CASE REPORT – OPEN ACCESS

International Journal of Surgery Case Reports 42 (2018) 79–81

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.casereports.com

A case report of successful management of clostridium difficile colitis with antegrade Fidaxomicin through a mucous fistula obviating the need for subtotal colectomy

Suzanne Arnott[a], Matthew Skancke[b,*], Sheena Chen[b], Bruce Abell[b]

[a] George Washington University School of Medicine and Health Sciences, United States
[b] Department of General Surgery, George Washington University Hospital, United States

ARTICLE INFO

Article history:
Received 27 September 2017
Received in revised form
22 November 2017
Accepted 23 November 2017
Available online 27 November 2017

Keywords:
Fidaxomicin
Clostridium difficile colitis

ABSTRACT

INTRODUCTION: Clostridium difficile is the most common cause of healthcare-associated infections and can have devastating morbidity and mortality. Traditional treatment algorithms involve intravenous metronidazole and enteric metronidazole or vancomycin. Fidaxomicin (Dificid[R]) targets "switch regions" within RNA polymerases and effectively kills clostridium difficile bacteria and is typically administered orally primarily or through a naso/oro-gastric conduit.
PRESENTATION OF CASE: 55-year-old with a recent elective surgical procedure was hospitalized with multifocal pneumonia and subsequently developed clostridium difficile colitis. This patient failed the standard medical therapy for clostridium difficile colitis, decompensated and required surgical exploration, partial colectomy and mucous fistula creation. Following her surgery, her clinical condition improved and her colitis resolved with the antegrade administration of fidaxomicin through her mucous fistula.
DISCUSSION: Fidaxomicin is a newer to market therapeutic agent that has been shown to be effective in the treatment of clostridium difficile colitis. Previously studies have shown benefit of oral fidaxomicin therapy for fulminant clostridium difficile but our study case report describes the index case of topical fidaxomicin through a mucous fistula.
CONCLUSION: In our case of fulminant clostridium difficile colitis, Fidaxomicin administered in an antegrade fashion through a mucous fistula may have reduced the need for total colectomy in the treatment of fulminant clostridium difficile colitis.

1. Introduction

Clostridium difficile (CD) is the most common cause of healthcare-associated infections with over half a million cases in the United States each year [1]. Oral fidaxomicin (Dificid[R]) was approved by the FDA for the treatment of CD in 2011 and, in comparison to rectal vancomycin [2,3], it targets "switch regions" within bacterial RNA polymerases. Fidaxomicin has been shown to effectively neutralizes CD species producing symptomatic cure and reduced recurrence. We present a case of fulminant CD colitis following treatment for hospital acquired multifocal pneumonia ultimately requiring an exploratory laparotomy and segmental colectomy. Following segmental colectomy, the patient was successfully treated with 10 days of antegrade fidaxomicin administered through the mucus fistula with subsequent stool polymerase chain reaction (PCR) testing showing remission of disease. The work in this case has been reported in line with the SCARE criteria [4].

2. Case report

A 55-year-old woman with a past medical history of hypertension, diabetes mellitus, prior transient ischemic attacks, and chronic kidney disease was admitted to the ICU for altered mental status after being found minimally responsive at home four postoperative days following an elective panniculectomy. Her initial workup was significant for a multi-focal pneumonia with concomitant acute kidney injury requiring initiation of hemodialysis. She was initially started on broad spectrum gram positive (vancomycin) and gram negative (piperacillin-tazobactam) coverage but on hospital day ten developed new onset watery diarrhea. Stool PCR testing was positive for CD and the patient was started on intravenous metronidazole (500 mg IV every six hours) and oral vancomycin (250 mg every six hours). After six days and despite double ther-

* Corresponding author at: General Surgery Resident George Washington University Hospital 22nd & I Street, NW 6th Floor Suite 6B Washington, DC, United States
E-mail address: mdskancke@gwu.edu (M. Skancke).

