



# Severe Diverticulitis Associated to *Clostridioides difficile* Infection in a 91 Year Old Patient (Clinical Case)

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**Aim.** To present a clinical case of a 91-year-old patient with a severe course of diverticulitis combined with the development of *Clostridioides difficile*-associated disease.

**Key points.** On admission the patient complained of pain in the left iliac region, increased body temperature, constipation and bloating. The medical history showed that constipation increased on the background of prolonged bed rest and discontinuation of psyllium. According to the laboratory and instrumental examinations, the patient had signs of acute diverticulitis, antibacterial therapy was corrected twice, positive dynamics of the condition was noted. However, a few days later, the patient developed a clinic of *C. difficile*-associated disease, which required the prescription of anticlostridial therapy (vancomycin), until the laboratory confirmation of the accession of this infection was obtained. Combined therapy of exacerbation of diverticular disease and *C. difficile*-associated disease made it possible to achieve a steady improvement of the condition.

**Conclusion.** The exclusion of possible development of *C. difficile*-associated disease on the background or prior antibiotic therapy is an important condition for correct and adequate management of a patient with exacerbation of diverticular disease. If the patient develops a clinical picture of *C. difficile*-associated disease, treatment may be initiated before laboratory confirmation.

**Keywords:** diverticular disease, *Clostridioides* associated disease, abdominal computed tomography

**Conflict of interest:** the authors declare no conflict of interest.

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## Тяжелое течение дивертикулита в сочетании с *Clostridioides difficile*-ассоциированной болезнью у пациентки 91 года

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**Цель.** Представить клиническое наблюдение пациентки 91 года с тяжелым течением дивертикулита в сочетании с развитием *Clostridioides difficile*-ассоциированной болезни.

**Основные положения.** При поступлении пациентка предъявляла жалобы на боль в левой подвздошной области, повышение температуры тела, запор и вздутие живота. Из анамнеза известно, что запор усугубился на фоне длительного постельного режима и прекращения приема препаратов псиллиума. По данным лабораторных и инструментальных исследований у пациентки признаки острого дивертикулита. Антибактериальная терапия была дважды скорректирована, отмечена положительная динамика состояния. Однако спустя несколько суток у пациентки развилась клиника *C. difficile*-ассоциированной болезни, что потребовало назначения ванкомицина еще до получения лабораторного подтверждения присоединения данной инфекции. Комбинированная терапия обострения дивертикулярной болезни и инфекции *C. difficile* позволила достигнуть стойкого улучшения состояния.

**Заключение.** Исключение возможного развития *C. difficile*-ассоциированной болезни на фоне антибиотикотерапии или после предшествующего назначения антибиотиков выступает важным условием правильного и адекватного ведения пациента с обострением дивертикулярной болезни. В случае развития у пациента клинической картины *C. difficile*-ассоциированной болезни лечение может быть начато до получения лабораторного подтверждения.

**Ключевые слова:** дивертикулярная болезнь, *Clostridioides difficile*, *C. difficile*-ассоциированная болезнь, компьютерная томография брюшной полости

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Diverticular disease (DD) has become one of the most prevalent digestive diseases in the last decade. The surgery rate for DD in the Western Europe and the USA has doubled in recent years [1]. Development of diverticula is promoted by increased intraluminal pressure along with impaired resistance of intestinal wall. Elevated intra-intestinal pressure results in intestinal mucosal prolapse. Along with age-related changes in intestinal architecture, impaired intestinal resistance may result of increased amount of food of animal origin in the daily diet that enhance proportion of 3<sup>rd</sup> type collagen in intestinal connective tissue on the background of genetic defects like Marfan syndrome or Ehlers — Danlos syndrome [2, 3].

