ORIGINAL PAPER
PŮVODNÍ PRÁCE

Clostridium difficile Colitis in Patients Undergoing Surgery for Adolescent Idiopathic Scoliosis

Kolitida způsobená *Clostridium difficile* u pacientů po operaci pro idiopatickou skoliózu

A. JURBAN, Y. ANEKSTEIN, Y. MORDISH, O. RABAU, Y. MIROVSKY, Y. SMORGICK

Department of Orthopedic Surgery and the Spine Unit and the Department of Pediatrics, Shamir (Assaf Harofeh) Medical Center, Zerifin, Israel, affiliated to the Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel

ABSTRACT

PURPOSE OF THE STUDY

To identify risk factors associated with developing *Clostridium difficile* infection (CDI) in adolescent idiopathic scoliosis patients after surgery and to describe the clinical presentation of CDI in these patients.

Clostridium difficile colitis is reportedly increasing in hospitalized patients and can have a negative impact on patient outcomes. No data exist on CDI rates and its consequences on patient undergoing surgery for adolescent idiopathic scoliosis.

MATERIAL AND METHODS

A retrospective database review of patients who underwent elective idiopathic scoliosis surgery between January 2019 to June 2021 was conducted. The population was divided into patients who developed *Clostridium difficile* colitis and those who did not.

RESULTS

A total of 128 patients were included in the study. We did not find notable risk factors for the development of CDI. In 2 patients diagnosis of CDI, was made. Length of hospital stays, and readmissions were significantly higher in patients with CDI.

CONCLUSIONS

CDI is a rare post-surgical complication in patients who undergo surgery for idiopathic scoliosis. Currently, we cannot identify predisposing factors for the development of CDI in adolescent idiopathic scoliosis patients.

A high index of suspicion is necessary for timely diagnosis and treatment in patients presenting with abdominal symptoms around post-operative day 5 after surgical treatment for idiopathic scoliosis.

Key words: *Clostridium difficile* infection, adolescent idiopathic scoliosis, abdominal pain, diarrhea.

INTRODUCTION

Clostridium difficile (CD) is a gram-positive anaerobic spore-forming microorganism. Although frequent in the microbiota of asymptomatic children (10), it can cause *Clostridium difficile* infection (CDI), a colitis resulting from disruption of normal gut flora, usually related to prior antibiotic use (8).

Orthopedic surgery has shown a strong association with CDI when compared to other surgical disciplines and rates of CDI have been shown to be highest in those undergoing spine interventions (33.8/1000 cases) (2, 6). Several studies have evaluated CDI in the context of spine surgery. The reported incidence of CDI in spine surgery ranges from 0.08% to 0.68% with association to increased hospital cost, length of stay, mortality, and readmission (1, 2, 5, 11). A study comparing surgical complication rates in the pediatric spine population as they are reported in institutional morbidity and mortality and National Surgical Quality Improvement Program found CDI as one of the most common under-reported complications (12). We were able to find only one case report describing CDI after surgery for adolescent idiopathic scoliosis (AIS) (9).

The aim of this study was to identify risk factors associated with developing CDI in AIS patients after surgery and to describe the clinical presentation of CDI in these patients.

MATERIAL AND METHODS

Patients

Following institutional review board (IRB) approval, a retrospective review of prospectively collected data from a single institution consecutive series of patients was undertaken. Due to the retrospective nature of the study, the need for informed consent was waived by the IRB.

Our study included 128 consecutive patients with AIS who underwent correction and fusion surgery between January 2019 to June 2021. There were 98 female patients and 30 male patients with a mean age of 15.6 years (range, 11 to 21 years) at the time of surgery. Patients' curves were classified according to the Lenke

Table 1. The demographic, clinical and surgical characteristics of patients with or without CDI

	Patients without CDI (n=126)	Patients with CDI (n=2)
Mean age (years)	15.6 ± 2.8	15 ± 2.8
Gender (male / female)	30 / 96	0 / 2
BMI (kg/m^2)	20.9 ± 4.5	18.1 ± 1.2
Level fused	11.43 ± 1.5	11
Estimated blood loss (ml)	960 ± 547	1100 ± 707
Duration of post-operative antibiotics	3.22 ± 0.4	3.5 ± 0.7
Length of stay	5.28 ± 0.9	9.5 ± 0.7
Readmissions	1	1

CDI – *Clostridium difficile* infection

classification system (7). Fifty-six were type 1, 21 type 2, 26 type 3, 4 type 4, and 21 type 6. Patient demographics are presented in Table 1.

