C. Difficile Infection

- **Basics**

Overview

Diarrhea is a frequent side effect of antibiotics, occurring 10–20% of the time. It usually gets better when the antibiotics are stopped. *Clostridium difficile* infection (CDI) is due to a toxin-producing bacteria that causes a more severe form of antibiotic associated diarrhea. The disease ranges from mild diarrhea to severe colon inflammation that can even be fatal. CDI usually occurs when people have taken antibiotics that change the normal colon bacteria allowing the *C. difficile* bacteria to grow and produce its toxins. Since 2000, there has been a dramatic increase in the number and severity of cases of *C. difficile* infection (CDI) in the US, Canada and other countries. *C. difficile* is a gram positive bacterium. This bacterium is everywhere in the environment, and produces spores that are hard to get rid of. *C difficile* produces two main toxins - toxins A and B - that cause inflammation in the colon.

Risk Factors

The major risk factor for CDI is taking antibiotics in the previous several weeks, but sometimes it occurs even without prior antibiotic use. High-risk antibiotics are clindamycin, cephalosporins, and quinolones (i.e. ciprofloxaxin, levofloxacin). Major risk factors are older age, weakened immune system, having other illnesses, and being in a hospital or a long-term care facility. However, even healthy individuals who have not had antibiotics can develop CDI. Patients with inflammatory bowel disease (Crohn's disease or ulcerative colitis) are more likely to get CDI, and may be sicker than patients with IBD alone or CDI alone. Many studies have also suggested that use of acid suppressive medications (proton pump inhibitors) may increase the risk of CDI. Individuals can pick up *C. difficile* by ingesting spores that are all around in the environment, especially in hospitals. Infected individuals excrete spores, and transmission among patients in hospital has been well documented.

Symptoms

Symptoms of CDI can vary. Diarrhea is the most common symptom; it is usually watery and, rarely, bloody, and may be associated with crampy abdominal pain. Associated symptoms are feeling poorly, fever, nausea and vomiting. Signs of severe disease include fever and abdominal distension and/or tenderness.

Screening/Diagnosis

C. difficile infection requires documenting the presence of toxin in the stools, usually by testing for the gene that produces toxin B, using a method called PCR. It is very sensitive, so it should not be used to test solid stools since that is likely a carrier state. An older test is an enzyme immunoassay test for toxin A and B, but it is less sensitive.

Treatment

First, it would be ideal to stop the antibiotic that led to the infection in the first place. This may not always be possible, however, as some infections, like severe bone or heart infections, need long-term antibiotics. If the symptoms are mild, metronidazole 500 mg, three times a day for ten days is recommended. If one cannot tolerate metronidazole's side effects, or early in pregnancy when it is not recommended, alternate treatment is vancomycin 125 mg, four times a day for ten days. If the patient does not get better after several days on metronidazole, a switch to vancomycin is recommended. Fidaxomicin is a new antibiotic that appears equivalent to vancomycin, but is much more expensive. Antidiarrheal drugs should never be used for CDI, as slowing down an inflamed colon may result in a severe complication called toxic megacolon.

Patients with severe disease may not have diarrhea if their colon is very inflamed. They are usually very sick, with fever, severe abdominal pain and tenderness. In such cases, oral vancomycin is the best choice. Sometimes intravenous metronidazole is added as well. In some patients, CDI is so severe that antibiotics do not work. When this happens, surgery to remove the colon may be needed to save the person's life.

While antibiotics are effective in treating most cases of CDI, the symptoms recur after the end of treatment in 10-20% of cases. This is called recurrent CDI and usually occurs 1–2 weeks after stopping treatment. After a recurrence, the chance of further recurrences goes up to 40-60%, perhaps because one is using an antibiotic to treat a disease caused by antibiotics. We presume that the normal colonic bacteria have not had a chance to recolonize. A common treatment is to give vancomycin in a pulsed regimen – taking it one day but then skipping a day, and increasing the number of days between doses. Perhaps this allows the normal bacteria to return on the "off antibiotic" days. The most effective treatment, however, is fecal microbiota transplant, also known as stool transplant. In studies, it has been effective in over 90% of patients who received the treatment, and has been proven effective with several randomized controlled trials.

Prevention

Wise antibiotic policies, by using narrow-spectrum agents when directed and avoiding unnecessary use of broad-spectrum antibiotics, are key in the prevention of CDI. Environmental cleaning is important – especially hand washing with soap and water, since alcohol gels do not inactivate spores. In hospitals, everyone entering the room of a patient with CDI should wear a gown, gloves, and use disposable equipment.

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