Autopsy Case Reports

Image in focus
Imagem em foco

Clostridium difficile infection

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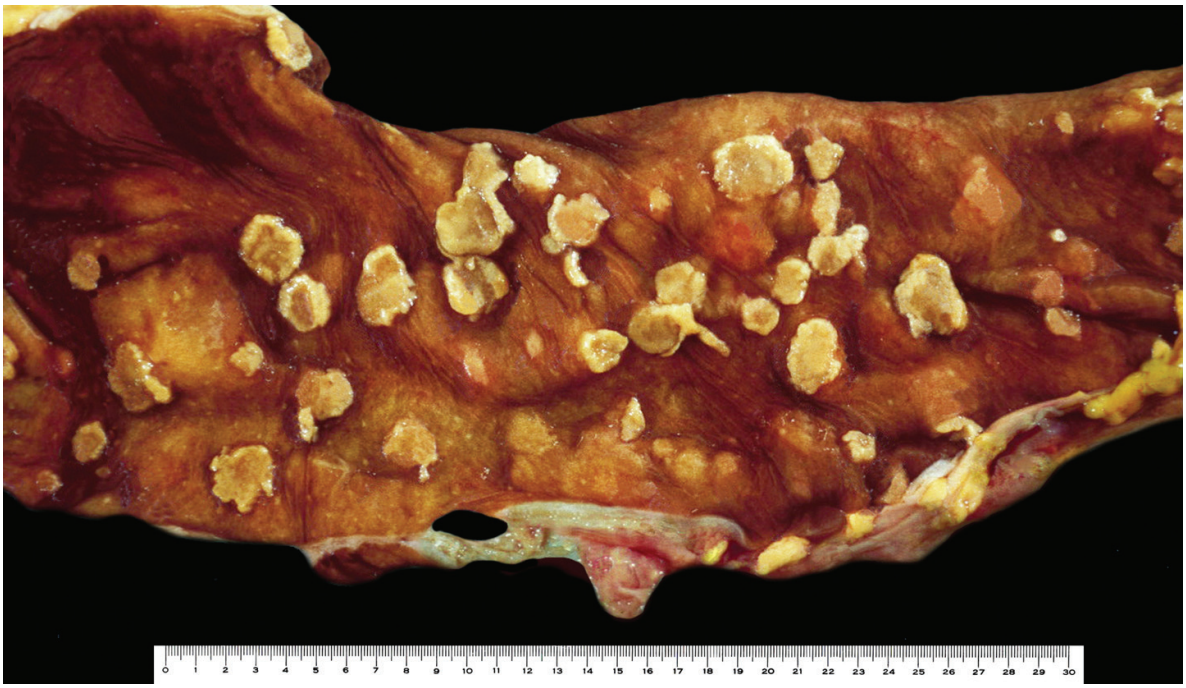

Picture provided by Dr. Stephen A. Geller - personal archive.

Clostridium difficile infection (CDI) is a significant and increasing medical problem, surpassing methicillin-resistant *Staphylococcus aureus* as the most common hospital-onset or facility-associated infection,[1-3] and a key element in the challenging battle against hospital-acquired infections. This Gram-positive, anaerobic, spore-forming colonizes the intestinal tract after antibiotics have altered the normal intestinal flora. CDI may be life-threatening; the death rate has dramatically increased from 3,000 per year in 1999-2000 to 14,000 per year in 2006-2007.[4] The use of antibiotics, although not the only risk factor, is the most significant triggering event, increasing in incidence with prolonged antibiotic use.[2,3,5] Many antibiotics have been implicated in the etiopathogenesis of CDI, especially ampicillin, amoxicillin, clindamycin, cephalosporin (particularly third generation cephalosporins) and quinolones.[2,3,6-8] However, not all cases of CDI are associated with

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antibiotics or their prolonged use. In 24% of cases of CDI there was no history of previous use of antibiotics and 9% had less than 3 days of use.[9] Most of these were hospitalized individual who had close contact with patients with diarrheal diseases. Other risk factor includes administration of antineoplastic agents like doxorubicin, cisplatin, cyclophosphamide, fluorouracil and chlorambucil, methotrexate.[10] Immunocompromised patients, either from cancer chemotherapy or, especially, after transplantation, also were prone to develop CDI. Other risk factors include: preceding inflammatory bowel disease (IBD) and other comorbidities, advanced age, enteral feeding (especially post pyloric), prior gastrointestinal surgery, and proton pump inhibitor users.[2,3,11]

Clinical presentation varies widely (Table 1). Asymptomatic (culture positive) carriers can have mild colitis without the characteristic inflammatory ("pseudo") membrane formation or fulminant toxic megacolon. Watery diarrhea is a cardinal manifestation accompanied by cramps and lower abdominal pain. Acute abdomen, requiring emergency surgery, has been described.[11,12] Symptoms generally start 2-10 days after antibiotic use. Although frankly bloody diarrhea is uncommon, occult blood is present in 26% of cases. As many as 50% of patients have a low-grade fever. When the temperature is greater than 38.5 °C there is usually severe disease. Leukocytosis, with increased band forms is frequent, as is hypoalbuminemia. Creatinine value elevations are seen with increasing severity of the diarrhea. Acute inflammatory exudate may be present in as many as 40% of stool samples.[11,13-15] Imaging studies are of little use in detecting CDI and endoscopy is indicated when rapid diagnosis is required. Findings may vary: normal mucosa (in mild cases), mild erythema, and friability can be seen before the appearance of the characteristic multiple, raised and centrally ulcerated, yellowish-white plaques (pseudomembranes).[16] The entire colorectal mucosa can be affected in the most severe cases but, most often, the lesions are patchy and separated by unremarkable mucosa, as in the image above. With effective therapy the mucosa heals completely.

Symptom recurrence may be due to reinfection by a different strain or can represent relapse with the original strain, and may be characterized by one or several episodes, starting days or weeks after treatment. Relapse may be more severe than the first episode.[17]

Currently, many laboratory assays have been used to diagnose CDI, but no single "gold standard" has been recognized.[2,3,11] *C. difficile* toxin is obtained from stool samples, which should be maintained at temperature under 4 °C if not immediately processed since the toxin is heat sensitive (a frequent cause of false-negative result). For this purpose the available tests are: Polymerase chain reaction (PCR), Enzyme immunoassay (EIA) for *C. difficile* glutamate dehydrogenase (GDH), Enzyme immunoassay (EIA) for *C. difficile* toxins A and B, Cell culture cytotoxicity assay and selective anaerobic culture.

Histologic examination is characteristic but, in biopsy samples, may be indistinguishable from acute ischemic colitis.

Less severe CDI may be treated with oral metronidazole or vancomycin with 90-98% cure rates. As the results are considered similar, metronidazole has been favored over vancomycin to limit the spread of vancomycin-resistant enterococci. Other treatment choices include fidaxomicin and rifaximin. Recently, fecal transplantation to either the upper or lower gastrointestinal tract has been shown to be dramatically effective in many cases of severe CDI.[18-20]

Table 1. Patterns of clinical presentation[2,3]

Carrier stage (asymptomatic)
C. difficile associated diarrhea (CDAD)
C. difficile associated colitis (CDAC)
Pseudomembranous colitis
Fulminant colitis
C. difficile associated enteritis (rare)
Acute appendicitis (rare)

Keywords: Enterocolitis, Pseudomembranous; Clostridium difficile; Cross Infection; Diarrhea.

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