Persistence of an Endemic (Toxigenic) Isolate of Clostridium difficile in the Environment of a General Medicine Ward

The epidemiology of Clostridium difficile-associated diarrhea (CDAD) in an endemic setting was investigated by use of DNA typing methods to determine the strain identity of C. difficile isolates. Two predominant toxigenic clones were found in the environment and accounted for 29.8% (type 1) and 15.5% (type 2) of CDAD cases, respectively. In endemic settings, the environment and cross-transmission may play a role in acquisition of CDAD.

Toxigenic Clostridium difficile is the cause of C. difficile-associated diarrhea (CDAD), which is a significant and increasingly common cause of morbidity in hospitals. Most studies concerning the epidemiology of CDAD have been outbreak investigations [1–3]. The epidemiology of this nosocomial infection in nonoutbreak situations is not well defined. Recently we reported the isolation of a wide variety of genotypes of C. difficile from patients and their environment on an oncology ward [4]. That study found no correlation between environmental and patient isolates, suggesting endemic CDAD was not spread clonally. In the present longitudinal study, we further investigate the epidemiology of endemic CDAD on a general medicine ward and found that the persistence and the prevalence of the 2 predominant endemic strains of C. difficile in the environment of this ward were correlated with their isolation from patients with CDAD.

The general medicine ward at the University of California Davis Medical Center (UCDMC) is a 41-bed unit that serves geriatric and general medicine patients and includes a 4–6 bed AIDS unit. The incidence of CDAD during the 2-year study period (April 1995 to April 1997) was 17.20 cases per 1000 discharges. Stool specimens from all patients with diarrhea on the ward were cultured for C. difficile on the selective medium cycloserine-cefoxitin-fructose (CCFA) agar plates [5]. Specimens from selected sites (bedroom and bathroom floors, toilet seats, and bedpans) in rooms were cultured every 2 weeks in rotation. Cultures were done using replicate organism detection counting contact plates containing the selective medium CCFA. All cultures were grown anaerobically at 37°C for 48 h. Presence of toxin A and B gene sequences and strain identity of patient and environmental isolates were determined, as described elsewhere [6–8], using PCR and arbitrarily primed PCR (AP-PCR), respectively.

During the study period, 84 cases of clinical CDAD were identified on this ward (9 stool specimens from case patients were lost). Ninety-two C. difficile strains were isolated from 206 stool specimens that were submitted to our laboratory. Seventeen isolates were from patients who had diarrhea but whose stool was negative for the presence of toxin B, according to the cytotoxicity assay. Seventy-nine isolates (82.3%) had the toxin A and B gene sequences targeted by our primers, and the other 13 (14.1%) were negative for these gene sequences. Among the 92 isolates, 42 AP-PCR types were identified. The predominant type (type 1) was associated with 29.8% cases of CDAD (25 of 84). A second endemic strain, type 2, was associated with 15.5% of cases of CDAD in this ward.

Culturing of specimens from 1202 sites in the ward environment yielded 196 C. difficile isolates, of which 173 (88.2%) had toxin A and B gene sequences, whereas only 23 (11.7%) were nontoxigenic. The predominant patient type, type 1, accounted for 51% of all the environmental isolates and was recovered throughout the ward during the 2-year period. Type 2, which was associated with a significant number of CDAD cases, accounted for 11.2% of environmental isolates. Figure 1 shows
Figure 1. Epidemic curve of cases of *Clostridium difficile*-associated diarrhea due to arbitrarily primed PCR types 1 and 2 isolated from patients and the environment (environmental sampling was not done April–June 1995).

The percentages of *C. difficile* type 1 and 2 isolated from patients and the environment. In addition to these 2 predominant endemic strains, 22 other AP-PCR types were identified among the environmental isolates.

No true outbreaks occurred in this ward during the study period; however, clustered cases of diarrhea due to the 2 predominant toxigenic strains of *C. difficile* were observed. The persistence of these strains in the ward and their isolation from a significant number of case patients suggest that the environment contributed to the acquisition of CDAD by patients in the ward. Our study also showed that the transmission of endemic *C. difficile* infection in this ward was restricted to specific strain types (types 1 and 2) that were associated with a high number of CDAD cases. These endemic strains were associated with CDAD cases that occurred in different rooms, suggesting the possibility of transmission by medical personnel as well, as has been reported by others [9]. In addition to the predominant types, a wide diversity of strain types were also identified in the patient population that were not present in the environment. This observation seems to indicate that a large number of the patients may be endogenously colonized with *C. difficile* and serve as a reservoir and source of *C. difficile*, as has been documented in the literature [10].

The findings of this study can be summarized as follows. In high-incidence settings of endemic CDAD, the environment and cross-transmission contribute to the acquisition of nosocomial CDAD. Two toxigenic strains found predominantly in the environment were associated with a significant number of cases. This epidemiological pattern resembles that observed in outbreak situations, where a high number of cases are associated with a single strain [1, 2]. The great diversity of strains simultaneously isolated from cases of clinical CDAD also points to an endogenous source of *C. difficile* infection. We continue to investigate patient-centered risk factors and medical and nursing practices, and we are initiating molecular studies on the virulence of these predominant strains.

Department of Internal Medicine, Division of Infectious and Immunologic Diseases, University of California Davis Medical Center, Sacramento, California

References

6. Tang YJ, Gumerlock PH, Weiss JB, Silva J Jr. Specific detection of *Clost-
Rapidly Progressive Necrotizing Fasciitis and Gangrene Due to Clostridium difficile: Case Report

A case of rapidly progressive necrotizing fasciitis and gas gangrene due to Clostridium difficile that responded very well to surgical intervention is described.

Antibiotic-associated diarrhea and pseudomembranous enterocolitis are known to be associated with Clostridium difficile infection. C. difficile organisms may be isolated from the intestinal tract of healthy neonates, neutropenic patients with hematologic malignancy [1, 2], elderly patients with diarrhea in long-stay units, and hospitalized patients. Very few cases of extraintestinal infection due to C. difficile have been reported in the literature [3, 4]. Cases have been reported of necrotizing fasciitis due to infection by Clostridium species, including C. perfringens, C. septicum, C. ramosum, and other species. We report a case of rapidly progressive necrotizing fasciitis and gas gangrene due to C. difficile infection.

A 59-year-old woman with no significant medical history was admitted to the hospital after a motor vehicle accident. She was initially treated for multiple injuries of the face, lower extremities, and abdominal bruises secondary to trauma, and wound debridement was required. On the third day, she was found to have gangrene of the left leg and thigh. The patient had a body temperature of 39.4°C and an elevated WBC count of 14,300/mm³. Blood culture did not show growth of any organism. Extensive debridement of skin and subcutaneous tissue and fasciotomy were done, and therapy was started with multiple antibiotics, including intravenous penicillin, vancomycin, and imipenem.

Figure 1. Gram-stained touch preparation of necrotic tissue from a patient with rapidly progressive necrotizing fasciitis and gangrene due to Clostridium difficile, showing gram-positive rods with subterminal spores (arrow) (original magnification, ×100).