

Toxic Megacolon – the Complication of an Infection with *Clostridium difficile* after an Odontogenic Abscess. Case Presentation

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ABSTRACT

Background: *Clostridium difficile* (CD) is the major cause of nosocomial antibiotic-associated infections, having as main manifestation diarrhea and life-threatening inflammation of the colon. Surgery may be necessary in up to 80% of patients due to the frequent complications associated with this condition. The mortality rate of this devastating disease could reach 50% even after proper treatment. **Case report:** We report a case of a 24-year-old female who was admitted with clinical signs of an odontal inflammatory process. After repeated surgical treatments and antibiotic therapy, she presented acute abdominal pain on the 14th postoperative day. The explorative laparotomy was negative. *Clostridium difficile* was isolated from her stool, and she was transferred to the Department of Infectious Diseases. After a few days without any favorable clinical outcome, she was transferred to the intensive care unit (ICU), where she developed acute respiratory distress syndrome. Despite the immediate surgical intervention and ICU care, she died within 15 days after admission. **Conclusions:** CD infection is considered a complication of antibiotic treatment, having as main cause the combination of fluoroquinolones with antiseptics. In the first phase, the changes of the colon can be minimal with the manifestation of a false acute surgical abdomen, but toxic colon can develop in evolution, leading to multi-system organ failure and death.

Keywords: *Clostridium difficile*, toxic megacolon, odontogenic abscess

INTRODUCTION

Clostridium difficile (CD) is a Gram-positive, strictly anaerobic spore-forming bacterium, which appears in the normal gastrointestinal flora in 1–3% of healthy adults and in 75% of children <12 months. It produces toxins A and B, which determine intestinal mucosal lesions. Toxin A produces blockage of intestinal fluid absorption and albumin secretion, whereas toxin B produces necrosis and accelerates intestinal transit.¹ CD is the most common cause of nosocomial diarrhea associated with antibiotic treatment through the alteration of colic microflora, and its survival in the hospital environment reaches up to 6 months.²

The source of CD infection is represented by the enormous amounts of *Clostridium* eliminated with stool, with the infection dose <10 spores. In contact

with air the bacteria turn into spores, which are found in a large number in the hospital environment.³

Among the risk factors for CD infection are age over 65, prolonged hospitalization and antibiotic therapy, immunosuppression, gastrointestinal surgery, treatment with proton pump inhibitors or H2-type antihistamines, and drastic diets. Antibiotics alter the balance of intestinal flora, destroying the normal flora and causing proliferation and colonization of the intestine with CD.^{4,5}

The clinical appearance of CD infection includes asymptomatic carriers, mild forms with moderate diarrhea, or pseudomembranous colitis which may be fatal.^{3,6} The average time between exposure and the occurrence of symptoms is about 2–3 days. Typical symptoms are watery diarrhea (15–20/day), often with blood and mucus, colicky abdominal pain of varying degrees of intensity, sometimes persistent and progressive pain, vomiting, fever, inappetence, meteorism, oligo-anuria, signs of intestinal occlusion or peritonitis.

Laboratory diagnosis is based on leukocytosis, hypoalbuminemia (<2.5 g/dL), increased serum creatinine, high serum lactate and procalcitonin, positive hemoculture, and presence of toxins in the patient's stool. The positive diagnosis is based on clinical, radiological, and laboratory test results.^{6,7}

The treatment consists in monitoring the stools and vital functions, hydro-electrolytic and acid-base re-equilibration, correction of hypoproteinemia, correction of organ failure, and antibiotic treatment. Antibiotic treatment consists in metronidazole 500 mg (every 8 hours for approximately 10 days in lighter forms), vancomycin 125 mg (every 6 hours for 10–14 days in severe infection or metronidazole failure, vancomycin in combination with metronidazole in toxic megacolon), or vancomycin enema. Surgical treatment should be considered when abdominal pain advocates an evolution toward surgical complications, perforation of the colon with progression to peritonitis, severe ileus with dehydration and shock, toxic megacolon with massive intestinal destruction, clinical signs of sepsis and organ dysfunction (renal and lung). In these cases, the surgical treatment consists in total or subtotal colectomy with ileostomy.⁸

CASE PRESENTATION

A 24-year-old female patient from a rural area presented urgently at a city hospital complaining of erythema, swelling, and pain in the left cheek, edema and palpebral cellulitis, fever, loss of appetite, the patient being unable to eat due to inability to open the mouth and masticate.

After the clinical and paraclinical investigations, her doctors established the diagnosis of odontogenic abscess, with possible bilateral jaw and left mandibular location, septic status (leukocyte count $15,000/\mu\text{L}$, neutrophil count $12,800/\mu\text{L}$, erythrocyte sedimentation rate 53), and acute dehydration syndrome.

