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Outbreak of *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* bloodstream infections at an outpatient chemotherapy center

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Abstract

Background: Four patients were hospitalized July 2011 with *Pseudomonas aeruginosa* bloodstream infection (BSI), 2 of whom also had *Klebsiella pneumoniae* BSI. All 4 patients had an indwelling port and received infusion services at the same outpatient oncology center.

Methods: Cases were defined by blood or port cultures positive for *K pneumoniae* or *P aeruginosa* among patients receiving infusion services at the oncology clinic during July 5-20, 2011. Pulsed-field gel electrophoresis (PFGE) was performed on available isolates. Interviews with staff and onsite investigations identified lapses of infection control practices. Owing to concerns over long-standing deficits, living patients who had been seen at the clinic between January 2008 and July 2011 were notified for viral blood-borne pathogen (BBP) testing; genetic relatedness was determined by molecular testing.

Results: Fourteen cases (17%) were identified among 84 active clinic patients, 12 of which involved symptoms of a BSI. One other patient had a respiratory culture positive for *P aeruginosa* but died before blood cultures were obtained. Available isolates were indistinguishable by PFGE. Multiple injection safety lapses were identified, including overt syringe reuse among patients and reuse of syringes to access shared medications. Available BBP results did not demonstrate iatrogenic viral infection in 331 of 623 notified patients (53%).

Conclusions: Improper preparation and handling of injectable medications likely caused the outbreak. Increased infection control oversight of oncology clinics is critical to prevent similar outbreaks.

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Keywords

Outpatient oncology care; Injection safety; *Klebsiella pneumonia*; *Pseudomonas aeruginosa*

On July 18, 2011, district health officials at the Mississippi State Department of Health (MSDH) were notified by a local hospital infection preventionist of a cluster of *Pseudomonas aeruginosa* bloodstream infections (BSIs) involving 4 patients hospitalized between July 9 and July 16, 2011. Two of these patients also had *Klebsiella pneumoniae* BSI. The 143-bed hospital serves as a regional referral center for several surrounding rural counties. All 4 patients had an indwelling infusion port and were receiving infusion services at the same local oncology clinic.

An initial investigation of the clinic by MSDH on July 18 did not identify a potential source for the infections; however, on that same day, 4 additional patients were admitted to the hospital with catheter-associated BSIs, all of whom received care at the same oncology center. Given the report of these additional infections, on July 20, the oncology clinic was closed under a public health order as an imminent public health threat. This report summarizes the findings of a public health investigation conducted to determine the cause and extent of the outbreak.

METHODS

For this study, a case was defined as a blood or port culture positive for *K pneumoniae* or *P aeruginosa* in a patient receiving infusion services at the oncology clinic during July 5-20, 2011. All patients actively receiving infusion services at the oncology clinic during this period were contacted and assessed for symptoms of a BSI or device-associated infection (eg, port-related infection). Regular communication was maintained with regional hospital infection preventionists to identify any hospital admissions from this group of patients. In addition, each patient's primary care physician was notified of the potential risk of infection and asked to monitor patients for relevant symptoms and to report any associated infections to public health authorities.

Patient isolates associated with the outbreak were sent to the Centers for Disease Control and Prevention (CDC) for analysis by pulsed-field gel electrophoresis (PFGE) to assess for genetic relatedness. In brief, chromosomal DNA from the *K pneumoniae* isolates was digested with the restriction endonuclease XbaI, under run conditions with switch times of 5 and 40 seconds and a total run time of 22 hours. DNA from the *P aeruginosa* isolates was digested with SpeI, and run conditions were switch times of 5 and 40 seconds for 21 hours. The genetic relatedness of the isolates was analyzed using BioNumerics software (Applied Maths, Austin, TX). Isolates were considered genetically related if their patterns were >90% similar.

After the clinic closed, MSDH conducted an extensive site evaluation, including in-depth interviews of current and former clinic staff, to identify potential modes of transmission. Infection control practices related to the storage and handling of parenteral medications,

including preparation of saline solution and heparin syringes for flushing central lines, as well as infusion techniques, were reviewed with clinic staff.

Infection control issues discovered during this investigation that might have predated the current outbreak prompted MSDH to notify all patients ever treated at the outpatient oncology center of their potential exposure to harmful practices and advising them to seek testing for viral blood-borne pathogens, including human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV). A review of clinic records was matched against the Mississippi vital statistics registry to identify all living patients who had received care at the clinic since it opened in January 2008. A letter was sent to all identified patients, and free blood-borne pathogen testing was offered at MSDH county clinics.

