

Update on *Clostridium difficile* Colitis

Clostridium difficile infection has recently emerged in populations without any known risk factors. This presentation will focus on the historical background, diagnosis, and treatment of *Clostridium difficile* colitis. The discussion will also address the means for control and prevention of infection.

Objectives:

- Develop an understanding of the differential diagnosis of pseudomembranous colitis
- Develop an understanding of the risk factors for *Clostridium difficile* infection
- Develop a basic understanding of the diagnosis and treatment of *Clostridium difficile* infection

**Update on the Newest Emerging
Infection: Community-Associated
Clostridium difficile Colitis**

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***Clostridium difficile* Colitis**

- Well-recognized iatrogenic complication of antibiotics use
- 15%-25% of all cases of antibiotic-associated diarrhea
- Wide spectrum of disease severity
- Likelihood increases with severity of the disease
- 95%-100% cause of antibiotic-associated pseudomembranous colitis

Historical Background

- 1935: *C. difficile* described
- 1943: Penicillin and typhlitis connection
- Early 1950s: Pseudomembranous colitis (PMC) & antibiotic use



Staphylococcus aureus suspected pathogen



Oral vancomycin standard therapy

***C. difficile* Era**

- 1974: Reports of high rates of PMC among patients on clindamycin
 - Stool cultures negative for *S. aureus*
- 1978: Cytopathic toxin that was neutralized with *Clostridium sordellii* antitoxin
- Search for the species began
- Reported in NEJM in 1978
- 2000: Emergence of a toxin hyperproducing strain (BI/NAP1/027)
 - Some with no history of antibiotic exposure

BI/NAP1/027

- More severe diseases, more refractory to therapy
- Higher rates of relapse, toxic megacolon
- Requiring colectomy, associated shock & death
- Produces more toxins A & B in vitro
- Absence of *tcdC*, a genetic sequence responsible for downregulation of toxin production
- Presence of binary toxin (role unclear)
- In vitro resistance to fluoroquinolones

Pseudomembranous Colitis

- Lesions nearly always limited to the colon
- *S. aureus* enterocolitis commonly involves small bowel
- Anatomic lesions best detected by colonoscopy
- 20%-30% of lesions limited to proximal colon
- Sigmoidoscopy may miss proximal lesions
- CT can also be helpful

Pseudomembranous Colitis Differential Diagnosis

- Intestinal obstruction
- Colon cancer
- Leukemia
- Severe burns, shock, uremia
- Heavy metal poisoning
- Hemolytic-uremic syndrome
- Crohn's disease
- Shigellosis
- Neonatal necrotizing enterocolitis, ischemic colitis
- Hirschsprung disease

Risk Factors

- Hospitalization, LTCFs
 - Risk increases with duration of hospital stay
- Age > 65 years
 - Neonates: High rates of *C. difficile* colonization
- Antibiotic exposure
 - Cephalosporins, broad-spectrum penicillins
 - Fluoroquinolones
 - Less common with other classes
- Methotrexate
- Use of acid-suppressive therapy (controversial)
- GI surgery or GI procedures

Clinical Presentation

- Watery diarrhea (gross blood is rare)
 - 15-30 bowel movements/day
- Abdominal cramps
- Lower quadrant abdominal pain (~22%)
- Low grade fever (~28%)
- Leukocytosis (~50%)
 - Can be in leukemoid range
- Low albumin

Potential Future Therapies

- Nitazoxanide, rifaximin
- Toxin-binding polymer
 - Tolevamer
- Poorly absorbed antimicrobials
 - OPT-8 (Difimicin)
 - Ramoplanin
- Monoclonal antibodies
- *C. difficile* vaccine

Complications

- Recurrence following discontinuation of therapy (~20%)
- Recurrence of identical symptoms within 8 weeks after therapy is discontinued
- 50% due to infection with new strain of *C. difficile*
- Failure to mount an immune response
 - Low levels of IgG against toxin A

Control & Prevention Measures

- Multifactorial
- Isolation, contact precaution
- Environment (room cleansing with 10% bleach)
- Personnel hygiene
- Ineffective: Alcohol-based hand sanitizers
- Effective: Hand washing with chlorhexidine or with soap and water
- Antimicrobial stewardship

Recommended Readings

- Al-Nassir WN, et al. *Clin Infect Dis* 2008;47:56-62.
- Bartlett JG. *Clin Infect Dis* 2008;46:1489-92.
- Pepin J. *Clin Infect Dis* 2008;46:1493-8.
- Bartlett JG, et al. *Clin Infect Dis* 2008;46:S1-S52.
- Blossom DB, et al. *Clin Infect Dis* 2007;45:222-7.
- Klein EJ, et al. *Clin Infect Dis* 2006;43:807-13.
- Bartlett JG. *Ann Intern Med* 2006;145:758-764.
