**Outbreak of Infection with *Klebsiella pneumoniae* Sequence Type 258 Producing *Klebsiella pneumoniae* Carbapenemase 3 in an Intensive Care Unit in Italy**

Gram-negative pathogens producing carbapenemases represent an alarming clinical threat with serious effects on patient outcomes (3, 7). In 2001, Yigit et al. (11) reported a novel β-lactamase termed “*Klebsiella pneumoniae* carbapenemase” (KPC-1) in North Carolina. KPC-producing strains are now emerging worldwide (5, 6, 8, 9). We report here an outbreak of infection and colonization with KPC-producing *K. pneumoniae* (KPC-Kp) occurring in Palermo, Italy.

Between 9 April and 1 September 2009, 13 inpatients who had been admitted at the second intensive care unit (ICU), ARNAS Civico and Benfratelli General Hospital of Palermo, Italy, were infected or colonized by a carbapenem-resistant *K. pneumoniae* isolate (Table 1). The ICU is a 10-bed medical-surgical unit with approximately 430 admissions per year. Pre-existing medical or surgical conditions were present in 50% approximately of all admissions. Organ failure was the leading cause of admission (70%), followed by treatment with mechanical ventilation (30%). The mean simplified acute physiology score (SAPS) of ICU patients was 39. ICU mortality was 24%. Nurse-to-patient ratio was 1:2. Ten out of the 13 patients were infected and five died, with the KPC-Kp infection being identified as a contributing factor. Five patients were transferred to other care units of the same hospital, but two moved to an external rehabilitation unit. All infections appeared to be nosocomially acquired based upon their onset compared to ICU admission day of the 10 patients. However, it was not possible to rule out the possibility that the index patient could have been colonized at the time of admission, because active surveillance cultures were not being routinely performed at the beginning of the outbreak.

Infection control measures, including undertaking contact precautions, grouping infected/colonized patients into cohorts, and using dedicated staff and equipment as much as possible, were implemented as indicated by the Centers for Disease Control and Prevention (CDC) guidelines for control of infection with carbapenem-resistant or carbapenemase-producing *Enterobacteriaceae* in acute care facilities (1). Active-surveillance rectal cultures were collected at admission and then on a weekly basis from all patients staying in the ICU more than 48 h. Microbiology records of the ICU for the preceding 12 months were reviewed, but carbapenem-nonsusceptible *K. pneumoniae* or other *Enterobacteriaceae* had not been previously detected. The outbreak was eventually controlled by September 2009.

Thirty-three isolates showing reduced susceptibility to ertapenem (i.e., MIC of >4 mg/liter) were collected from the 13 patients, predominantly from respiratory secretions and blood. Identification (ID) and antimicrobial susceptibility testing (AST) were routinely performed using the Vitek-2 system (bioMérieux, France). The 33 KPC-Kp strains were resistant to imipenem (MICs, ≥16 μg/ml), meropenem (MICs, 32 μg/ml), and ertapenem (MICs, ≥8 μg/ml). They were also resistant to amikacin (MICs, ≥64 μg/ml), amoxicillin-clavulanic acid (MICs, ≥32 μg/ml), cefepime (MICs, 8 μg/ml), cefotaxime (MICs, 8 μg/ml), ceftazidime (MICs, ≥64 μg/ml), ciprofloxacin (MICs, ≥4 μg/ml), levofloxacin (MICs, ≥8 μg/ml), piperacillin-tazobactam (MICs, ≥128 μg/ml), tobramycin (MICs, ≥16 μg/ml), and trimethoprim-sulfamethoxazole (MICs, ≥320 μg/ml). They were susceptible to gentamicin (MICs, 4 μg/ml) and colistin (MICs, ≤0.5 μg/ml) but showed full or intermediate susceptibility to tigecycline (MICs, ≤4 μg/ml).

XbaI pulsed-field gel electrophoresis (PFGE) typing attributed the 33 KPC-Kp isolates to three closely related pulsotypes differing from each other by one to three bands. All isolates were positive for the presence of the KPC, TEM, and SHV sequences by PCR amplification while testing negative for the

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**TABLE 1. Clinical characteristics and outcomes of patients with infection or colonization by KPC-producing *Klebsiella pneumoniae***

