Teachable Moment

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Clostridium difficile Testing: A Hard Look at Loose Stools

Story From the Front Line

CB is a 75-year-old woman with multiple medical problems, including chronic constipation. Her outpatient daily bowel regimen included senna-docusate, bisacodyl suppositories, and polycarbophil. She presented to Greenville Memorial Hospital secondary to mental status changes and increased abdominal girth. Her caregiver stated that the patient had not had a bowel movement in several days.

CB was admitted to the intensive care unit for septic shock secondary to a urinary tract infection (UTI) and evidence of a right lower lobe pneumonia based on chest X-ray. Allergies to penicillins and cephalosporins were documented in the electronic medical record, so broad-spectrum antibiotics of aztreonam, vancomycin, and ciprofloxacin were initiated on hospital day 2 because of illness severity. Ciprofloxacin and vancomycin were discontinued on hospital days 3 and 4, respectively, and aztreonam was continued until day 7 to treat an Escherichia coli UTI.

Tube feedings were started on hospital day 1 and continued until day 10 when the tube was displaced and not replaced. Proton-pump inhibitor therapy was started on hospital day 1 and continued until discharge. CB was not taking acid-suppressive medications before hospital admission.

On hospital day 2, an abdominal and pelvis CT scan showed gaseous distention of the transverse colon with formed stool throughout the left colon. The rectum and sigmoid colon were distended with formed stool suggesting constipation. There was no evidence of small bowel obstruction. A bowel regimen consisting of daily polyethylene glycol (17 g packets), bisacodyl suppositories (10 mg), and senna tablets (8.6 mg) was started in addition to a 1-time dose of lactulose solution (40 g) and of sodium polystyrene suspension (30 g).

The patient had 6 documented loose bowel movements on hospital day 2. CB continued to have 0–2 soft or loose stools documented per day until hospital day 11 when 3 watery stools were charted. A Clostridium difficile (C difficile) polymerase chain reaction (PCR) test was ordered. Daily bisacodyl and polyethylene glycol doses were discontinued after administration on hospital day 11. After discontinuation, the documented bowel movements were again 0–2 soft or loose stools per day for the remaining hospital stay. Senna was administered until hospital day 14.

On hospital day 12, the C difficile PCR test resulted positive, and the patient was started on metronidazole by mouth (500 mg every 8 hours).

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Clostridium difficile is the most common pathogen implicated in hospital-acquired infections. National surveillance data estimates C difficile was responsible for 500 000 infections and 29 000 deaths in 2011. The 30-day crude case fatality rate for C difficile infections is 9.3%. The cost of C difficile infection (CDI) is high, with data from 2008 estimating up to $4.8 billion in excess cost for acute care facilities.

Antibiotic exposure remains the most important risk factor for CDI. Combination antibiotic use and prolonged antibiotic therapy increase the risk of CDI; however, perioperative antibiotic exposure also introduces risk for infection. One study demonstrated the rate of CDI in patients who received only perioperative antibacterial prophylaxis to be 7.3 per 1000 surgical procedures.

Antibiotic agent selection may also be a contributing risk factor, as clindamycin, fluoroquinolones, cephalosporins, and aminopenicillins have been shown to be associated with CDI. Use of proton pump inhibitors has been shown in some...
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studies to increase the risk for CDI because of modification of normal stomach acidity and gastrointestinal microbiota. Advanced age is another risk factor, with patients over 65 years having an 8-fold increased risk of CDI when compared to younger patients.1

While C. difficile is most commonly associated with the healthcare setting, community-associated infection is also on the rise with 159,700 community-associated cases reported in 2011.1 C. difficile in the community setting, however, tends to affect younger patients and risk factors remain unclear.8

The endotoxins released by the bacteria, and the resultant inflammatory changes in the colonic epithelium, cause colitis and diarrhea in susceptible patients with clinical CDI.9 A significant number of people are asymptomatic carriers of C. difficile but do not develop overt clinical signs of infection. Therefore, detection of C. difficile from stool is just one way to diagnose CDI.