The surgery was performed by two fellowship trained spine surgeons with more than 10 years' experience. The surgical technique was identical for all cases, including instrumented posterior spinal fusion with all pedicle screws double rod construct. Patients were enrolled into the study if instrumented posterior spinal fusion for late-onset juvenile or AIS was performed.

Patients were characterized as those with and without CDI diagnosed within 30 days of surgery. To establish positive CDI, we used an enzyme immunoassay and polymerase chain reaction (PCR). An enzyme immunoassay was performed on the stools, to detect simultaneously toxins A and B. To verify the diagnosis, CDI was tested in the stool by PCR. Infection was diagnosed when both PCR and toxins were present.

Patient demographics including age, gender, and body mass index (BMI; kg/m2) were compared between CDI patients and controls. We have documented estimated blood loss during surgery, type and duration of post-surgical antibiotic treatment, treatment with proton pump inhibitors (PPI), length of stay (LOS) and readmissions within 30 days. Index surgeries were further categorized by number of instrumented levels. Since the study population was young and healthy, comorbidities were not documented.

We have also documented the symptoms of patients with CDI, their duration, treatment, and response to treatment.

Statistical analysis

Statistical analysis was performed using SPSS software (version 20; SPSS, Chicago, IL, USA) with a 5% significance level.

We used comparisons of age, BMI, blood loss during surgery, duration of post-surgical antibiotic treatment, number of instrumented levels, and length of stay with t test between the infected and non-infected group. Chi-square (χ^2) test was used to evaluate differences in type of antibiotics, treatment with proton pump inhibitors (PPI), gender and readmissions with 30 days between the infected and non-infected group.

RESULTS

During the study period, 128 patients underwent instrumented posterior spinal fusion with all pedicle screws double rod construct. Among those, two cases were diagnosed with CDI (1.5%). The demographic, clinical and surgical characteristics of the 126 patients who did not have the CDI are described in Table 1.

We did not find a correlation between age, gender, blood loss during surgery, type and duration of post-surgical antibiotic treatment, treatment with PPI and CDI. However, length of hospital stays, and readmissions were significantly higher in patients with CDI.

Two patients, described below as patient A and patient B, developed symptoms on post-operative day 5 and diagnosis of CDI was made.

Patient A was a 17-year-old healthy adolescent, with no comorbidities, who underwent an uneventful posterior spinal fusion from T4 to L3 (Solera, Medtronic). We were able to correct her right thoracic curve from 56 degrees to 26 degrees. The patient received intravenous (IV) cefazolin 1 g intraoperatively and was prescribed cefazolin 1 g every 8 hours until the removal of her drainage on post-operative day 3.

On post-operative day 5 the patients developed spiking fever with temperature of 38.5 C, accompanied by nausea, vomiting and diarrhea. On her labs, the white blood cell (WBC) count was 18.400 cells/µl and the C-reactive protein (CRP) was 57.24 mg/l. Chest X-ray did not demonstrate any infiltrates or effusion and the urine analysis was normal. The surgical wound did not show any sign of infection throughout her post-operative course. Other causes of diarrhea like *Salmonella, Shigella, Campylobacter, Rotavirus* and *Adenovirus* were ruled out. The stool sample was positive for *Clostridium difficile* toxin, and PCR verified the diagnosis. She was then started on a regimen of oral vancomycin tablets, 125 mg every 6 hours.

On post-operative day 8 the diarrhea and her abdominal pain resolved. Repeat labs showed a WBC of 14.400 cells/µl. She was discharged home and continued to receive oral vancomycin for another 7 days, to a total of 10 days.