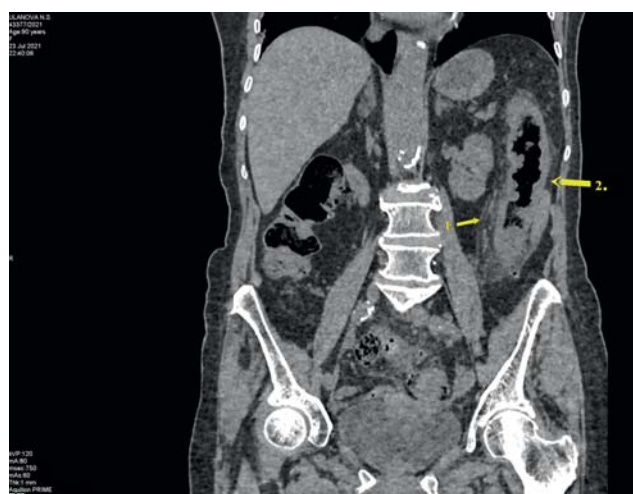
Long term intake of non-steroid anti-inflammatory drugs (NSAIDs) that is common in elderly patients is regarded to be another risk factor [4]. DD frequency is significantly more prevalent in the old age groups (less than 5 % in patients under 40 years old, while the prevalence in patients after 80 years of age is around 60–65 %). On the other hand,

elder age in hospital conditions, severe relapses of DD, along with steel lifestyle and constipation, frequent use of antibiotics may result in development of *C. difficile*-associated disease. Older age, long time hospital stay, history of antibiotic treatment act as a proven etiological factors for *C. difficile* disease [5].

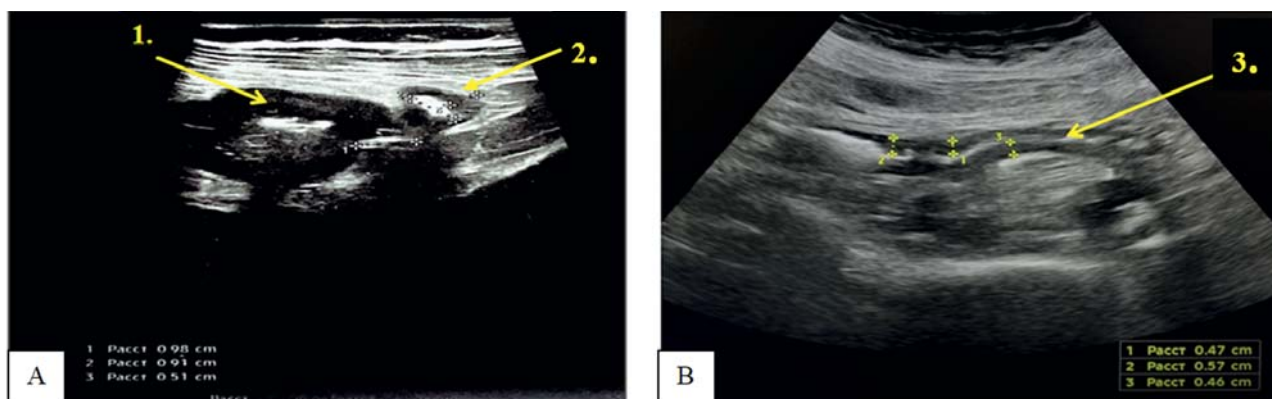
**Patient U**, female, 91 years old, admitted to the Vasilenko Clinic of Internal Diseases Propedeutics, Gastroenterology and Hepatology complaining of intensive boring left iliac pain without irradiation that relieved after bowel movements (7 to 8 points according to the visual analog scale). Patient had a fever up to 38 °C without rigors mostly in the evening time, constipation for up to 5 days, flatulence and general weakness. The patient had a history of long time constipation, self-treated by psillium 10 g per day, was subject to no medical examination. In July 2021 a patient developed a traumatic fracture of L1 vertebra that was diagnosed by MRI of the spine. Patient was at the bed rest for 3 weeks, received NSAID along with proton-pump inhibitors (PPIs), followed by physical-therapy course in rehabilitation hospital where patient noted progression of constipation after 3 days of staying and flatulence.