A variety of testing methods are available, but diagnostic tests capable of detecting toxins are the most clinically useful. Currently, toxigenic culture and cell cytotoxicity assay are considered the gold standard testing methods. These tests are time-intensive and are mainly used for epidemiologic purposes.

Enzyme immunoassay-based tests offer a shorter turnaround time, but at the expense of sensitive results. Nucleic acid amplification testing methods, such as PCR, are more sensitive and specific, but can identify C. difficile toxin in the stool of asymptomatic patients. Some clinical microbiology laboratories utilize a 2-step testing method to increase sensitivity, combining a test for detection of organism that, if positive, reflexes to a test for presence of toxin.10

Greenville Health System utilizes a PCR test for C. difficile that detects the genes that regulate production of toxin A and toxin B and the presence of genes for the B1/NAP1/027 hypervirulent strain. Because PCR can detect the toxin genes in stool of asymptomatic patients, adequate patient selection and sample collection are paramount to accurate diagnosis of C. difficile infection.

The Infectious Diseases Society of America recommends that C. difficile testing only be performed on diarrheal stools.11 Diarrhea is defined as the acute onset of 3 or more loose stools in a 24-hour period. Diarrheal stools are watery, loose, or unformed; one rule of thumb is that the stool specimen should take the shape of the sample container.10 C. difficile testing on formed stools decreases the specificity of diagnosis. Asking patients questions that characterize their acute diarrhea can be an important part of subjective assessment.

It is important to understand the factors that can confound assessment of a patient with acute diarrhea; these include medications, diet, and disease. A scheduled bowel regimen that includes laxatives and stool softeners can cause loose stools. If clinical suspicion exists that a patient has acute diarrhea, it would be prudent to discontinue the bowel regimen and observe the patient for another 24–48 hours.

Diarrhea is a chief complaint of patients on enteral tube feeds because of the absence of fiber and starches. Use of enteral tube feeds may promote a colonic environment susceptible to CDI resulting from increased small bowel colonization by colonic flora and decreased motility.12 Oncology patients are also at risk of developing acute diarrhea, as this condition can be an adverse effect of their chemotherapy regimen or a complication of their malignancy.

The importance of assessing other causes of diarrhea is important from a regulatory, public reporting, and financial standpoint. At the Centers for Disease Control and Prevention (CDC), C. difficile case definition is based only on laboratory identification (LabID) of a positive C. difficile result.13 Therefore, a patient with clinical CDI and a patient colonized with C. difficile would both count as CDC LabID event.

C. difficile cases are further classified as either community onset—identification occurs on or before hospital day 3—or facility-associated—if identification occurs on or after hospital day 4.14 Facility-associated C. difficile rates are now reportable to the public. Greenville Memorial Hospital was included on a 2016 Consumer Reports list of hospitals in the United States that received the lowest or second-lowest rating in preventing facility-associated C. difficile.15 The Centers for Medicare & Medicaid Services no longer reimburses hospital systems for facility-associated C. difficile cases.15

In summary, C. difficile infection is a clinical syndrome. As such, laboratory testing should be
coupled with patient assessment. Inappropriate laboratory testing can be minimized by taking an accurate patient history and minimizing factors that exacerbate acute diarrhea.

CB had a history of chronic constipation with inpatient and outpatient use of aggressive laxative therapy. The number of stools per day decreased with the discontinuation of part of her bowel regimen; however, because the C difficile PCR test was positive, she was labeled as a facility-associated C difficile case.

Incidence of CDI is on the rise; therefore, prevention is paramount. C difficile is the focus of antimicrobial stewardship programs across the country as judicious use of antimicrobials can minimize the risk of infection. Using antibiotics only when necessary and for the shortest effective duration are principles that can help curb incidence of CDI.

References