Two weeks later, the patient was readmitted because of fever, abdominal pain, diarrhea, and vomiting. Her labs showed a WBC of 18.400 cells/µl and an elevated CRP of 65.11 mg/l. She was restarted on oral vancomycin, leading to resolution of her diarrhea and abdominal pain on the second hospitalization day. The stool examination for *Clostridium difficile* toxin at this time was negative and the vancomycin treatment was stopped. The patient remained under supervision for another day and was later discharged. In the following year, there has not been recurrence of symptoms.

Patient B was a 13-year-old healthy girl, with no comorbidities, who underwent an uneventful posterior spinal fusion from T4 to L3 (Solera, Medtronic), during

which her right thoracic curve was corrected from 75 degrees to 30 degrees. The patient received IV cefazolin 1 g intraoperatively and was prescribed cefazolin 1gr every 8 hours until the removal of her drainage on post-operative day 4.

On post-operative day 1, she received a transfusion of 1 unit of packed red blood cells for a hemoglobin of 6.4 g/dl.

On post-operative day 5 the patient developed spiking fever with temperature of 39 °C, as well as abdominal pain and diarrhea. Her WBC count was 13.200 cells/μl and the CRP was 77.79 mg/l. Chest X-ray did not demonstrate any infiltrates or effusion and the urine analysis was normal. The surgical wound did not show any sign of infection throughout her post-operative course. Other causes of diarrhea like *Salmonella, Shigella, Campylobacter*, *Rotavirus* and *Adenovirus* were ruled out. The stool sample was positive for *Clostridium difficile* toxin, and PCR verified the diagnosis. Prompting oral treatment with vancomycin 125 mg every 6 hours. On post-operative day 8 the diarrhea stopped. On post-operative day 9 the patient was discharged home with oral vancomycin for a total of 10 days. In the following year there has not been recurrence of symptoms.

DISCUSSION

The incidence of CDI in patients undergoing elective spine surgery ranges from 0.11% to 0.68%, with lower incidence of infection reported in patients undergoing cervical spine surgery (0.08%) and lumbar spine surgery (0.11%) (1, 2, 5, 11). To date, CDI following surgery for idiopathic scoliosis has only been reported in one case report which included 2 patients (9). On the other hand, CDI is one of the most commonly under-reported complications in the pediatric spine population (12). The relatively high incidence of 1.5% found in our study is probably an overestimation of the true incidence, possibly related to the prolonged treatment with post-operative antibiotics and subject to selection bias.

We did not find a statistically significant correlation between any of the variables that were studied and the development of CDI. All cases in our study as well in the previous case reports were treated with prolonged antibiotic prophylaxis treatment after surgery, in contrast to the Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery, which recommends a single dose of cefazolin or another first-generation cephalosporin 1 hour prior to the surgical incision (3). This implies that a prolonged post-surgical antibiotic prophylaxis treatment may put patients at risk of developing CDI. Nevertheless, the pros and cons of prolonged post-operative antibiotic prophylaxis remains a controversial subject (11).

All patients in our study as well as cases of CDI after surgery for adolescent idiopathic scoliosis reported in the literature were diagnosed during post-operative hospitalization, usually between post-operative days 5 to 7 (9). However, 70% of CDI cases after spine surgery were diagnosed post-discharge (2). Our experience supports early diagnosis and treatment as central to the prevention a more invasive infection. We have also found that the detection of *Clostridium difficile* toxin is possible in early diagnosis and that treatment with oral vancomycin is effective (4).

Previous studies and the current results show post-operative CDI is significantly associated with extended hospital stay and readmissions (1, 2, 5,11). We have demonstrated that high level of suspicion for CDI leading to early diagnosis and treatment will result in prompt resolution of symptoms in our patient population.

The limitations of our study are its retrospective design, the relatively small cohort.

CONCLUSIONS

CDI is a rare post-surgical complication in patients who undergo surgery for idiopathic scoliosis. Currently, we cannot identify predisposing factors for the development of CDI in AIS patients.