Blood samples positive for blood-borne pathogens were sent to the CDC for verification and molecular testing. Because HCV was the sole blood-borne pathogen in which active infection was identified in more than 1 patient, molecular testing was performed for HCV-positive samples only. HCV RNA was extracted from positive samples, and the NS5b gene region was amplified as described previously.[1] Samples that were NS5b- positive were subjected to HVR1 quasi-species amplification. The E1/E2 junction region, which contains the HVR1 region, was amplified using the endpoint limiting-dilution (EPLD) real-time nested polymerase chain reaction (PCR) protocol described by Ramachandran et al.[2] Nested NS5b and HVR1 amplicons derived from the PCR amplification were purified (PCR Purification Kit; Qiagen) and sequenced with their respective nested primers using the BigDye v3.1 chemistry sequencing kit and an ABI 3130xl automated sequencer (Applied Biosystems, Foster City, CA) as described previously.[1]Maximum likelihood phylogenetic trees were then constructed using MEGA version 5 (http://www.megasoftware.net/).

RESULTS

Fourteen cases were identified among 84 patients who received infusion services at the oncology clinic between July 5 and 20, 2011. Initial dates of culture positivity ranged from July 9 to August 26, 2011 (Fig 1). Among the 14 cases, cultures identified *K pneumoniae* in 3 patients, *P aerguinosa* in 4 patients, and both *K pneumoniae* and *P aeruginosa* in 7 patients. All 14 patients had an indwelling port; 11 patients had their first positive culture from blood, and 3 had their first positive culture from an explanted port. Twelve of the patients had symptoms consistent with a BSI, including fever, nausea, vomiting, and lethargy, in addition to pain at the port implantation site. Two patients were asymptomatic and underwent elective port removal, which was found to be culture-positive. One patient with *K pneumoniae* bacteremia also had *P aeruginosa* growth from a respiratory specimen. One other patient died from sepsis before the acquisition of blood cultures; this patient had a respiratory specimen that yielded *P aeruginosa* and was classified as a probable case. No other known exposure besides the oncology clinic was identified in the 15 patients, including the probable case. Patient age ranged from 46 to 91 years. All 15 patients were hospitalized, with admission dates between July 9, 2011, and August 25, 2011.

PFGE analysis of available *K pneumoniae* and *P aeurginosa* isolates from 8 different patients demonstrated indistinguishable banding patterns (Figs 2 and 3). A *P aeruginosa*

isolate from a respiratory specimen of a patient with *K pneumoniae* BSI also matched the outbreak strain.

The oncology clinic was a freestanding facility operated by a single physician, who served as the medical director, assisted by 2 registered nurses and several administrative staff members. All port access and infusion services were rendered by the 2 nurses and by an administrator who had been trained by previous staff and the physician medical director. Both nurses were recent associate degree graduates from nursing school with no previous experience with chemotherapy or infusion services. Neither had received any specialty training in chemotherapy administration. Minimal onsite training was provided by the physician medical director and the non–medically trained administrator.

In-depth interviews identified a recent change in protocol that might have led to unsafe injection practices. As a reported costcontainment measure, starting on July 5, 2011, staff nurses were directed by the physician medical director to use common-source 1-L saline and 1-L heparin flush bags rather than single-dose vials for all port and line flushes. These bags were used over several days for multiple patients. A single syringe was dedicated to each patient to draw up the saline flush for the entire day; each syringe could be reused multiple times to access the common bag of saline solution before being discarded at the end of the day. Other syringes were dedicated to drawing up the heparin flush for all patients from the common-source heparin flush bag. These heparin syringes were shared among multiple patients over an indeterminate period of time, and in many cases were discarded only if visible blood was seen in the syringe. In addition, some syringes were dedicated for mixing nonchemotherapy medications in smaller, individual-unit doses. These syringes were used over many days and stored up to several months at a time in a nonsterile drawer. There was no indication that any of these specific syringes were used directly on patients.