Since the development of spine trauma patient stopped taking soluble plant fiber and had minimal physical activity. Body temperature was normal as did the serological tests, however on the 3<sup>rd</sup> day of hospital stay, severe iliac pain developed associated to fever of 38 degrees, blood test demonstrated increase of white blood cell count up to  $17 \times 10^9/l$  and elevation of CRP up to 117 mg/l. Abdominal CT (Fig. 1) showed multiple colonic diverticula up to 10 mm in size in all parts of the large intestine with mild exudation along the descending colon, increase in density and edema of paracolic fat tissue, thickening up to 12 mm and edema of the left side of the colon. Sigmoid colon demonstrated impaired layer pattern, the lumen was not visible.

Then the patient was referred to the Vasilenko Clinic of Internal Diseases Propedeutics, Gastroenterology and Hepatology for further

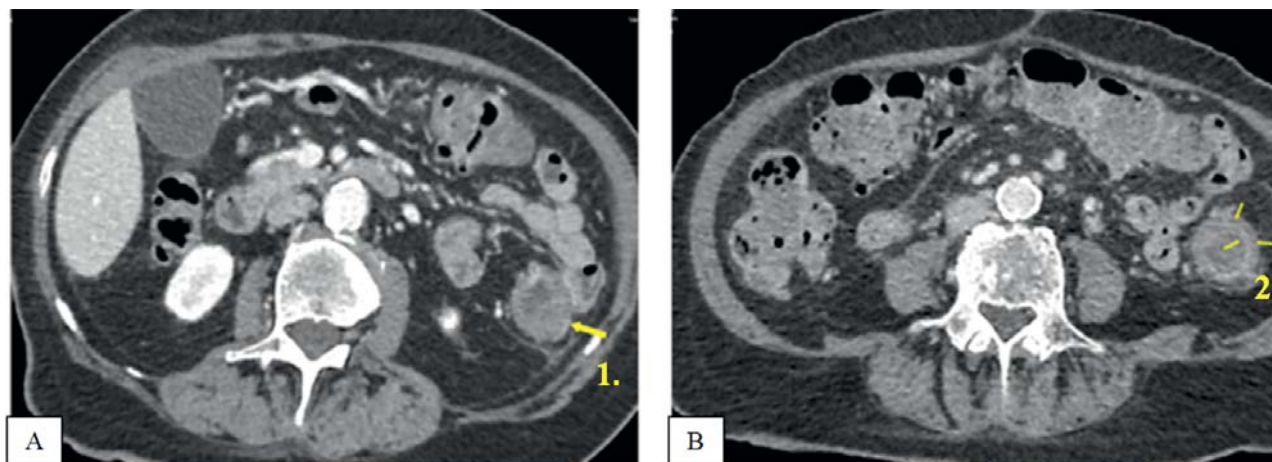


**Fig. 1.** Abdominal CT: mild exudation along the descendent colon was determined. Multiple diverticula of all parts of the large intestine up to 10 mm in size were noted. There was increase density and edema



*Fig. 2.* Abdominal US before treatment onset (A): there was uneven outline of intestinal wall, circularly thickened up to 9 mm with reduced echogenicity and loss of differentiation into layers (1). Multiple diverticula of the sigmoid colon were visualized, with a severe thickening of the walls (2). Walls of the transverse colon were thickened up to 5–6 mm, differentiation into layers was not clear. A small amount of free fluid was determined in the abdominal cavity and small pelvis

After treatment (B): in the projection of the descending and sigmoid colon, the contour of the intestinal wall was even, the walls were thickened to 6 mm, with slightly reduced echogenicity (3). The intestinal lumen was spasmodic, the paracolic tissue was slightly thickened. Free fluid at the time of screening was determined in the minimal amount. The walls of the localized diverticula of the sigmoid colon were not thickened