A high index of suspicion is necessary for timely diagnosis and treatment in patients presenting with abdominal symptoms around post-operative day 5 after surgical treatment for idiopathic scoliosis.

The pros and cons of prolonged antibiotic prophylaxis should be considered in view of the risk for CDI.

References

1. Bell J, Vatani J, Raad M, Labaran L, Puvanesarajah V, Hassanzadeh H. Clostridium difficile Infection following spine surgery: incidence, risk factors, and association with preoperative antibiotic use. Spine (Phila Pa 1976). 2020;45:1572–1579. doi: 10.1097/BRS.0000000000003627. PMID: 32756273.
2. Bovonratwet P, Bohl DD, Russo GS, Ondeck NT, Singh K, Grauer JN. Incidence, risk factors, and impact of Clostridium difficile colitis after spine surgery: an analysis of a national database. Spine. 2018;43:861–868.
3. Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, Fish DN, Napolitano LM, Sawyer RG, Slain D, Steinberg JP, Weinstein RA; American Society of Health-System Pharmacists; Infectious Disease Society of America; Surgical Infection Society; Society for Healthcare Epidemiology of America. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm. 2013;70:195–283.
4. Crobach MJ, Planche T, Eckert C, Barbut F, Terveer EM, Dekkers OM, Wilcox MH, Kuijper EJ. European Society of Clinical Microbiology and Infectious Diseases: update of the diagnostic guidance document for Clostridium difficile infection. Clin Microbiol Infect. 2016;22(Suppl 4):S63–S81.
5. Guzman JZ, Skovrlj B, Rothenberg ES, Lu Y, McAnany S, Cho SK, Hecht AC, Qureshi SA. The burden of Clostridium difficile after cervical spine surgery. Global Spine J. 2016;6:314–321.
6. Kim DY, Lee Y-M, Kim YJ, Lee M, Lee HJ, Park KH. Prevalence, risk factors, and outcome of postoperative Clostridium difficile infection after orthopedic surgery. Open Forum Infect Dis. 2018;5(Suppl 1):S176.
7. Lenke LG, Betz RR, Harms J, Bridwell KH, Clements DH, Lowe TG, Blanke K. Adolescent idiopathic scoliosis: a new classification to determine extent of spinal arthrodesis. J Bone Joint Surg Am. 2001;83-A:1169–1181.
8. McDonald LC, Gerding DN, Johnson S, Bakken JS, Carroll KC, Coffin SE, Dubberke ER, Garey KW, Gould CV, Kelly C, Loo V, Shaklee Sammons J, Sandora TJ, Wilcox MH. Clinical practice guidelines for Clostridium difficile infection in adults and children: 2017 update by the Infectious Diseases Society of America

(IDSA) and Society for Healthcare Epidemiology of America (SHEA). Clin Infect Dis. 2018;66:e1–48.
9. Osebold WR, Cohen AN, Gillum MD, Hurley JH, Locher NJ. Postoperative Clostridium difficile pseudomembranous colitis in idiopathic scoliosis. A brief clinical report. Spine (Phila Pa 1976). 1993;18:2549–2552. doi: 10.1097/00007632-199312000-00031.
10. Sammons JS, Toltzis P, Zaoutis TE. Clostridium difficile infection in children. JAMA Pediatr. 2013;167:567–573.
11. Skovrlj B, Guzman JZ, Silvestre J, Al Maaieh M, Qureshi SA. Clostridium difficile colitis in patients undergoing lumbar spine surgery. Spine. 2014;39: E1167–1173.
12. Welling SE, Katz CB, Goldberg MJ, Bauer JM. NSQIP versus institutional morbidity and mortality conference: complementary complication reporting in pediatric spine fusion. Spine Deform. 2021;9:113–118. doi: 10.1007/s43390-020-00197-z. Epub 2020.

Corresponding author:
Yossi Smorgick, MD
The Spine Unit, Shamir (Assaf Harofeh) Medical Center
Zerifin 70300, Israel
E-mail: ysmorgick@gmail.com