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Spread of a *Klebsiella pneumoniae* Strain Producing a Plasmid-Mediated ACC-1 AmpC β-Lactamase in a Teaching Hospital Admitting Disabled Patients

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We describe a large outbreak involving a *Klebsiella pneumoniae* strain producing a plasmid-encoded ACC-1 type AmpC β-lactamase in a hospital caring for patients with motor impairment. The epidemic strain was isolated from 57 patients in six wards between September 1999 and May 2003 and caused clinical infections in 19 patients.

Large nosocomial epidemics involving AmpC-producing *Klebsiella pneumoniae* strains have never been reported to date. The first reported nosocomial outbreak due to AmpC-producing *K. pneumoniae* strains occurred at the Miriam Hospital (Rhodes, Greece) in 1988 and involved 11 patients (8). A number of other outbreaks have since been described, but they rarely involved more than 10 individuals (7). We report the largest outbreak involving a plasmid-encoded AmpC-producing *K. pneumoniae* strain and the first such case in a department of physical medicine and rehabilitation (PMR).

The Raymond Poincaré hospital (Garches, France) is a 440-bed teaching hospital that includes a 150-bed PMR department caring for patients with motor impairment. In November 1999, a 26-year-old patient with tetraplegia transferred from Tunisia to the PMR department was found to have urine samples positive for an ACC-1-producing *K. pneumoniae* strain. After the identification of three other cases from January to March 2000 in the PMR department, the screening strain. After the identification of three other cases from January to March 2000 in the PMR department, the screening strain and the first such case in a department of physical medicine and rehabilitation (PMR).

The epidemic involved a total of 57 cases (at least one clinical sample and/or rectal swab positive for ACC-1-producing *K. pneumoniae*) from September 1999 to May 2003, mainly in the PMR department (46 cases) but also in other hospital units (surgical intensive care unit, 7 cases; medical intensive care unit, 3 cases; and septic orthopedic surgery, 1 case). The epidemic was controlled by strictly isolating carriers of ACC-1-producing *K. pneumoniae*, a measure implemented only at a late stage because it is in contradiction with our reeducation strategy. ACC-1-producing *K. pneumoniae* isolates were detected in diagnostic cultures (12 cases), screening cultures (24 cases), or both (21 cases). Nineteen patients met the criteria for nosocomial infection (4) (urinary tract infection, 16 cases; pyelonephritis with bloodstream infection, 2 cases; and paravertebral abscess, 1 case). The mean (± the standard deviation) delay between admission and the first positive sample was 28 (±40) days (range, 1 to 229 days). Most patients were male (sex ratio, 0.86). The median age was 34 years (range, 17 to 94 years). All patients had a neurological disease, mostly spinal cord injury.

All ACC-1-producing *K. pneumoniae* isolates collected during the outbreak showed the same pattern of resistance to β-lactams with the disk diffusion method and were resistant to gentamicin, tobramycin, netilmicin, trimethoprim-sulfamethoxazole, and rifampin; most isolates were resistant to tetracycline and/or intermediate or resistant to ciprofloxacin. MICs of ceftazidime, cefotaxime, cefoxitin, and cefotetan. Epidemic ACC-1-producing *K. pneumoniae* was suspected in the presence of the susceptibility pattern shown in Fig. 1.

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K12C600 (Str<sup>r</sup>) by conjugation and to <i>E. coli</i> NM554 (Str<sup>r</sup>) by transformation. Transconjugants and transformants were selected on Drigalski agar plates containing streptomycin (100 mg/liter) and ceftazidime (10 mg/liter). Transconjugants (obtained only with isolate 2) and transformants displayed the same pattern of resistance to β-lactam agents as the donor <i>K. pneumoniae</i> isolates. Other resistance markers were cotransferred: (i) gentamicin, tobramycin, and netilmicin (isolates 1, 2, and 3); (ii) rifampin (isolates 1, 2, and 3); (iii) sulfamethoxazole (isolates 1 and 2); (iv) trimethoprim (isolate 3); and (v) tetracycline (isolate 3). Each of the transconjugants and transformants contained a single additional plasmid of approximately 100 kb (data not shown), suggesting that all of the transconjugants and transformants yielded an amplicon of 1,276 bp with the primer set TCC-ACC2, SHV01-SHV02, and TEMA1-TEMB1 (Table 2). The amplification conditions were 45 cycles of 30 s at 94°C, 30 s at the annealing temperature, and 30 s at 72°C and a final extension step at 72°C for 10 min. The PCR products were sequenced with the Big Dye terminator sequencing kit (Perkin-Elmer/Applied Biosystems, Courtaboeuf, France) using the primers listed in Table 2 and an ABI Prism sequencer (Perkin-Elmer/Applied Biosystems). The three β-Lactam resistance gene Primer name and sequence<sup>a</sup> <i>T<sub>m</sub></i> (°C) Fragment size (bp) Reference or source

<table>
<thead>
<tr>
<th>β-Lactam resistance gene</th>
<th>Primer name and sequence&lt;sup&gt;a&lt;/sup&gt;</th>
<th>&lt;i&gt;T&lt;sub&gt;m&lt;/sub&gt;&lt;/i&gt; (°C)</th>
<th>Fragment size (bp)</th>
<th>Reference or source</th>
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<td>&lt;i&gt;bla&lt;/i&gt;&lt;sub&gt;SHV&lt;/sub&gt;</td>
<td>SHV-F: 5′-CACTCAAGGAGATTGTATTGTG-3′&lt;br&gt;SHV-R: 5′-TTAGCGTGCTGACGTGCTG-3′</td>
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<td>1,075</td>
<td>12</td>
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<tr>
<td></td>
<td>A1: 5′-ATAAAATCTTTGAGAAGC-3′&lt;br&gt;B1: 5′-TTACCAATGGCATTATCA-3′&lt;br&gt;V167*: 5′-ACATTTCTTTGAGGTTTGCC-3′&lt;br&gt;V267*: 5′-GCTTTTCTTTGACTGTTGAG-3′</td>
<td>42</td>
<td>822</td>
<td>10</td>
</tr>
<tr>
<td>&lt;i&gt;bla&lt;/i&gt;&lt;sub&gt;ACC-1&lt;/sub&gt;</td>
<td>ACC3: 5′-ACATTTGGAATCTTTTCCG-3′&lt;br&gt;ACC2: 5′-GTGCAAAACATCGCTGATGTT-3′&lt;br&gt;ACC7*: 5′-GGCCTCTTCAATCGCAT-3′</td>
<td>55</td>
<td>1,276</td>
<td>This study</td>
</tr>
</tbody>
</table>

<sup>a</sup> An asterisk indicates that the primer was used only for sequencing.
This is the first large, nosocomial outbreak involving a unique strain of *K. pneumoniae* producing a plasmid-mediated AmpC \( \beta \)-lactamase. The epidemic strain harbored a plasmid-borne \( \text{bla}_{\text{ACC-1}} \) gene, known to be derived from the chromosomal \( \text{bla} \) gene of *Hafnia alvei* (9). This strain was imported from a region of Tunisia that constitutes a persistent focus of multidrug-resistant *K. pneumoniae* strains, including strains harboring the plasmid-borne \( \text{bla}_{\text{ACC-1}} \) gene (11). The fact that our institution is geared toward the rehabilitation of patients with motor impairment probably strongly affected the dissemination of the strain in an endemic-epidemic manner, with transfers and prolonged stays of patients providing mobile reservoirs for bacteria (6).  

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REFERENCES