Interviews with former staff members suggested that the identified injection safety lapses, particularly the overt reuse of syringes among patients, could have occurred at any time before July0 5,2011. In light of this, 623 living patients who had been seen at the clinic between January 2008 and July 2011 were notified of a recommendation for testing for blood-borne pathogens. Of the 331 of these 623 patients with available test results, 37 had evidence of current or resolved HBV or HCV infection, with 4 demonstrating evidence of previous infection with both. Twenty-eight patients had evidence of resolved HBV infection (hepatitis B surface antigen negative and core antibody positive), and 1 patient had chronic HBV infection (hepatitis B surface antigen positive). No temporal clustering of patients with resolved HBV infection was identified. Twelve patients had detectable antibodies to HCV. Five of these patients had detectable HCV RNA, of whom 4 had sufficient RNA for HVR1 quasi-species determination by EPLD. Phylogenetic analysis of the NS5b and intrahost HVR1 sequences revealed the absence of intermixing of HCV variants among individuals and no evidence of genetic relatedness to suggest iatrogenic transmission.

Additional risk factor data were available for 32 of the 37 patients who had current or resolved HBV or HCV infection, 8 of whom were previously aware of their infection. Eighteen patients had some potential additional risk factor for the acquisition of bloodborne pathogens, including blood transfusions before 1992 (n = 7), HCW (n = 5), tattoos (n = 11),

household contact with hepatitis (n = 2), and intravenous drug abuse (n = 1). No patient tested positive for HIV.

DISCUSSION

We describe an outbreak of *K pneumoniae* and *P aeruginosa* BSIs in patients undergoing infusion procedures at an outpatient chemotherapy infusion center. We identified 14 confirmed cases and 1 probable case involving a fatality in a patient with *P aeruginosa* isolated from a respiratory specimen. All available clinical isolates of *P aeruginosa* and *K pneumoniae* shared indistinguishable PFGE patterns, consistent with a common source outbreak. We identified several lapses in the preparation and handling of injectable medications that could have resulted in crosscontamination with subsequent spread of infection to multiple patients. Similar lapses in injection safety have been implicated in previous outbreaks of invasive bacterial infections,[3-6] including BSIs, meningitis, and epidural abscess, and have led to transmission of blood-borne viruses.[7-9]

Of most concern were our findings of syringe reuse among patients as well as syringe reuse to access shared medications (eg, saline bag), demonstrating a lack of adherence by clinic staff to fundamental principles of injection safety.[9,10] Because of the severity of these lapses and the associated risk of blood-borne pathogen exposure,[7,9] and because these lapses may have occurred after the clinic first opened, 623 clinic patients were notified to undergo blood-borne pathogen testing. To our knowledge, this is only the second patient notification for blood-borne pathogen testing owing to unsafe injection practices in the context of a bacterial outbreak. The first patient notification event that involved a bacterial outbreak was also prompted by the finding of syringe reuse to access shared medication vials.[5]

To prevent transmission of infections to patients, all providers should adhere to safe injection practices as part of Standard Precautions.[10] These include using a new syringe and needle for each patient and for accessing medication vials or bags, promptly disposing a syringe and needle after each use, and not using saline or heparin bags as a common source supply for multiple patients.[9-12]

This study has some limitations. Given the multiple ongoing injection safety lapses, the exact route of transmission for this outbreak cannot be determined. Among patients who were notified for blood-borne pathogen testing, results were available for only 53%; only a small number of these patients had detectable virus (ie, HCV) that could be assessed for genetic relatedness. Thus, the transmission of blood-borne pathogens in this clinic cannot be definitively excluded.

Outpatient settings are accounting for an increasing proportion of total health care delivery. In Mississippi, as in most states, there is no official oversight of infection control practices in outpatient facilities that are not certified by the Centers for Medicare & Medicaid Services, such as outpatient oncology clinics. In Mississippi, the facility medical director and nurses have direct responsibility for maintaining proper infection control procedures; however, no specific nurse training is required to provide infusion services. The state board of medical licensure and the state nursing boards serve as the only backstop to address unacceptable

practices of the individual provider, but these functions are typically exercised only after an untoward effect has occurred. In addition, most outpatient facilities lack a system for detecting infections associated with care. In many cases, outbreaks originating in outpatient settings are detected by hospitals to which affected patients have been admitted, as was the case in this outbreak. The vigilance of the hospital infection preventionist and her close relationship with the local health department was critical to the successful detection and control of this outbreak.