Surgery was performed under general inhalation anesthesia, performing the incision of mandibular abscess with evacuation, lavage, and drainage. Postoperatively, hydro-electrolytic equilibration treatment was administered. *Proteus mirabilis* was isolated from the cultivation of bacteria, and antibiotic treatment (fluoroquinolones) was administered according to the antibiogram.

The postoperative outcome was favorable with reduction of local inflammatory phenomena, and the resumption of oral food intake. Subsequently, the patient presented a reheating of the infection, fever, and chills. Computed tomography (cerebral + cervical column) described a periapical cystic lesion with dimensions of approximately 6×7 mm, located near the mandibular nerve channel, without boundary to it; the lesion showed communication with the vestibular cavity in the mandibular cortex through a solution of continuity of about 3–4 mm diameter.

Surgery was performed in general anesthesia by incision, lavage, and drainage of the lesion. The subsequent progression was favorable, and the patient was discharged in a relatively good overall state, with no fever and preserved appetite, showing surgical healing with an open facial wound and no signs of infection at the cavity of the abscess.

After 22 days, she referred to another hospital in emergency condition with the symptoms of acute surgical abdomen, diffuse abdominal pain, and intestinal transit disorders. Abdominal ultrasound revealed intraabdominal free fluid and left parauterine lesion, while abdominal radiography showed air-fluid levels. Immediate exploratory laparotomy was performed, highlighting ascites fluid, normal-sized thin intestine, normal-looking parenchymatic organs, and a thickened, edematous colon, without signs of ischemia.

Gastroenterological consult was required, followed by rectosigmoidoscopy, which established the diagnosis of pseudomembranous colitis. HIV and VDRL tests, and quick test for the determination of *Clostridium* Toxin A and B were all negative. However, as the postoperative evolution did not show any sign of improvement, the *Clostridium* quick tests for both A and B toxins were repeated, and this time they were positive.

The patient was transferred to the Department of Infectious Diseases, where antibiotic treatment with metronidazole and vancomycin was initiated. However, as



FIGURE 1. Computed tomography in the case of toxic megacolon caused by *Clostridium difficile* infection. **A** – thoracic computed tomography showing left pleural effusion; **B** – Abdominal computed tomography showing ascites and distension of the colon; **C** – Abdominal computed tomography with the aspect of megacolon in vertical plan

the evolution was stationary (persistent abdominal pain, meteorism), she was transferred to the Department of Surgery of the Mureș County Hospital, and then to the Intensive Care Unit in an altered general status, with no fever, conscious, cooperative, hemodynamically and respiratory stable. Antibiotic treatment was continued with vancomycin 4×250 mg + metronidazole 3×500 mg, in association with albumin and Kabiven for hypoproteinemia.

A day later, the thoracic radiography showed a homogeneous opacity located in the basal third of the left pulmonary field, associating deletion of the left diaphragmatic outline, highly suggestive of a basal pulmonary condensation area. Therefore, drainage of the left hemithorax was performed.

After another 6 days, the patient's status became altered, developing fever (37.8°C), dyspnea, desaturation

(SpO_2 82% without O_2 , 91% with O_2 8 L/min on facial mask). Emergency surgery was decided due to acute respiratory insufficiency (toxic megacolon with diaphragm compression, pneumonia, and toxic septic shock). The tomographic aspect of toxic megacolon is represented in Figure 1. The evolution of leukocyte levels is presented in Figure 2. Subtotal colectomy with terminal ileostomy was performed, and the operatory specimen is presented in Figure 3. The postoperative thoracic radiography showed bronchopneumonia in both pulmonary fields with merging tendency in the right perihilar, right infrahilar, and left basal segments (Figure 4). Emergency tracheostomy was performed due to the impossibility of mechanical ventilation.

In spite of the complex therapeutic procedures performed, the patient died on the 8th postoperative day due

