CLOSTRIDIUM DIFFICILE INFECTION: CLINICAL SYMPTOMS

YEVSTIHNIEIEV I.V.
candidate of Medical Sciences,
assistant of the Therapy Department 3
State Institution "Dnipropetrovsk Medical Academy of the Ministry of Health Ukraine"
Dnipro, Ukraine

In the last decade, the frequency and severity of *Clostridium difficile infection* (CDI) as a nosocomial infection has increased worldwide [1,2]. The most important risk factors for CDI are antibiotic therapy, old age, hospital or nursing home care. With CDI, variability of clinical manifestations is observed from asymptomatic carriage and mild to pseudomembranous colitis and toxic megacolon. More often, CDI is detected in patients after frequent and prolonged courses of antibacterial therapy and against the background of immunosuppression. *Clostridium difficile* colonizes the intestinal mucosa with significant violations of the intestinal microbiota, after surgical operations on the organs of the abdominal cavity, against the background of chemotherapy.

After violation of the species diversity of microbiota, the colonization resistance of the mucous membrane decreases. Rapid proliferation of *Clostridium difficile* in the colon begins with the production of toxins A (enterotoxin) and B (cytotoxin) and the occurrence of diarrhea and colitis. In severe forms, pronounced necrosis of colonocytes with clinical symptoms of pseudomembranous colitis and toxic megacolon is observed.

Risk factors that predispose to the occurrence of clinical symptoms of CDI include:

- long-term systemic antibiotic therapy in the last 1-3 months. Manifestations of CDI can be not only after the end of the course of antibiotic therapy, but also coincide with the beginning or continuation of the next course of antibiotic therapy;

- long-term use of proton pump blockers and H2-histamine receptors;
- immunosuppression of any genesis;
- prolonged hospitalization in hospital;
- elderly and senile age in patients with comorbid conditions;
- conducting radiation and chemotherapy;
- active phase of chronic inflammatory bowel disease.

Antibacterial therapy in the last 1-3 months is not a prerequisite for the occurrence of clinical symptoms of CDI in the presence of other risk factors.

The disease can manifest itself in several clinical forms.:

1. *CDI-associated diarrhea* with unformed stools more than 3 times a day, the most frequent and easiest of clinical forms;
2. *CDI-associated colitis* is manifested by an increase in bowel movements from 3 to 15 or more times a day with watery bowel movements, spastic pain in the lower abdomen, low-grade fever, moderate leukocytosis. With fibrocolonoscopy in the colon, lesions of the mucous membrane from hyperemia and swelling of the mucosa to ulcers are determined, depending on the severity of the lesion.
3. *Pseudomembranous colitis* is more severe than *CDI-associated colitis*. An endoscopic examination determines round, slightly rising yellow plaques (epithelial necrosis with fibrin impregnation). *These pathomorphological changes are called pseudomembranes and are a pathognomonic symptom of CDI.* However, in about 1/3 of patients with clinical symptoms of pseudomembranous colitis, these formations on the mucous membrane are detected only in the proximal colon. Sigmoidoscopy and fibrosigmoidoscopy make it possible to examine only the rectosigmoid section, therefore, the implementation of fibrocolonoscopy is more preferable in cases of suspected pseudomembranous colitis.

Computed tomography with contrasting the intestine makes it possible to identify areas of pronounced thickening of the colon wall, which is one of the markers of this disease. Fulminant forms of CDI-associated pseudomembranous colitis are characterized by increased diffuse abdominal pain or localized in the lower abdomen, watery diarrhea, sometimes with an admixture of blood, expressed by

leukocytosis. With severe hypovolemia, diarrhea may be minor or absent. In some patients, the absence of diarrhea is caused by a loss of colon tone with the development of dilatation of the most affected sections with accumulation of fluid and the occurrence of intestinal obstruction..

