Pseudomembranous Colitis: Causes, Diagnosis, and Treatment

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Pseudomembranous colitis also referred to as clostridium difficile infection or colitis is a potential complication of recent antibiotic use. Students should be aware of its causes, consequences, and management.

Definition

Pseudomembranous colitis refers to inflammation of the colon (colitis) due to infection with Clostridium difficile bacteria. The condition is characterized by pseudomembranes that can be seen both macroscopically and microscopically. Pseudomembranous colitis occurs when there is a disruption to the normal bowel flora of the gut through the use of antibiotics.

Epidemiology

The first case of C. difficile colitis was reported in 1978. Its incidence and severity have been increasing since then, and currently, it is the most common hospital-acquired (nosocomial) diarrheal illness. There are approximately 3 million cases of
pseudomembranous colitis each year in the United States. 

*C. difficile* is a commensal gut bacteria that is present in about 5%-15% of normal healthy adults, and up to 57% of patients in hospitals and long-term facilities. The spores of *C. difficile* are present in both the natural environment and in medical facilities such as hospitals and nursing homes. **Advanced age** is a major risk factor for developing pseudomembranous colitis.

**Etiology**

![Image: Clostridium difficile colonies after 48 hours of growth on a blood agar plate; magnified 4.8X. By: CDC. License: Public domain.](Image)

Pseudomembranous colitis most commonly arises due to the **use of broad-spectrum antibiotics, which leads to infection with** *C. difficile*, a *gram-positive, anaerobic, rod-shaped bacteria (bacillus)* that produce spores (see image). Antibiotics can disrupt or kill the natural gut flora, allowing *C. difficile* to proliferate. The most commonly implicated antibiotics include **ampicillin, cephalosporins (2nd and 3rd generation), fluoroquinolones, and clindamycin.**

**Pathology and Pathophysiology**

Exposure to **broad-spectrum antibiotics disrupts the normal flora of the bowel**, predisposing the patient to infection through colonization with a **toxigenic strain of C. difficile.**

In the colon, *C. difficile* proliferates and produces 2 exotoxins, **toxins A (an enterotoxin) and B (a cytotoxin).** These exotoxins are responsible for the adverse effects that occur. They induce inflammation in the colon, causing increased vascular permeability. Pseudomembranes are formed and consist of inflammatory cells including neutrophils along with cellular debris, fibrin, and mucin. Macroscopically, the pseudomembranes appear as **white or yellow plaques** that adhere to the underlying inflamed colonic mucosa. Of the 2 exotoxins that produce **tissue** damage, toxin A is the most responsible, as it induces tissue damage, while toxin B helps perpetuate the damage once the mucosa is already injured.

The development of clinical disease depends on a patient’s immune system and the toxigenic potential of the *C. difficile strain*. Otherwise, a patient may become an asymptomatic carrier, in which case there is usually no toxin production.
Symptoms

Signs and symptoms of pseudomembranous colitis are usually apparent 4–9 days after beginning antibiotic treatment. However, they can also develop as early as 2 days after antibiotic use, or as late as 8 weeks.

Common symptoms include the following:

- Diarrhea
- Abdominal pain and tenderness
- Fever
- Nausea and vomiting

Diarrhea is one of the key clinical features of pseudomembranous colitis, and can vary in its severity. It is usually high-volume, watery, and foul-smelling, and rarely is bloody. However, if diarrhea is absent, this may herald a serious complication such as paralytic ileus or toxic megacolon.

Abdominal pain also varies in its severity, and can be colicky in nature; however, it may be absent in some cases. Patients may also have an accompanying fever, while nausea and vomiting uncommonly occur.

In cases of fulminant colitis, the patient may have severe abdominal pain and tenderness. They may also display signs of shock, including hypotension and tachycardia.

Diagnosis

Diagnosis of pseudomembranous colitis can be made with history and physical exam. Other tests, such as those listed below, may also be helpful, but are not necessary for diagnosis.

Blood Tests

Patients with pseudomembranous colitis usually have a raised white blood cell count, but this is not a specific or sensitive finding for the condition. In cases of fulminant colitis, the white blood cell count may be significantly high.

Stool Tests

Stool tests play a key role in the diagnosis of pseudomembranous colitis. Stool samples in a patient are generally positive for the presence of leukocytes. Specific stool tests to detect *C. difficile* include a cytotoxin tissue culture assay, immunoassay for toxins A and B, polymerase chain reaction test, and glutamate dehydrogenase test.

Treatment for pseudomembranous colitis should not be delayed by waiting for stool test results. In other words, a positive stool test is not needed for diagnosis.

Radiology

An abdominal X-ray may be done in cases where there is abdominal distension; it can detect colonic wall thickening, air in the bowel, and the degree of dilatation.

An abdominal computed tomography (CT) scan may be considered in patients with
severe disease or those displaying signs of complications, such as absent bowel sounds, worsening abdominal pain, and/or abdominal distension. A CT scan may reveal colonic wall thickening, dilatation of the bowel, ascites, or bowel perforation.

Additional Tests

A sigmoidoscopy or colonoscopy may reveal evidence of pseudomembranous colitis with characteristic pseudomembrane formation and ulcerations (see image). These investigations may be performed when there is treatment failure or when there is suspicion of other causes for the patient’s presentation. A biopsy may also be performed.

Differential Diagnoses

- Antibiotic-associated diarrhea (diarrhea with the presence of nausea and absence of fever; negative C. difficile toxin test)
- Gastroenteritis (viral or bacterial; a history of consumption of contaminated foods, recent travel, or infectious contacts)
- Ischemic colitis (bloody diarrhea)
- Inflammatory bowel disease (chronic diarrhea; extraintestinal features may be present)

Therapy

The patient’s antibiotics should be discontinued. If the patient requires antibiotics, a substitute that is not associated with causing pseudomembranous colitis should be used. Ampicillin, clindamycin, 2nd- and 3rd-generation cephalosporins, and fluoroquinolones should be avoided.

The antibiotics used against C. difficile will depend on the severity of the infection. For mild and moderate cases, oral vancomycin or oral fidaxomicin is the first-line option of treatment, or oral metronidazole (second-line). In severe cases, oral vancomycin is used. Fulminant cases require a combination of oral vancomycin and intravenous metronidazole.
Supportive care measures are important as well. Patients’ fluid status and electrolytes should be monitored closely and kept stable. It is also necessary to practice infection control through the use of barrier precautions and hand hygiene.

Recurrent *C. difficile* infection occurs in approximately 20% of patients. Treatment options include *vancomycin* and *fecal microbiota transplant (FMT)*; also known as stool transplant. FMT can be done endoscopically or via a nasogastric tube and has been found to have success rates of 70%–90%. The goal is to restore normal, healthy intestinal bacteria.

Progression and Prognosis

Pseudomembranous colitis is especially dangerous in older patients or those who are immunocompromised. In outbreaks of the disease, mortality rates can reach 6.9%. Fortunately, most patients generally recover.

Cases of fulminant colitis, though uncommon, carry a high risk of mortality (35%–80%). Risk factors for the development of fulminant colitis include inflammatory bowel disease, a significantly elevated white blood cell count, and recent gastrointestinal surgery.

Recurrent disease occurs in 15%–30% of patients after treatment. This may be due to relapse of the infection or re-infection with a new strain of *C. difficile*.

References


**Correct answers:** 1C, 2C, 3B

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