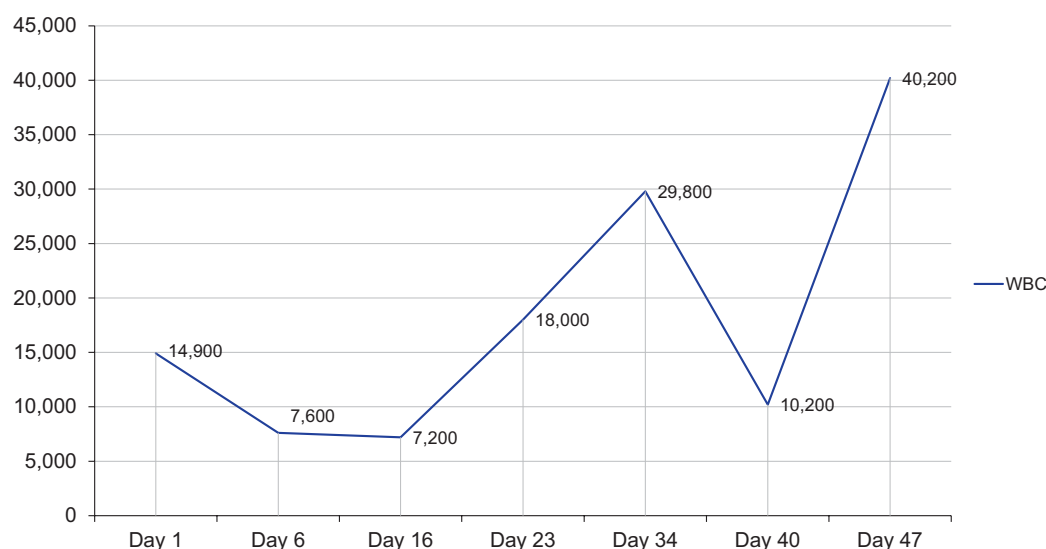


FIGURE 2. Evolution of leukocyte count during the progression of the disease



FIGURE 3. Operatory specimen after subtotal colectomy

to acute respiratory distress syndrome (ARDS) and multi-system organ failure (MSOF).

The patient's relatives and the institution agreed to the publication of the data, and the manuscript was written according to the ethical principles stated in the Declaration of Helsinki.

DISCUSSION

During the past two decades, CD infection has evolved from a relatively uncommon hospital-acquired infection to a major cause of morbidity and in-hospital or out-of-hospital mortality.⁹

Advanced age is a known risk factor for poor outcomes of colitis, including CD infection.¹⁰ However, a recent study has shown a high rate of CD among young adults presenting with diarrhea at two hospitals in Kenya.¹¹

Mortality associated with CD infection is high worldwide, particularly in elderly patients who present frequent comorbid conditions.¹² In the United States, a study based on the collection of multiple cause-of-death mortality data indicated a significant increase in the estimated number of deaths attributed to CD, from 3,000 deaths per year between 1999 and 2000 to 14,000 between 2006 and 2007, with nearly 90% of deaths occurring in patients aged ≥ 65 years.¹³



FIGURE 4. Chest radiography showing bilateral pulmonary consolidation

Regarding the antibiotic treatment, metronidazole hydrochloride has historically been considered first-line therapy for patients with mild to moderate CD infection, but is currently inferior to vancomycin hydrochloride.¹⁴ New studies show that fidaxomicin and fecal microbiota transplants can offer promising results in severe CD colitis.¹⁵

In cases of toxic megacolon, a systematic review published in 2012 supports total colectomy with end ileostomy as the primary surgical treatment for patients with severe CD infection; other surgical procedures are associated with high rates of reoperation and mortality.¹⁶

More recently, Kaiser *et al.* concluded that the involvement of a surgical team can bring significant benefits for the most severe forms with toxic colitis. Swift open total abdominal colectomy with end ileostomy in patients with severe or fulminant CD colitis has the best chance to reduce mortality if it is not delayed and can be performed before the development of shock, end organ damage, vaso-pressor requirement, or alteration of mental status.¹⁷

In an article published in 2017, Ferrada *et al.* compare loop ileostomy with total colectomy as surgical treatment for CD-associated diseases and affirm that loop ileostomy is associated with lower mortality than total colectomy.¹⁸

In order to evaluate the risk of mortality after colectomy from fulminant CD infection, there are several risk calculators available using preoperative variables, which can be useful in preoperative decision making.¹⁹

Our patient was a young adult, who developed the CD infection as a complication of postoperative antibiotic treatment, probably resulting from the association of fluoroquinolones with gastric antisecretory drugs. In this case, there were no other comorbidities or risk factors present (such as age, HIV, tuberculosis, neoplasms, immunosuppression) that could have influenced the severity of CD infection.

CONCLUSION

Based on clinical outcomes, this case illustrates with high clarity the role of complex diagnosis in the interpretation of CD infection and its complications.

Although initially the quick tests for toxins A and B were negative, they did not indicate the absence of infection or disease progression. Although rapid tests for A and B toxins based on enzyme immunoassay are widely used for the diagnosis of CD infection, they have suboptimal sensitivity and more false negative results compared with real-time polymerase chain reactions.

In the first phase, changes in the colon, sometimes associated with negative CD tests, may be minimal, with the manifestation of a fake acute surgical abdomen; however, with the appearance of toxic colon, the development can be complicated by ARDS and MSOF, as in our case.

Despite the younger age of the patient, restraining the surgeon as the first step in achieving subtotal colectomy is unjustified even in the absence of obvious macroscopic changes in the colon.

This case shows that even after using all the available resources, the evolution of CD infection can be lethal and when ARDS is installed the survival is not improved by radical surgery or subtotal colectomy.

CONFLICT OF INTEREST

The authors declare no conflict of interests.

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