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Clostridium difficile Bacteremia in an Immunocompetent Child

Clostridium difficile is an anaerobic gram-positive rod known to colonize the gastrointestinal tract and is a major cause of antibiotic-associated diarrhea and the primary cause of pseudomembranous colitis (3). It is currently recognized as an important nosocomial enteric pathogen (4, 9, 11). In contrast, very few cases of *C. difficile* bacteremia or other extraintestinal illness have been reported (2, 6, 7), and these have occurred mainly when a severe underlying disease was present. In most cases of septicemia, the source of infection has been found to be the gastrointestinal tract, as suggested by isolation of *C. difficile* with other intestinal bacteria (9).

We report a case of *C. difficile* bacteremia in a nonneutropenic patient who had received a prolonged course of antibiotics. The patient, a 3-year-old boy, had been well until 11 days earlier, when he began to experience fever and odynophagia. A physician made a diagnosis of tonsillitis and prescribed amoxicillin-clavulanic acid. Three days later, amoxicillin-clavulanic acid was replaced by cefixime. Seven days later fever disappeared and cefixime was suspended. After 24 h, the child's temperature rose to 38.4°C and he was admitted to the hospital, where a diagnosis of acute pericarditis with pericardial effusion was made.

The patient's additional past medical history consisted only of talasemia minor and five episodes of tonsillitis during the year before admission.

In addition to having a temperature of 38.4°C, the patient had a pulse rate of 163/min, a respiratory rate of 40/min, and blood pressure of 127/61 mm Hg. No dyspnea or cyanosis was present.

On cardiac examination, a pericardial friction was detected but no murmur was heard. The abdomen was normal except that a nontender liver edge descended 4 cm below the right costal margin. Findings of the remainder of the examination were unremarkable. An electrocardiogram revealed sinus tachycardia, and an echocardiogram showed severe pericardial effusion.

The patient's urine was normal. The hematocrit was 29.9%, and the leukocyte count was 14,140, with 69% neutrophils, 2% band forms, 22% lymphocytes, and 7% monocytes. The platelet count was 173,000, and the erythrocyte sedimentation rate was 79 mm/h. The hemoglobin level was 8.8 g/dl, and the hemoglobin A2 was 2.93%. Blood urea nitrogen, glucose, sodium, potassium, and calcium and serum aspartate aminotransferase were within normal limits. Tests for antinuclear antibodies and rheumatoid factor were negative. Serologic tests for toxoplasma, mycoplasma, and varicella virus were negative. The echovirus titer was 1/8, and tests for coxsackie virus groups B1 to B6 yielded titers of 1/16 for B2 and 1/32 for B3.

Specimens of blood were sent for culture; fluid, acetylsalicylic acid, and ranitidine were given to the patient. Antibiotic therapy with cefotaxime (800 mg every 8 h intravenously [i.v.]) was administered. On the following days, pericardial effusion decreased but the patient remained febrile. On the fifth hospital day, new specimens of blood were sent for culture (three different sets of aerobic and anaerobic flasks). Mild gastrointestinal signs were noted, but no stool specimens were sent to the laboratory. On the seventh hospital day, all the second anaerobic blood cultures (BacT/Alert blood culture system; Organon Teknika Corporation, Durham, N.C.) yielded an anaerobic gram-positive rod. The colonies appeared dry and were grey-brown on anaerobic blood agar; they smelled like horse manure. *C. difficile* was identified by the Vitek ANI card (bioMérieux Vitek-Aust. Pty. Ltd.), and toxin A was detected in the strain isolated from blood cultures (Meridian Diagnostics Premier C. difficile Toxin A EIA). Susceptibility testing was performed by E test (AB Biodisk, Solna, Sweden), by following the manufacturer's instructions. The strain was sensitive to penicillin G (MIC = 0.75 mg/liter), piperacillin-tazobactam (MIC = 6 mg/liter), clindamycin (MIC = 2 mg/liter), and metronidazole (MIC = 0.125 mg/liter) and resistant to cefoxitin (MIC > 256 mg/liter) and imipenem (MIC > 32 mg/liter).

In view of these results, cefotaxime was suspended and the patient was treated with vancomycin (200 mg every 6 h i.v.). After 24 h, the patient became afebrile and treatment with vancomycin was continued for 12 days. The patient was discharged.

C. difficile is a spore-forming organism that can be found in the environment, with a limited number of species commonly encountered as agents of infection in properly collected clinical specimens from humans (5). It is responsible for asymptomatic colonization, but in nonhospitalized asymptomatic adults carriage is uncommon (8). On the other hand, prevalence in hospitals is particularly high (10 to 15%), with the organism playing a major role in intestinal diseases ranging from antibiotic-associated diarrhea to pseudomembranous colitis (10).

Since 1962, only a few cases of septicemia have been described, with reports of isolation of the organism from patients after war wounds, crush injuries, abscesses, or penetrating abdominal traumas. It is also recognized that the bowel is the primary site of colonization of *C. difficile* and that the infections usually involve other pathogens.

In the case presented here, the patient had received a prolonged course of treatment with cephalosporins, which probably caused a change in the microflora of the bowel which allowed the bacteremia to occur. Although the possibility exists that the isolation of *C. difficile* represents contamination of blood cultures rather than a true infection, it seems improbable in this case because all blood cultures (three different sets) were positive and vancomycin clearly was effective in decreasing fever. Although the patient presented only mild symptoms of gastrointestinal disease, there have been reports of bacteremia and other extraintestinal infections by *C. difficile* that were not always associated with diarrhea or intestinal pathology (1).

The prolonged course of treatment with antibiotics that our patient underwent occurred mainly before admission to the hospital. Physicians should be aware of the potential of *C. difficile* to cause invasive disease and consider the possibility of adverse effects after antibiotic therapy.

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