https://doi.org/10.1016/j.ijscr.2017.11.042

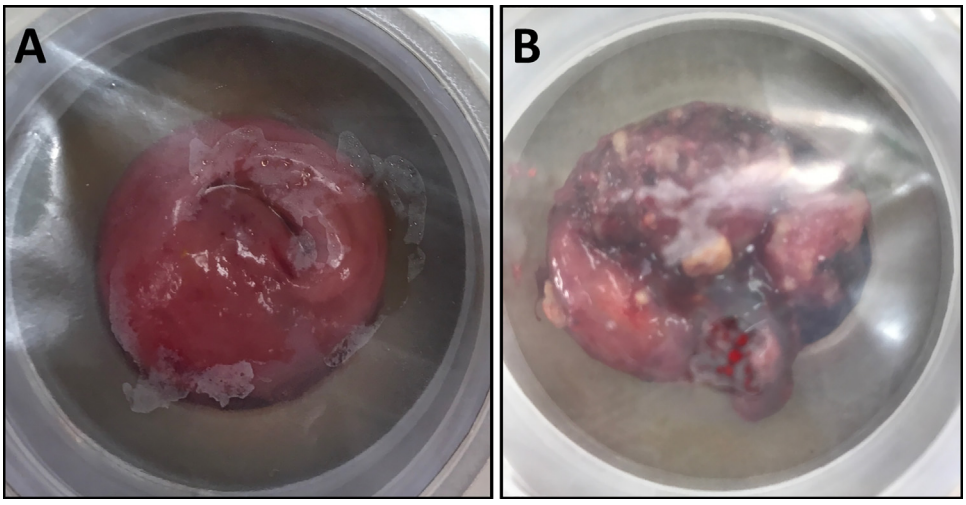

Fig. 1. Matured end ileostomy (A) and mucous fistula (B) following segmental right colectomy for fulminant clostridium difficile colitis. Note the presence of continued pseudomembranous disease on the mucous fistula prior to administration of antegrade fidaxomicin.

apy, the patient's disease progressed to fulminant CD colitis with advanced imaging showing pancolitis without evidence of megacolon or perforation. Rectal vancomycin (500 mg every six hours) and oral fidaxomicin (200 mg twice daily) were added however within two days the patient had decompensated, her leukocytosis had progressed to 54,000/ul, and she required multiple vasoactive medications to sustain a mean arterial pressure greater than 65 mmHg. The decision was made to proceed to the operating room for laparotomy and subtotal colectomy with an end ileostomy. The procedure was performed by a general surgeon with more than twenty years of experience with critical care surgery.

During laparotomy, the right colon appeared edematous with evidence of significant inflammation with a transition point to healthy appearing colon distal to the hepatic flexure. Similarly, the small bowel appeared healthy proximal to the ileocecal valve. The ascending colon and small bowel extending 10 cm proximal to the ileocecal valve were resected leaving the patient in enteric discontinuity. The abdomen was then irrigated and a temporary abdominal closure vacuum dressing was placed and the patient was taken back to the ICU for continued resuscitation. While in the operating room, the resected colon and small bowel were opened on the back table revealing a significant burden of pseudomembranous disease within the ascending colon. Postoperative pathological analysis of the resected colon and small bowel confirmed our clinical suspicions identifying acute enterocolitis with transmural inflammation and luminal pseudo-membrane formation.

The patient remained hemodynamically stable overnight and was taken back to the operating room the following day for re-evaluation of the abdomen and potential abdominal closure. On second look, the terminal ileum and transverse colon appeared healthy without progression of clinical colitis. The terminal ileum and transverse colon stumps were externalized and matured following successful primary fascia closure (Fig. 1). Following the second operation, the mucus fistula developed new pseudomembranes consistent with persistent colitis. Over ten days, crushed fidaxomicin (200 mg twice daily) was administered through the mucous fistula by a red-rubber catheter in an antegrade fashion. During the ten-day course of antegrade fidaxomicin, the clinical burden of pseudomembranous disease on the mucous fistula receded, hemodynamic lability improved, and the leukocytosis cleared. Upon completion of the ten-day course of antegrade fidaxomicin by mucous fistula, repeat stool CD PCR studies from the mucous fistula were negative for CD.