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (yr)</th>
<th>Gender</th>
<th>Date of admission</th>
<th>Cause(s) of admission</th>
<th>Site(s) or type(s) of infection/colonization</th>
<th>Rectal colonization</th>
<th>Empirical treatment</th>
<th>Antimicrobial therapy after ID/AST</th>
<th>Length of stay (days)</th>
<th>Patient outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>67/F</td>
<td>April 9</td>
<td>RF, C</td>
<td>UTI</td>
<td>Present</td>
<td>BSC</td>
<td>GEN</td>
<td></td>
<td>110</td>
<td>Transferred to the respiratory ICU</td>
</tr>
<tr>
<td>2</td>
<td>69/F</td>
<td>June 13</td>
<td>MT</td>
<td>Sputum, BSI</td>
<td>Present</td>
<td>TYP</td>
<td>COL</td>
<td></td>
<td>15</td>
<td>Alive and still in ICU at the end of the study period</td>
</tr>
<tr>
<td>3</td>
<td>57/M</td>
<td>June 15</td>
<td>PT</td>
<td>Sputum, BSI</td>
<td>Not tested</td>
<td>TYP</td>
<td>COL</td>
<td></td>
<td>45</td>
<td>Transferred to the thoracic surgery unit</td>
</tr>
<tr>
<td>4</td>
<td>17/M</td>
<td>June 25</td>
<td>RF, C</td>
<td>Sputum, BSI</td>
<td>Present</td>
<td>BSC</td>
<td>COL</td>
<td></td>
<td>30</td>
<td>Transferred to an external neurorehabilitation unit</td>
</tr>
<tr>
<td>5</td>
<td>81/M</td>
<td>June 27</td>
<td>HF, RF</td>
<td>UTI</td>
<td>Present</td>
<td>Not done</td>
<td>GEN</td>
<td></td>
<td>30</td>
<td>Death</td>
</tr>
<tr>
<td>6</td>
<td>55/M</td>
<td>July 10</td>
<td>HT</td>
<td>Rectum</td>
<td>Present</td>
<td>BSC</td>
<td>Not done</td>
<td></td>
<td>25</td>
<td>Transferred to the ICU</td>
</tr>
<tr>
<td>7</td>
<td>67/F</td>
<td>July 24</td>
<td>HF, RF</td>
<td>Sputum, BSI</td>
<td>Present</td>
<td>TYP</td>
<td>COL</td>
<td></td>
<td>25</td>
<td>Transferred to the neurology ward</td>
</tr>
<tr>
<td>8</td>
<td>35/F</td>
<td>July 24</td>
<td>SS</td>
<td>Peritonitis</td>
<td>Not tested</td>
<td>Not done</td>
<td>COL</td>
<td></td>
<td>28</td>
<td>Transferred to the ICU</td>
</tr>
<tr>
<td>9</td>
<td>63/F</td>
<td>July 31</td>
<td>IH</td>
<td>UTI</td>
<td>Not tested</td>
<td>BSC</td>
<td>GEN</td>
<td></td>
<td>52</td>
<td>Death</td>
</tr>
<tr>
<td>10</td>
<td>78/F</td>
<td>August 8</td>
<td>HF, RF</td>
<td>Nases (colonized)</td>
<td>Not tested</td>
<td>Not done</td>
<td>Not done</td>
<td></td>
<td>20</td>
<td>Transferred to the ICU</td>
</tr>
<tr>
<td>11</td>
<td>68/M</td>
<td>August 13</td>
<td>PT</td>
<td>Rectum</td>
<td>Present</td>
<td>TYP</td>
<td>COL</td>
<td></td>
<td>16</td>
<td>Death</td>
</tr>
<tr>
<td>12</td>
<td>45/M</td>
<td>August 27</td>
<td>PT</td>
<td>Peritonitis</td>
<td>Not tested</td>
<td>TYP</td>
<td>COL</td>
<td></td>
<td>33</td>
<td>Transferred to an external neurorehabilitation unit</td>
</tr>
<tr>
<td>13</td>
<td>66/F</td>
<td>September 1</td>
<td>SS</td>
<td>Peritonitis, BSI</td>
<td>Not tested</td>
<td>Not done</td>
<td>COL</td>
<td></td>
<td>9</td>
<td>Death</td>
</tr>
</tbody>
</table>

* Abbreviations: F, female; M, male; C, coma; RF, respiratory failure; MT, medullary trauma; PT, polytrauma; HF, heart failure; HT, head trauma; SS, septic shock; IH, intracranial hemorrhage; UTI, urinary tract infection; BSI, bloodstream infection; BSC, broad-spectrum cephalosporin; COL, colistin; GEN, gentamicin; TYP, tazobactam-piperacillin.

Only NA, not available, because the patient was still in the ICU at the end of the study.
VIM, IMP, and \textit{qnr} genes (10). Previously described primers were also used to amplify an 851-bp fragment containing the \textit{waaE} gene (10). Sequencing of all ampiclons obtained from three representative isolates, which had been selected on the basis of variation in PFGE pattern, revealed that \textit{bla}_{KPC-3}, \textit{bla}_{TEM-1}, and \textit{bla}_{SHV-11} were present. In comparison with a reference sequence (GenBank accession number AF146532), the \textit{waaE} sequence contained five nucleotide changes: four were silent, but one was predicted to determine an Arg (48) \rightarrow Gly substitution. The substitution is different than that observed by Woodford et al. (10) in isolates from ICUs in New York—Ile (31) \rightarrow Val—and thus could likely be useful as an epidemiological strain marker. Multilocus sequence typing (MLST) was performed according to the protocol described on the \textit{K. pneumoniae} MLST website (http://www.pasteur.fr/recherche/genopole/PF8/mlst/Kpneumoniae.html) (2) and attributed the three representative isolates to sequence type 258 (ST258).

This study reports for the first time an outbreak of KPC-Kp infection and colonization in an ICU in Italy. Indeed, only one case of infection in an inpatient, at the University Hospital of Florence, has been previously reported in Italy (4). The characteristics of our strains are consistent with isolates from several geographic areas, such as the United States and Israel (5, 6). Clone ST258 has been shown to account for approximately 70\% of the KPC-Kp strains sent to the CDC (5). In Europe, it has also been found in Norway, Sweden, and Finland from patients transferred from Greece, Israel, and Italy (8, 9).

There is need of urgent action to be undertaken to slow down and eventually control the epidemic worldwide spread of KPC-Kp in health care institutions and the community. Antibiotic use policy and strict infection control measures are critical in the fight against carbapenemase-producing organisms.

\textbf{REFERENCES}


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