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Carbapenem-Resistant Enterobacter cloacae Isolates Producing KPC-3, North Dakota, USA

To the Editor: Carbapenem-resistant Enterobacteriaceae (CRE) continue to emerge as a serious public health threat throughout the world (1). CRE infections in the United States are often mediated by acquisition of Klebsiella pneumoniae carbapenemase (KPC) expressed by Klebsiella spp., although KPC is also found in other genera (2). The spread of KPC-producing, gram-negative bacteria in hospitals has been linked to severity of illness, co-existing medical conditions, exposure to antimicrobial drugs, and need for chronic care (3).

After reporting of CRE infections to the North Dakota Department of Health became mandatory in 2011, a total of 20 CRE cases were noted in 12 of 53 counties (2.9 cases/100,000 population) (4). Most cases involved infection with Enterobacter cloacae and occurred in Cass County, where the state’s largest city, Fargo, is located. We describe an outbreak of clonal carbapenem-resistant E. cloacae in a health care system in Fargo.

Sanford Health is a 583-bed, acute-care facility, representing 70% of acute-care beds in Fargo. The hospital handles >27,000 admissions/year and serves as a referral center for a large area of the state, and the only long-term acute-care (LTAC) facility in the eastern half of the state operates on its campus. During December 2011–December 2012, all isolates of Enterobacteriaceae with reduced susceptibility to ertapenem (MIC ≥1 µg/mL) identified at the hospital’s clinical microbiology laboratory were screened for carbapenemase production by using the modified Hodge test (mHT), according to Clinical and Laboratory Standards Institute recommendations (5). Identification and susceptibility testing were done with the MicroScan system (Siemens Healthcare Diagnostics, Tarrytown, NY, USA); MICs of carbapenems were confirmed with Etest (bioMérieux, Durham, NC, USA). Three carbapenem-resistant E. cloacae isolates from documented cases of CRE infection at the hospital during 2010 were analyzed for comparison.

To characterize carbapenem-resistant and mHT-positive isolates, we used PCR to amplify and sequence the carbapenemase genes bla_{IMP}, bla_{NDM}, bla_{VIM}, and bla_{KPC} by using established methods (6). The upstream sequence of bla_{KPC}-positive strains was analyzed to determine the isoform of the transposon Tn4401 that harbored bla_{KPC} (7). We investigated genetic similarity among isolates by repetitive sequence-based PCR; isolates with >95% similarity were considered clonal (6). We also sequenced the highly conserved hsp60 gene (8) and attempted conjugative transfer of the bla_{KPC} gene by growing KPC-producing E. cloacae along with sodium azide-resistant Escherichia coli J-53. As part of the study, we examined records of patients from whom carbapenem-resistant E. cloacae was isolated. The study was approved by the Institutional Review Board at Sanford Health.

During December 2011–December 2012, a total of 19 single-patient E. cloacae isolates and 1 E. aerogenes isolate had positive mHT results. bla_{KPC} was detected in 17 of the 19 E. cloacae isolates and in the 3 carbapenem-resistant E. cloacae isolates from 2010. For all 20 of those isolates, sequencing revealed bla_{KPC3} in association with isoform d of the transposon Tn4401, and all isolates were clonally related (Figure). All 20 isolates also had an identical hsp60 sequence belonging to cluster VI in the Hoffman and Roggenkamp scheme (8). Conjugation of a bla_{KPC}-containing plasmid into E. coli J-53 was successful for 1 strain.

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All 20 of the patients from whom KPC-producing CRE isolates were obtained (17 from this study, 3 from 2010) had been hospitalized at Sanford Health during the 3 months before CRE isolation; 13 (65%) were admitted to intensive care. In addition, 13 (65%) patients had been admitted to the LTAC during the year before CRE isolation. Co-colonization with multidrug-resistant bacteria was documented in 16 (80%) patients, including extended-spectrum β-lactamase–producing and carbapenem-resistant organisms in 4 and 2 patients, respectively. Seven (35%) patients died; 3 (15%) deaths were attributed to CRE infection. One of the patients was a neonate 30 days of age.

The finding of KPC-3–producing \textit{E. cloacae} in North Dakota contrasts with the predominant epidemiology of CRE across the United States. Most CRE cases nationwide are caused by KPC-producing \textit{K. pneumoniae} (2). KPC-type β-lactamases were previously identified in diverse strains of \textit{Enterobacter} spp. from an urban health care system in Detroit, accounting for ≈15% of CRE (9). In contrast, our genetic analysis reveals a uniform genetic background among KPC-producing \textit{E. cloacae}, which suggests horizontal dissemination of an outbreak strain.

Because active surveillance programs do not exist at our facility, this study probably underestimates the extent of CRE spread. We found that patients with KPC-producing \textit{E. cloacae} in this sample were exposed to an LTAC and concomitantly were colonized or infected with other multidrug-resistant organisms (9). Although the spatio-temporal origin of the outbreak (acute care vs. LTAC) remains undefined, these findings likely reflect longer exposure to the continuum of care and higher rates of co-existing conditions within the LTAC population. This outbreak of KPC-producing \textit{E. cloacae} infections in a health care system in North Dakota highlights the infection control challenges of long-term care facilities and the potential role they play in CRE dissemination.

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**Figure.** Genetic typing of carbapenem-resistant \textit{Enterobacter cloacae} identified from patients at Sanford Health in Fargo, North Dakota, USA. Repetitive sequence–based PCR was used. The dendrogram at left displays the percentage similarity among band patterns shown at right. Isolate numbers ND 1, ND 4–5, ND 7–14, and ND 18–23 indicate \textit{Klebsiella pneumoniae} carbapenemase (KPC) 3–producing \textit{E. cloacae} isolates isolated during December 2011–December 2012; ND A–C indicate KPC-3–producing \textit{E. cloacae} isolated during 2010. All KPC-3–producing \textit{E. cloacae} isolates share >97% similarity, indicating a clonal strain. ND 15 and 16 are \textit{E. cloacae}, and ND 17 is \textit{E. aerogenes}, genetically distinct and without carbapenemases.
Urethritis Caused by Novel Neisseria meningitidis Serogroup W in Man Who Has Sex with Men, Japan

To the Editor: We report a case of urethritis caused by a novel multilocus sequence type (ST), 10651, of the ST11/electrophoretic type (ET)–37 complex Neisseria meningitidis serotype W. The patient was a man who has sex with men. We also report on the patient’s male partner, who was colonized with the same bacteria.

In March 2013, a 33-year-old Japanese man sought medical care at Shirakaba Clinic (Tokyo) after experiencing a urethral discharge for 4 days. The man was HIV positive (CD4 count 649 cells/mL) but was not receiving antiretroviral therapy. Physical examination showed a mucous urethral discharge. Gram staining of a sample revealed many gram-negative diplococci phagocytosed by polymorphonuclear leukocytes. Eleven days before seeking care, the patient had oral and anal intercourse with his male partner. A diagnosis of suspected urethritis caused by Neisseria gonorrhoeae was made, and a sample of the urethral discharge was sent for culture and testing (Strand Displacement Amplification) for N. gonorrhoeae and Chlamydia trachomatis. The patient was intravenously administered a single dose of ceftriaxone (1 g) (intramuscular administration of ceftriaxone is not approved in Japan). He was also given a single dose of azithromycin (1 g orally) for possible C. trachomatis urethritis (I).

Six days after receiving treatment, the patient showed improvement. Results of the Strand Displacement Amplification test were negative for N. gonorrhoeae and C. trachomatis. Eight days after receiving the patient received treatment, the culture for the urethral discharge sample was shown...