How do we handle *Clostridium difficile* infections in IBD?

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Overview

I. Background – C. difficile

II. Impact of C. difficile on IBD

III. Diagnostic considerations C. difficile

IV. Treatment considerations
In the past: *C. difficile* linked to antibiotic use. Most cases treated successfully with metronidazole

- Doubling of *C. difficile* associated disease between 1996 - 2003
- >500,000 cases in US annually
- >15,000 deaths in US annually
- Diminished therapeutic response to metronidazole (50% failure rate with initial course of treatment)
- Increasing impact on IBD patients reported

**Clostridium difficile and IBD**

- *C. difficile* and IBD present in identical fashion ranging from mild diarrhea to fulminant colitis.
- Early studies performed 2 decades ago indicated little overlap between *C. difficile* and IBD. It concluded “No need for routine screening for *C. difficile* in IBD population”.
- Recent studies: Increasing incidence and severity of *C. difficile* in IBD population
- *C. difficile* recently identified to have a significant negative impact on IBD morbidity

Increasing Impact of *Clostridium difficile* on IBD

$P \leq 0.01$

Increasing Impact of *Clostridium difficile* on IBD

Increasing Proportion of *Clostridium difficile* Patients With IBD

<table>
<thead>
<tr>
<th>Year</th>
<th>Total C. diff patients</th>
<th>IBD patients with C. diff</th>
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</thead>
<tbody>
<tr>
<td>2000</td>
<td>50</td>
<td>2</td>
</tr>
<tr>
<td>2001</td>
<td>100</td>
<td>5</td>
</tr>
<tr>
<td>2002</td>
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<td>2004</td>
<td>250</td>
<td>20</td>
</tr>
<tr>
<td>2005</td>
<td>300</td>
<td>30</td>
</tr>
</tbody>
</table>

*P* ≤ 0.01

Complications: *C. difficile*-Infected Patients With IBD*

Hospitalizations

Colectomies

1998 1999 2000 2001 2002 2003 2004 2005

Number of Patients

0 5 10 15 20 25 30

2004 2005

# of Patients With IBD With C. diff

# of Colectomies

36% 15%

*Preliminary data.
Endoscopic Appearance of Clostridium difficile

Endoscopic appearance of C. diff in control patients

Endoscopic appearance of C. diff in patients with IBD

Ulcerative Colitis

Crohn’s Disease

Extensive cryptitis crypt abscesses in Crohn’s colitis patient with active *C. difficile*. No inflammatory pseudomembranes are identified.

Demographic Data: IBD Patients With *C. difficile*

91% Colonic IBD

61% recent antibiotic exposure

Stool ELISA Testing in IBD Patients for *C. Difficile* Toxins A and B

Special IBD Scenarios with *C. difficile*

- **C. difficile** in ileo-anal pouchitis
  - Two case reports
  - Chronic refractory pouchitis
  - Unresponsive to broad spectrum antibiotics
  - In both cases *C. difficile* developed while patients were on metronidazole therapy

- **C. difficile** in segments of diverted bowel
  - One case report of *C. difficile* in UC pt following subtotal colectomy with end-ileostomy
  - Treated successfully with 10 day course of metronidazole suppositories

C. *difficile* Enteritis: An Early Postoperative Complication in IBD Patients Following Colectomy

- Rare but associated with significant morbidity with mortality rates ranging from 60%-83%
- MCW institutional series of six patients (2004-2006)
  - *C. difficile* manifested in high volume watery ileostomy output, ileus and fever with leukocytosis
  - No mortality with prompt diagnosis and therapy

Clostridium difficile in IBD: Morbidity and Mortality

- IBD patients with *C. difficile* compared with IBD alone:
  - Longer hospital stay
  - Increased hospitalization costs
  - Higher colectomy rates
  - Increased mortality rate –
  - 118 IBD *C. diff* deaths in NIS 2004
  - (>500 IBD *C. diff* deaths in U.S. 2004)

Clostridium difficile in IBD: Increasing U.S. hospitalizations 2004 - 2007

Proportion C. difficile (per 1000 hospitalizations)

- IBD
- Crohn's
- UC
- All patients

Year
- 1998
- 2004
- 2007

Decreasing colectomy rate among hospitalized IBD patients with C. difficile

- Number of infections and rate of hospitalization remained constant, but significant decrease in colectomy rate
  - High index of suspicion
  - Use of oral vancomycin – superiority over metronidazole
  - Decreased corticosteroid dosing

C. difficile and IBD: Summary I

- C. difficile has doubled in North American Medical Centers in the past decade.
- IBD colitis patients are affected at highest rate.
- C. difficile in IBD is associated with high rates of hospitalization, colectomy and increased mortality.
- Antibiotic use may not be required to precipitate infection.
- Endoscopic and Histologic appearance is not classical – pseudomembranes are rare in IBD.
- Multiple stool ELISA samples for toxin analysis are required to make a diagnosis.
C. difficile and IBD: Summary II

- Metronidazole failure rate is 50%; Oral vancomycin may be superior in hospitalized patients.
- *C. difficile* enteritis may occur in post-colectomy patients and patients with ileoanal pouch reconstruction.
- *C. difficile* recurrence rates are high.
- Early surgical consultation for patients developing severe disease (>10 BM/day, WBC>20K, severe abdominal pain, ileus).
- Hand washing with soap and water is essential to prevent nosocomial transmission.