3. Discussion

Over the last decade, there has been a notable increase in the severity of CD infections in addition to the discovery of new virulent strains [5]. With the high incidence and increased severity, the literature has proposed multiple new agents and strategies for managing CD infections that have failed to improve with metronidazole and vancomycin treatment alone [6]. Fidaxomicin was approved by the FDA for the treatment of CD in 2011 after it was shown to be non-inferior to rectal vancomycin in two large randomized controlled trials [7,8]. While most of these initial patients only had mild to moderate illness, fidaxomicin has proven efficacy for symptomatic cure in addition to reducing disease recurrence compared to rectal vancomycin [3]. As a result, despite the higher cost of fidaxomicin, it has gained significant popularity for complicated CD infections [9].

Fidaxomicin is currently FDA approved for oral administration and has been demonstrated to have a 98–100% recovery when crushed and dispersed into various liquid vehicles [10]. Furthermore, multiple case reports have demonstrated successful medical management of severe CD colitis with crushed fidaxomicin through a nasogastric tube [11,12]. Since CD colitis is a toxin mediated disease, postoperative antibiotics are usually also recommended even in the cases of subtotal colectomy which should in theory provide mechanical source control [13]. Given the morbidity of a subtotal colectomy, there has recently been a push towards bowel sparing treatment regimens, most notably being loop ileostomy with intraoperative colonic lavage and 10 days of vancomycin antegrade washes [14].

While the initial administration of oral fidaxomicin in this case did not prevent the need for surgical intervention, it is possible that doses prior to surgery had not reached the affected colon secondary to the ileus from the patient's inflammatory state. Following segmental resection, topical administration of fidaxomicin was possible, bypassing any prior absorption or transit issues with oral administration. Topical application of fidaxomicin has rarely been described in patients with severe disease requiring bowel resection. One prior case in the Czech Republic was described by Longin et al. where topical fidaxomicin 200 mg in small volume enemas was started after the patient failed to improve with metronidazole and vancomycin for eleven days after bowel resection. This patient eventually tested negative for CD by NAAT amplification and had successful gastrointestinal tract restoration after five months [15].

In this case, our patient failed to improve with intravenous metronidazole and rectal vancomycin alone, prompting the addition of oral fidaxomicin as a third agent for CD treatment. However, when the patient became hypotensive and refractory to resuscitation, surgical intervention was required. After the creation of her end-ileostomy and mucus fistula, crushed fidaxomicin successfully supplemented enteric vancomycin resulting in symptomatic and bacteriologic cure. This case report demonstrates a new administration route for fidaxomicin through mucous fistula that may prove effective in curing fulminant CD colitis obviating the need for subtotal colectomy.

Conflicts of interest

We have no conflicts of interest for this manuscript.

Funding

We have no sources of funding for this research.

Ethical approval

The George Washington University IRB department does not require IRB approval for studies or analyses of less than 8 individuals. As this is a case report with one individual we believe this would be exempt from IRB approval provided that no identifying patient information is disclosed.

Consent

The George Washington University Operative Consent form stipulates that patients "Agree to the appropriate disposal of any tissue or part removed from my body, to the taking of photographs during the procedure/operative/treatment for research, teaching, or scientific purposes as long as my identity is not disclosed.Ẅritten informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Arnot, Suzanne – Manuscript production, study design, data analysis, patient care

Skancke, Matthew – Manuscript production, study design, data analysis, patient care

Chen, Sheena – Study design, patient care

Abell, Bruce – Manuscript production, study design, data analysis, patient care

Guarantor

Matthew Skancke and Bruce Abell

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