MINISTRY OF HEALTH OF UKRAINE

DANYLO HALYTSKYI LVIV NATIONAL MEDICAL UNIVERSITY

PEDIATRIC INFECTIOUS DISEASES DEPARTMENT

GUIDELINES

FOR SELF STUDY FOR 6th YEAR STUDENTS SPECIALTY "GENERAL MEDICINE"

PROFILE COURSE OF CHOISE **"OBSTETRICS AND GYNECOLOGY" "SURGERY"**

"Acute intestinal infection caused by *Clostridium difficile*."

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These guidelines are made according to the working curriculum on children's infectious diseases for students of the second (master's) level of higher education in the field of knowledge 22 "Health" specialty 222 "Medicine"

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Actuality of theme.

Clostridium difficile infection (CDI) is considered to be the main cause of bacterial infectious diarrhea in nosocomial settings. Since the beginning of the new century a continuous rise in the incidence of severe CDI has been observed worldwide. Even though some CDI cases are not associated with previous antibiotic exposure, this remains as the principal risk factor for the development of CDI. The rate of recurrences represents perhaps one the most challenging aspect on the management of CDI

CDI is considered to be the main cause of bacterial infectious diarrhea in nosocomial settings. *C. difficile* is implicated as the causative organism in 10–25% of patients who develop antibiotic-associated diarrhea (AAD), 50–75% of those with antibiotic-associated colitis and 90–100% of those with antibiotic-associated PMC

Elderly hospitalized patients receiving antibiotics remain the main group at risk of infection, and have the greatest associated mortality. However, recent evidence shows an increased incidence of CDI in younger populations with no previous contact either with the hospital or with antibiotics. Furthermore, the incidence of CDI in other groups, previously considered at low risk, such as children[5] and pregnant women,[6] has increased.

Questions for self-preparation:

- What disease it causes *C difficile?*
- What are the risk factors for the disease in children?
- What are the main symptoms of the disease?
- With what diseases the differential diagnosis is carried out?
- What laboratory tests are used to confirm the diagnosis?
- What are the main directions of treatment of the disease?

Contents of the topic.

Etiology

C difficile colitis results from a disruption of the normal bacterial flora of the colon, colonization with *C difficile*, and release of toxins that cause mucosal inflammation, mucosal damage, and diarrhea.

Risk factors

- *Antibiotic exposure*

The primary risk factor for *C difficile* colitis is previous exposure to antibiotics; the most commonly implicated agents include the cephalosporins (especially second and third generation), the fluoroquinolones, ampicillin/amoxicillin, and clindamycin. Less commonly

implicated antibiotics are the macrolides (ie, erythromycin, clarithromycin, azithromycin) and other penicillins. Agents occasionally reported to cause the disease include aminoglycosides, trimethoprim-sulfamethoxazole, metronidazole, chloramphenicol, tetracycline, imipenem, and meropenem.

- *Proton pump inhibitors*
- *Antidepressants*
- *Other risk factors*

Severe illnesses, immune suppression, and gastric acid suppression (or bypassing gastric acid via enteral feeds) are also well-established risk factors. In addition, in recent years, inflammatory bowel disease (IBD) has been implicated as a strong risk factor for *C difficile* infection (CDI). Early emergency general surgery has also been associated with a high incidence of CDI, particularly in patients who receive 3 or more postoperative antibiotics and those who undergo bowel resections.

Epidemiology.

CDI is more common in elderly people, and old age may promote susceptibility to colonization and disease. Cross-infection by *C difficile* is common in neonatal units, but neonates do not seem to develop *C difficile* –associated diarrhea. More recently, there have been specific populations affected by *C difficile* that were previously believed to be at low risk, such as young, healthy persons not exposed to a hospital environment or antimicrobial therapy and young women in a peripartum setting.

Clinical presentations

C difficile colonization results in a wide spectrum of clinical conditions, including an asymptomatic carrier state; mild, self-limited diarrhea; pseudomembranous colitis; and fulminant colitis. Most patients develop diarrhea during or shortly after starting antibiotics. However, 25-40% of patients may not become symptomatic for as many as 10 weeks after completing antibiotic therapy.

