



# ***Clostridium difficile* infection occurred after radical hysterectomy for cervical cancer—a case report**

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**Background:** *Clostridium difficile* infection (CDI) is a global health challenge. In recent years, the incidence of CDI is increasing rapidly. *Clostridium difficile* (*C. difficile*) is now a common cause of nosocomial infection. Surgery is a known risk factor for the development of CDI. However, the rate of CDI that occurred after Gynecological surgeries has been reported significantly less.

**Case Description:** We presented a case of a 44-year-old woman with FIGO stage IB1 invasive cervical cancer who suffered from high fever, chills and severe diarrhea after receiving laparoscopic radical hysterectomy with bilateral salpingectomy and pelvic lymph node dissection. The symptoms of surgical complications and bowel diseases overlap with those of patients in the case.

**Conclusions:** CDI in gynecological surgery patients is often misdiagnosed and ignored due to the absence of prominent symptoms and signs, as well as the low rate of positive examination results. Therefore, it is necessary for early confirmation and treatment of CDI. PCR and two-step algorithm (GDH detection followed by nucleic acid amplification test) have been reported to be the rapid and accurate laboratory examination for the diagnosis of CDI. Owing to the rare property of this disease, we present this case to underscore the importance of early diagnosis and intervention for CDI after gynecological surgeries.

**Keywords:** *Clostridium difficile* infection (CDI); gynecological surgery; bowel injury; inflammatory bowel disease (IBD); case report

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## **Introduction**

*Clostridium difficile* (*C. difficile*), an anaerobic gram-positive bacillus, was detected in feces specimens of healthy infants for the first time in 1935 (1). *Clostridium difficile* infection (CDI) causes increasing life-threatening incidence worldwide, with the postoperative CDI being a common nosocomial infection (2). Reports have associated the development of CDI in surgical patients with multivariable factors including prophylactic antibiotics, older age, chronic immunosuppression, hypoalbuminemia ( $\leq 3.5$  g/dL) and so on. Compared with other surgeries, the occurrence of CDI after

Gynecological operations has the lowest rate (0.1%), more insights are needed regarding the clinical significance of this disease (3,4). Herein we present a rare case of patient who developed CDI after laparoscopic radical hysterectomy for cervical cancer. We present the following article in accordance with the CARE reporting checklist (available at <https://gpm.amegroups.com/article/view/10.21037/gpm-20-24/rc>) (5).

## **Case presentation**

A 44-year-old woman with FIGO IB1 stage invasive

carcinoma of the uterine cervix underwent laparoscopic radical hysterectomy (radical hysterectomy with bilateral salpingectomy and pelvic lymph node dissection). The operation was uneventful. She received Cefmetazole (1,000 mg q8h) in the course of perioperative management and regular cervical cancer aftercare in the hospital. On postoperative day 2, she developed a fever and lasted for 6 days. The use of antibiotic was replaced with Cefoperazone Sodium/Tazobactam Sodium (2,000 mg q8h) during medical treatment. On postoperative day 9 her vital signs were normal and she was tolerating a regular diet. She was discharged subsequently.

Sixteen days later, she was admitted to the emergency department with a high fever and chills that had started 5+ hours earlier, but she had no other specific symptoms. Laboratory examination revealed a white blood cell of  $18.2 \times 10^9/L$  and a serum albumin of 28.6 g/L. Urine cultures were positive, while blood cultures were negative. Intravenous Piperacillin Sodium/Tazobactam Sodium (4,500 mg q8h) and rehydration were administered empirically. Approximately 9 hours after being transferred to intensive care unit (ICU), the patient appeared septic shock with nausea, vomiting and diarrhea. Physical examination found mild distended abdomen with hypoactive bowel sounds, rebound tenderness was also present in lower quadrant. A computed tomographic (CT) scan of the chest, abdomen and pelvis showed the following findings: dilated and edematous colons, a small amount of free fluid without air, lymphocele, and there's no signs of peritonitis and pneumonia. An abdominal ultrasound examination showed that the thickness of colon wall was 0.8 cm. Stool and urine cultures were negative. As the source of infection was unsuspected, empirical therapy was performed. The patient received dieting, gastrointestinal decompression, fluid resuscitation, and a series of supportive therapies. After she was given antibiotic and supportive treatment for 5 consecutive days, her vital signs were stable without notable symptoms and she started to eat liquid food.