*Fig. 3.* Abdominal CT before treatment (A): diverticula of all parts of the large intestine up to 10 mm in size were observed. Haustra of the left half of the large intestine were smoothed, the layers of the bowel wall were not differentiated in the sigmoid colon, and the lumen was not visualized (1). In the abdominal cavity, a small amount of fluid was unchanged, the amount of fluid in the small pelvis had increased

After treatment (B): compaction and edema of paracolic tissue in the descending and sigmoid colon decreased. There was a three-layer pattern of the walls of the left half of the colon (2), haustra were smoothed. The minimal amount of free fluid in the abdominal cavity and small pelvis was determined

examination and treatment. At admission, according to physical examination, patient was in moderately severe state, body mass index was 21 kg/m<sup>2</sup>, abdominal distension and tenderness in the left iliac region were noted. Auscultation revealed weakening of intestinal sounds. Peritoneal signs were negative. The hereditary history was uncomplicated, there was drug allergy (urticaria) at administration of cephalosporins in the past history.

ECG showed no pathological changes. Blood test demonstrated progression of leukocytosis up to  $22 \times 10^9/l$ , ESR was elevated up to 60 mm/h, CRP was at the level of 170.8 mg/ml. Patient underwent abdominal ultrasound (Fig. 2A) according to which sigmoid and descending colon have uneven contour with walls of reduced echogenicity, circularly thickened to 7–9 mm without clear differentiation into layers.



Multiple diverticula of sigmoid colon were visualized with thickening of the wall as well as thickening of the transverse colon wall up to 5–6 mm with blurred layer differentiation. A small amount of free exudate was detected in the abdominal cavity and small pelvis. Control abdominal CT scan (Fig. 3A) showed multiple diverticula in all parts of the colon, induration and edema of paracolic fat tissue in the area of the sigmoid and descending colon were observed. Mild exudation along the descendent colon without change and increase of small pelvis exudation were visualized. Thus, according to instrumental data, the patient had signs of progression of acute diverticulitis of the sigmoid colon and partly — of the descending colon.

The patient received ciprofloxacin 500 mg bid, metronidazole 500 mg bid, drotaverine 40 mg per day, mesalazine 1.5 g per day, psyllium 10 g per day. Despite of therapy the patient's condition did not improve, febrile temperature and severe pain in the left iliac region persisted. Lack of clinical improvement required to adjust the antibacterial therapy: ciprofloxacin was cancelled, and the patient was put to ertapenem treatment ( $\beta$ -lactam antibiotic of the carbapenem group), at a dosage of 1 g per day. At ertapenem therapy, the pain decreased and the body temperature returned to normal.

However, on the third day after the antibiotic therapy change, the patient noted onset of watery stool up to 5 times per day without mucus or blood. Diarrhea was considered as a manifestation of *C. difficile*-associated disease, taking into account such risk factors as repeated courses of antibiotic therapy and prolonged hospital stay. Analysis for *C. difficile* toxin A and B was performed, however, in accordance with the guideline of the Russian Gastroenterological Association on the diagnosis and treatment of *C. difficile*-associated disease, vancomycin at a dosage of 2 g/day was added to therapy until laboratory confirmation of the diagnosis was obtained [5].

On the second day of the therapy patient's condition significantly improved: the stool consistency and frequency returned to normal, the abdomen became soft and painless on palpation, body temperature was 36.6 °C. According to the control blood test all parameters were within the normal range. Control abdominal US (Fig. 2B) showed positive dynamics at the therapy background: in the projection of the sigmoid and descending colon the bowel outline was clear, the walls were moderately thickened up to 6 mm with slightly reduced echogenicity, the lumen was spasmodic and the paracolic fat tissue was marginally thickened. The walls of the localized diverticula of the sigmoid colon were not thickened. Exudate was determined in the minimum

amount. According to the results of abdominal CT (Fig. 3B) after the treatment differentiation of the intestinal wall of the sigmoid colon into layers and reducing edema of paracolic fat tissue were noted. The laboratory test was positive for *C. difficile* toxin A and B.