In response to reports of outbreaks involving outpatient oncology settings,[3,4,7,8] the CDC launched a campaign in October 2011 that featured new tools and resources to prevent infections among oncology patients.[11] These features include a basic infection control plan containing key policies and procedures that any outpatient oncology facility can implement to standardize and improve its infection prevention practices.[12] Continued efforts to increase facility awareness of these infection control resources and implementation of recommended practices are needed to protect this vulnerable subset of outpatients.

Acknowledgments

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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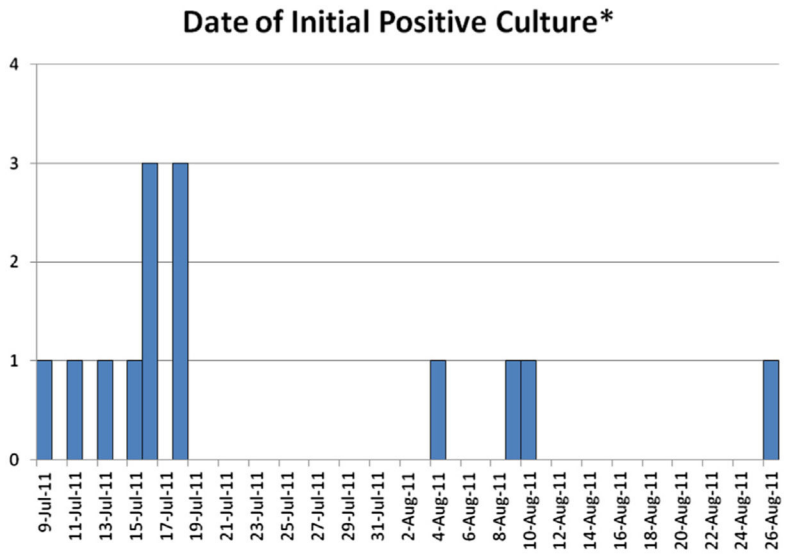

Fig 1.

K pneumoniae and *P aeruginosa* cases by date of first positive blood or port culture, July-August 2011. *Initial positive cultures obtained on August 4, August 10, and August 26, 2011, were obtained from explanted ports that had been removed electively or because of local inflammation.

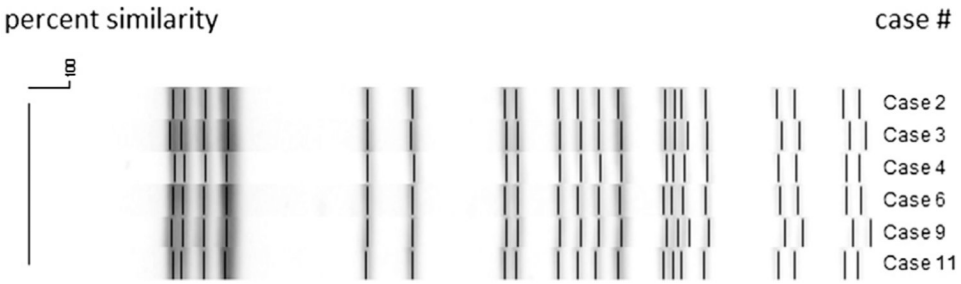

Fig 2.
PFGE of available *K pneumoniae* outbreak isolates, July-August 2011.

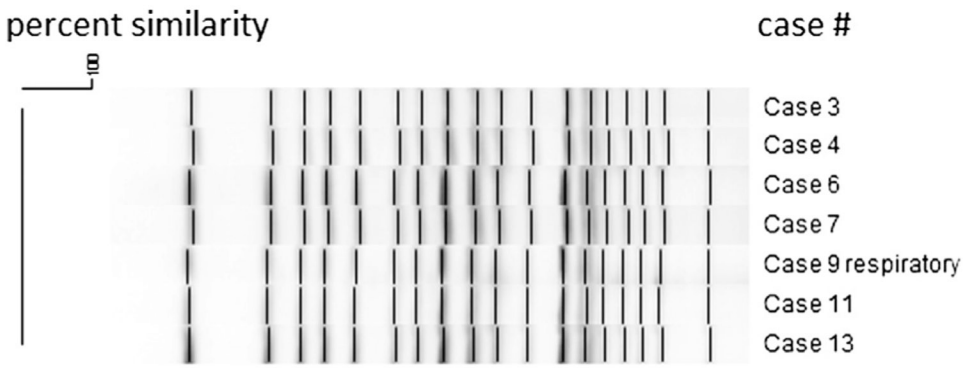

Fig 3.
PFGE of available *P aeruginosa* outbreak isolates, July-August 2011.