However, on the 11th day after the patient presented to the hospital, she reoccurred worsening diarrhea (>5 in 24 h) and stool culture revealed moderate dysbiosis. She was unresponsive to probiotic products and antidiarrheal drugs. Due to a sudden onset of high fever (>39.5 °C), chills, septic shock and her severe abdominal distension and pain on the 17th day following admission, blood, urine and stool cultures were collected. Laboratory examination showed a white blood cell of  $33.8 \times 10^9/L$  and a serum albumin of 21.5 g/L. Urine culture and blood cultures were

negative. Enzyme immunoassays (EIA) for both toxin A/B and glutamate dehydrogenase (GDH) of stool cultures were positive for *C. difficile*. Oral Vancomycin (400 mg qd) and intravenous Meropenem (1,000 mg q8h) were started. On the 31th day her vital signs were normal, but she still complained of diarrhea (>5 in 24 h). Thus, therapy of antibiotics was switched to Vancomycin (400 mg qd) orally and Piperacillin Sodium/Tazobactam Sodium (4,500 mg q8h) intravenously. The patient recovered on the 49th day, she was taking regular food and normalizing stool form. Due to her gut microbiota dysbiosis, she had to keep receiving probiotic products after discharged.

All procedures performed in the case involving human participants were in accordance with the ethical standards of the institutional and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient.

## Discussion

In this case report, we described a female after radical hysterectomy for cervical cancer who presented with high fever, chills and severe diarrhea proved to be associated with CDI. Due to the lack of typical clinical manifestation and rare occurrence of CDI after gynecologic surgeries, differential diagnosis is of important value for early identification and implementation.

Empirically, the common short-term (<30 days) surgical complications which develop in women after radical hysterectomy for cervical cancer include urinary tract infection with catheterization, chronic pulmonary disease, vascular disease and lymphedema. Main symptoms of these postoperative complications include high fever, abnormal laboratory and auxiliary examination results, which are similar to unspecific symptoms of CDI. Therefore, it is difficult to distinguish between them. Diarrhea, as a prominent symptom of CDI, may be absent initially, due to the disturbance of colonic motility caused by either cervical cancer itself or previous underlying conditions (6). Besides, it is noted that abnormally high WBC counts and decreased serum albumin of the case were inconsistent with the common infection. Thus, CDI should be considered in patients with severe infection when diarrhea occurs.

The extensive scope of radical hysterectomy places patients at risk of bowel injury intraoperatively. The most frequent damaged region of bowel injury in Gynecological surgeries is the small intestine. Peritonitis, abdominal pain, fever, and abdominal distension are the most frequent

symptoms presented in patients with intestinal injury (7), which overlap the symptoms of patient in this case. As pneumoperitoneum is rare in small intestine injuries, the sensitivity and specificity of imaging methods are low. The same is true for colon and rectum with pinhole-size perforation, which diagnosis is frequently delayed by late-onset clinical manifestations. Although bowel injury may be excluded by abdominal exploration and endoscopy, these are not optimal ways for patients with unclear surgical indications. Besides, it might impose great risks on patients especially with signs of infections. Observations and other managements might be the best options for patients who are similar to this case.

Risk factors for the development of inflammatory bowel disease (IBD) include prior antibiotic use and dysbiosis. Main clinical symptoms of severe Crohn's disease (CD) are fever, diarrhea, vomiting and abdominal pain. CT or Ultrasound results of CD show increased bowel wall thickness and enlarged lymph nodes (8). Similar changes can be observed in cases of CDI, thus, it is hard to differentiate the CDI from IBD. In addition, CDI in patient with IBD may be asymptomatic, and even microscopic abnormalities can be indistinguishable (9). We suggest that the diagnosis and treatment of IBD could be made until CDI is excluded.

A precise diagnosis of CDI is based on a positive laboratory examination. EIA for toxin A/B is a fast, convenient, inexpensive but too insensitive laboratory test. GDH is a screening test, which is sensitive compared with EIA for toxin A/B. PCR and two-step algorithm (GDH detection followed by nucleic acid amplification test) are reported to be the rapid and accurate diagnosis of CDI (10). Though EIA for toxin A/B implemented in relation to GDH indicates a quick test with high accuracy, the sensitive of this method is still lower than PCR and two-step algorithm (11). To determine an optimal test is necessary for early confirmation and treatment of CDI.

In conclusion, as the difficulty in differentiation between CDI and many other diseases overlap, the diagnosis of CDI in Gynecological surgery patients requires a high index of suspicion. PCR or a two-step algorithm performed in postoperative patients with severe diarrhea and related risk factors is essential to confirm and exclude the diagnose of CDI.

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## Footnote

*Reporting Checklist:* The authors have completed the CARE reporting checklist. Available at <https://gpm.amegroups.com/article/view/10.21037/gpm-20-24/rc>

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Informed consent was obtained from the patient. All procedures performed in the case involving human participants were in accordance with the ethical standards of the institutional and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient.

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