Thus, according to the data of examination and observation in the clinic, the final clinical diagnosis was formulated: **Main disease:** Diverticular disease of the colon: diverticulitis. **Background:** Chronic constipation. **Complication:** Antibiotic-associated diarrhea, *C. difficile*-associated disease.

Complete clinical remission was achieved, the patient was discharged in a satisfactory condition with the following prescriptions: vancomycin 1000 mg per day (250 mg qid) for 6 days, then 500 mg per day (125 mg qid) for 14 days — considering the likelihood of recurrence of Clostridial infection, gradual reduction of vancomycin dose was recommended. As a maintenance therapy, the patient was recommended to take mesalazine 1000 mg per day for 10 days every month for 6 months, constant intake of psyllium 10 g per day.

## Discussion

The development of both uncomplicated and complicated forms of DD is based on inflammatory changes in the diverticula wall. Narrowing of the neck of the diverticulum impairs evacuation of its contents into the bowel lumen. Obstruction of the diverticulum neck and block of its emptying lead to inflammation both in the tissues of the diverticulum and in the surrounding tissues with their impregnation with inflammatory exudate.

Diverticulum destruction, in particular — destruction of its basement membrane and lamina propria (since there is no muscular and submucosal layers in the diverticulum) leads to outpouring of the aggressive contents of the intestine to peri-intestinal tissue with its subsequent inflammation [6]. In presented clinical case, multiple diverticula with their synchronous inflammation caused widespread colonic damage.

In our clinical case, multiple diverticula with simultaneous inflammation caused the development of inflammatory changes throughout a large segment of the colon (Figs. 1 and 3A). Systemic therapy with carbapenem antibiotics resulted in regression of the clinical and laboratory manifestations of diverticulitis (abdominal pain, fever, C-reactive protein level), but the treatment resulted in severe diarrhea, which was considered to be a manifestation of *C. difficile*-associated disease (it was later confirmed by laboratory examination of stool for *C. difficile* toxin A and B). Therefore, Vancomycin therapy was prescribed, which resulted in a significant improvement of the patient's condition.

The exclusion of the possible *C. difficile*-associated disease (especially in the presence of appropriate clinical signs) on the background of antibiotics intake or previous antibiotic therapy is important prerequisite for correct and adequate management of a patient with relapse of DD [5]. According to Makar et al. 1.14 % of patients with acute diverticulitis develop *C. difficile*-associated disease [7].

Patients with concomitant *C. difficile*-associated disease have increased risk of diverticulitis morbidity (OR 1.45, 95 % CI [1.21; 1.74]) and mortality in hospital (OR 2.78, 95 % CI [1.30; 5.95]) [7]. The likelihood of developing *C. difficile*-associated disease (except for antibiotic therapy) significantly increases such disease predictors as long-term hospital stay and compromised immune status (e.g. due to old age).

According to the study by Lessa et al. patients of 65 years of age and older were about nine times more likely to develop *C. difficile*-associated disease than the younger group of patients (OR 8.65; 95 % CI [8.16; 9.31]) [8]. It should be noted that if a patient develops a clinical signs of *C. difficile*-associated disease, treatment may be started pending laboratory confirmation. Negative laboratory test results do not exclude the diagnosis [5, 9].

## Conclusion

We presented a clinical case of DD relapse (acute diverticulitis) in 91 year-old sedentary woman receiving NSAIDs for back pain. At the background of severe aggravation of constipation patient developed clinical symptoms of diverticulitis, accompanied by widespread inflammatory changes in the intestinal wall.

On the background of antibiotic therapy severe diarrhea was developed. This condition required

anticrostrial therapy (vancomycin), pending laboratory confirmation of the infection. Combined therapy of DD aggravation and *C. difficile*-associated disease provided to achieve a stable improvement in the condition.

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