension. The vancomycin dosage is 500 mg orally 4 times per day and 500 mg in approximately 100 mL normal saline per rectum every 6 h as a retention enema.¹⁷ For patients with *C. difficile* colitis with ileus where oral drugs do not reach the colon, it is essential to recognize severe disease which does not respond to oral metronidazole

and vancomycin therapy. In such cases, the administration of vancomycin in an intra-colonic way is an important alternative option in order to prevent subtotal colectomy.^{18–20} If the intracolonic vancomycin treatment fails in severe CDI with PMC, and there are clinical signs of sepsis, organ dysfunction, or mental status changes, surgical treatments such as subtotal colectomy and end-ileostomy should be considered.^{12,13} Furthermore, colonoscopic vancomycin might be an excellent therapy in serious environments that lack access to safe surgery. Metronidazole is rapidly absorbed from the gastrointestinal tract and excreted through the biliary system, while only about 14% of the drug is excreted in the stool. Vancomycin and metronidazole have similar response rates in CDI treatment.¹² The European Society of Clinical Microbiology and Infectious Diseases²¹ and Infectious Diseases Society of America¹⁷ recommend one of these regimens for “severe, and/or complicated or refractory CDI”: IV metronidazole plus per rectum vancomycin or oral vancomycin plus per rectum vancomycin. Another suggested treatment for CDI is fecal microbiota transplantation (FMT)²² and fidaxomicin.¹² FMT represents the most promising candidate among non-antibiotic treatment options for patients having multiple relapses or recurrences.²³ Fidaxomicin which is classified as a macrolide antibiotic has activity against *C. difficile*, while having limited or no activity against normal fecal microflora. Fidaxomicin is minimally absorbed following oral administration and is excreted almost solely in the feces. Fidaxomicin therapy has significantly lower recurrence rate compared with vancomycin therapy.²⁴ Vancomycin given by both orally and intra-colonoscopically is a promising alternative in clinical cases with suspicion of CDI-associated PMC.²⁵

Conclusion

Oral and intra-colonoscopy vancomycin treatment presents a promising alternative in the presence of ileus. However, we need diagnostic strategies to differentiate patients who will benefit from this treatment. To our knowledge, this is the first reported case of a complicated pseudomembranous colitis in a child patient treated by intra-colonic and oral vancomycin therapy in the literature.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Our institution does not require ethical approval for reporting individual cases.

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Informed consent

Written informed consent was obtained from the patient’s legally authorized representative to publish in this article.

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