Symptoms often include the following:

- Mild to moderate watery diarrhea that is rarely bloody
- Cramping abdominal pain
- Anorexia
- Malaise
- Fever, especially in more severe cases

Physical examination is generally nonspecific in patients with mild *C difficile* infection. Fever, signs of dehydration, lower abdominal tenderness, and/or rebound tenderness (raising the possibility of colonic perforation and peritonitis) may be present.

More concerning signs include marked dehydration, marked abdominal tenderness, and distention, as well as marked rigidity and decreased bowel sounds. These may indicate the presence of complications such as toxic megacolon, and bowel perforation.

Differential Diagnoses

- Crohn Disease
- Diverticulitis
- Irritable Bowel Syndrome (IBS)
- Malabsorption
- Peritonitis and Abdominal Sepsis
- Salmonella Infection (Salmonellosis)
- Shigellosis
- Ulcerative Colitis
- Vibrio Infections
- Viral Gastroenteritis

Laboratory studies

Laboratory testing for evaluating patients with CDI includes the following:

- Complete blood count: Leukocytosis may be present (the levels can be very high in severe infection)
- Electrolyte levels, including serum creatinine: Dehydration, anasarca, and electrolyte imbalance may accompany severe disease
- Albumin levels: Hypoalbuminemia may accompany severe disease
- Serum lactate level: Lactate levels are generally elevated (≥5 mmol/L) in severe disease
- Stool examination: Stool may be positive for blood in severe colitis, but grossly bloody stools are unusual; fecal leukocytes are present in about half of cases

Stool assays for *C difficile*, from the most to the least sensitive, include the following:

- Stool culture: The most sensitive test (sensitivity, 90-100%; specificity, 84-100%), but the results are slow and may lead to a delay in the diagnosis if used alone
- Glutamate dehydrogenase enzyme immunoassay (EIA): This is a very sensitive test (sensitivity, 85-100%; specificity, 87-98%); it detects the presence of glutamate dehydrogenase produced by *C difficile*

- Real-time polymerase chain reaction (PCR) assay: This test is an alternative gold standard to stool culture (sensitivity, 86%; specificity, 97% [3]); it may be used to detect the *C difficile* gene toxin
- Stool cytotoxin test: A positive test result is the demonstration of a cytopathic effect that is neutralized by a specific antiserum (sensitivity, 70-100%; specificity, 90-100%)
- EIA for detecting toxins A and B: This test is used in most laboratories (moderate sensitivity, 79-80%; excellent specificity, 98%)
- Latex agglutination technique: Another means of detecting glutamate dehydrogenase; however, the sensitivity of this test is poor (48-59%), although the specificity is 95-96%

Imaging studies and procedures

Abdominal computed tomography (CT) scanning is the imaging modality of choice for *C difficile* colitis when pseudomembranous colitis (see the image below), complications of CDI, or other intra-abdominal pathology is suspected. [4] In patients with sepsis due to suspected megacolon, abdominal radiography may be performed instead of CT scanning to establish the presence of megacolon in a timely manner.

Endoscopy is less sensitive for diagnosing *C difficile* than are stool assays. Endoscopy may demonstrate the presence of raised, yellowish white, 2- to 10-mm plaques overlying an erythematous and edematous mucosa. These plaques are termed pseudomembranes. Endoscopic findings may be normal in patients with mild disease or may demonstrate nonspecific colitis in moderate cases.

Management

Treatment for CDI varies according to its severity. Interventions include the following:

- Asymptomatic carriers: No treatment is necessary
- Mild, antibiotic-associated diarrhea without fever, abdominal pain, or leukocytosis: Cessation of antibiotic(s) may be the only treatment necessary
- Mild to moderate diarrhea or colitis: Metronidazole (oral or intravenous) or vancomycin (oral) for 10 days
- Severe or complicated disease: Vancomycin is considered to produce faster symptom resolution and fewer treatment failures than metronidazole; in fulminant cases, combined therapy with intravenous metronidazole and oral (or per rectum) vancomycin may be considered
    - Either metronidazole or vancomycin is recommended for the treatment of children with an initial episode or first recurrence of nonsevere CDI.