4. *Toxic megacolon* is a complication of fulminant CDI-associated pseudomembranous colitis. Atony and dilatation of the large intestine of more than 7 centimeters in the largest diameter are characteristic of this complication. There is a translocation of microbes from the intestine into the systemic circulation with the development of endotoxemia and septic shock. On the survey roentgenogram of the abdominal organs, the extension of the transverse colon is determined, the haustra are not determined, the dentate striation of the colon, fluid levels are observed.

5. *Colon perforation* is a complication of CDI-associated pseudomembranous colitis. There is severe abdominal pain, symptoms of peritoneal irritation. On the survey roentgenogram of the abdominal organs, free gas is often determined above the liver in the form of a sickle-like enlightenment.

The criteria for severe CDI-associated colitis include:

- symptoms of peritonitis and intestinal obstruction;
- unstable hemodynamics with progression to toxic shock;
- fever above 38.50C
- pronounced leukocytosis (above 15.0×10^9 / l);
- pronounced leukocyte shift to the left (more than 20% of stab forms of neutrophils);
- increase in serum creatinine level (increase of more than 50% of the initial level);
- an increase in serum lactate levels of more than 5 mmol / l;
- a decrease in serum albumin content of less than 30 g / l;
- respiratory failure if mechanical ventilation is needed;
- dilatation of the transverse colon more than 7 cm during x-ray examination;
- endoscopic manifestations of pseudomembranous colitis.

The clinical symptoms of CDI are variable, mild forms may not be diagnosed and progress to CDI-associated pseudomembranous colitis with the development of toxic megacolon and perforation of the large intestine [3,4,5]. There may be clinical manifestations of toxic megacolon with the development of acute intestinal obstruction during CDI debut without diarrhea, and differential diagnosis should be carried out quickly. Unreasonable prescription of antibacterial drugs, unreasonable surgical intervention aggravate the condition of patients [7.8]. Timely assessment of the manifestation of clinical symptoms of CDI, laboratory, endoscopic, if necessary, x-ray examination and computed tomography with contrasting the intestines make it possible to prescribe adequate treatment in a timely manner.

References

1. Czepiel J, Drozdz M, Pituch H et al. Clostridium difficile infection: review. *Eur J Microbiol Infect Dis.* 2019 Jul; 38(7): 1211-1222. doi: 10.1007/s10096-019-03539-6.

2. Davis L, Loo VG, Embil J et al. Association of Medical Microbiology and Infectious Diseases. Canada treatment practice quidelines for Clostridium difficile infection. *Official J of the Association of Med Microb[ol and Infect Dis.* Canada; 3.2.2018:1-22.

3. Ofosu A. Clostridium difficile infection: a review of current and emerging therapies. *Ann Gastroenterol.* 2016 Apr-Jun; 29(2): 147-154.

4. Mada PK, Alam MU. Clostridium Difficile. [Updated 2019 Jun 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Pablishing; 2019 Jan. Available from: https: //www.ncbi.nlm.nih.gov/NBK31054/.

5. Kong LY, Eyre DW, Corbeil J et al. Clostridium difficile: Investigating Transmission Patients Between Infected and Colonized Patients Using Whole Genome Sequencing. *Clin Infect Dis.* 2019 Jan 7; 68(2): 204-209. doi: 10.1093/cid/ciy457. PMID: 29846557.

6. McDonald LC, Diekema DJ. Point-Counterpoint Active Surveillance for Carriers of Toxigenic Clostridium difficile Should Be Performed To Guide Prevention 26; Efforts. *Clin Microbiol.* 2018 Jul; 56(8). pil: e00782-18. doi: 10.1128/JCM.00782-18. Print 2018 Aug. PMID: 29769275.

7. Mathias F, Curti C, Montana M et al. Management of adult Clostridium difficile digestive contaminations: a literature review. *Eur J of Clin Microbiol and Infect Dis.* Febr 2019; 38(2): 209-231.

8. Goval H, Perisetti A, Rehman MR, Singla UJ. New and emerging therapies in treatment of Clostridium difficile infection. *Eur J Gastroenterol Hepatol.* 2018 Jun; 30(6): 589-597. doi: 10.1097/MEG. 0000000000001103.