- For children with an initial episode of severe CDI or with a second or greater episode of recurrent CDI, oral vancomycin is recommended over metronidazole.

Prevention

C difficile is now recognized as a major nosocomial pathogen, and universal precautions against it should be implemented. The following guidelines are recommended when dealing with patients with *C difficile* colitis [5, 30] :

- Use disposable gloves, laboratory coats, and proper washing techniques
- Educate the medical and nursing staff, as well as family and visitors, regarding the disease and its epidemiology, and emphasize compliance with hand hygiene practices (such as washing with soap or antimicrobial soap and water)
- Hospital transmission is likely associated with the survival of spores on inanimate objects; therefore, close attention to cleanliness and disinfective measures are important (eg, use of contact precautions for 48 hours or longer following resolution of diarrhea, disposable electronic rectal thermometers, chlorine-containing cleansers or other sporicidal agents), particularly during the patient's diarrheal period
- Isolation of patients who are infected is strongly recommended but often impractical at most hospitals; in such situations, a dedicated commode for each patient should be provided.

Tests for self-control

1. "What drugs are ineffective in treating pseudomembranous colitis?"

- Ciprofloxacin
- Metronidazole
- Vancomycin
- Bacitracin
- Cholestyramine
- Probiotics

2. "Specify the route of administration of vancomycin in the treatment of Clostridium Difficile?"

- Orally

- Parenterally
- Intramuscular
- Intravenously
- Subcutaneously
- Endolymphatic

3. "Specify antibiotics that do not cause antibiotic-associated colitis:"

- Amoxiclav
- Tetracycline
- Vancomycin
- Ciprofloxacin
- Erythromycin
- Doxycycline

4. A healthy 16-year-old boy after a long term antibacterial therapy (21 days) developed diarrhea with blood impurities, excruciating abdominal pain and fever. After a few weeks of illness, he went to the doctor, who during proctosigmoscopy found bleeding and loose mucous membranes. Probable diagnosis?

- pseudomembranous colitis
- viral gastroenteritis
- Campylobacter infection
- Ulcerative colitis

Case

Patient K., 15 years old, complained of watery stools, up to 10 times a day, with mucus,blood in the stool, bloating, moderate cramping pain abdomen, more in the projection of the large intestine. The pain intensifies to and decrease after defecation. It is known that a week before the treatment she was treated at the place of residence concerning chronic pyelonephritis in the form of oral administration of cefazolin, and then intramuscular administration of cefotaxime. Two days later from. At the beginning of antibiotic treatment, the patient noted

loose stools up to three times per day. Antibiotic therapy was not stopped. Liquid stool was noted in during the entire treatment period. A few days later she noticed a deterioration state. On examination: satisfactory condition, t - 36.8 ° C, height 161 cm, weight 51 kg, skin and visible mucous membranes pale pink. Vesicular respiration in all departments, no wheezing. BP 18 in 1 min. Heart -tones are sonorous, the rhythm is correct. Heart rate 92 in 1 min. AD 108/65 mm Hg The tounge moderately diffusely coated with a grayish plaque, moist. The stomach is involved in breath, evenly swollen, at a superficial palpation soft, moderate morbidity on the left flank of a stomach, at deep palpation soreness in the left iliac region, where it is palpated densely elastic, painful sigmoid colon. The sizes of a liver and a spleen according to Kurlov: 9x8x7 cm and 6x4 cm, respectively. The edge of the liver is not defined. The lumbar symptom is negative.In the general analysis of blood: erythrocytes 3,22x1012 / l, Hb 113 g / l, leukocytes 15.6x109/ l. ESR 35 mm / hour. General analysis of urine - without pathology. Biochemical blood test: Total protein 60.1 g / l, Reactive protein (25 mg / l). Coprogram: feces liquefied, unformed, leukocytes up to 30-40 in the field of view, erythrocytes in small quantities, mucus in large quantities. Ultrasound: swollen loops are detected in all parts of the abdominal cavity large and small intestine. Abdominal radiography: no signs of intestinal obstruction.

Questions:

1. What the diagnosis.

2. How to confirm the diagnosis.

3. What additional research methods would you prescribe to this patient?

4. Determine the patient's management plan using medical and non-medical methods.

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