Detection of OXA-48 Carbapenemase in the Pandemic Clone
*Escherichia coli* O25b:H4-ST131 in the Course of Investigation of an Outbreak of OXA-48-Producing *Klebsiella pneumoniae*

Reports of carbapenemase-producing *Enterobacteriaceae* (CPE) have increased dramatically in the past decade. OXA-48 was first described in Turkey in 2008, and outbreaks of OXA-48-producing *Enterobacteriaceae* have since been reported worldwide, including Ireland (3, 12, 16). *Escherichia coli* O25b:H4-ST131 is a very successful uropathogenic clonal group, and its close association with the extended-spectrum β-lactamase (ESBL) CTX-M-15 has been implicated in the dissemination of this enzyme (2, 14). We report, for the first time, OXA-48 carbapenemase in a member of the sequence type 131 (ST131) clonal lineage.

An 81-year-old male patient (patient 1) (Table 1) was admitted to the medical ward in October 2011 with a diagnosis of lower respiratory tract infection. He had multiple comorbidities and had been treated initially with co-amoxiclav and subsequently with piperacillin-tazobactam. A *Klebsiella pneumoniae* isolate (isolate number 31799) resistant to amoxicillin, co-amoxiclav, piperacillin-tazobactam, and ertapenem was isolated from a midstream urine and sputum specimen cultured on day eight after admission. On the basis of a preliminary identification as a probable carbapenem-resistant *K. pneumoniae* isolate, rectal screening of all patients cared for on the same ward was initiated together with measures to control transmission of infection in accordance with draft national guidance (http://www.hpsc.ie/hpsc/A-Z/MicrobiologyAntimicrobialResistance/StrategyforthecontrolofAntimicrobialResistanceinIrelandSARI/CarbapenemResistantEnterobacteriaceaeCRE/). In the course of investigation, carbapenem-resistant *K. pneumoniae* isolates were identified from six other patients, including patient 2 (Table 1).

Patient 2 was an 82-year-old man admitted in late October 2011 with a diagnosis of lower respiratory tract infection. He had multiple comorbidities and had been treated empirically with piperacillin-tazobactam for 7 days, as he had recently been discharged from a health care facility (9). He had a history of peripheral vascular disease with gangrene of his right foot and multiple comorbidities. He had a recent lengthy hospital stay (August to October 2011) for management of lower limb soft tissue infection and ischemia. On day 10 of his October admission, he developed a progressive soft tissue infection of his right foot. He was treated with broad-spectrum antibiotics for 10 days and required subsequent forefoot amputation. On day 22, in response to the progressive soft tissue infection, piperacillin-tazobactam treatment was commenced and further debridement of his foot was performed. The rectal swab was taken 5 weeks after admission, and in addition to *K. pneumoniae* (isolate number 110833-3), an *Escherichia coli* (isolate number 110833-1) isolate was found.

Isolate identification was confirmed by Vitek2 (bioMérieux, Hampshire, United Kingdom). Isolates were identified as carbapenemase producers by the modified Hodge method of the Clinical and Laboratory Standards Institute. Results of a commercial synergy test (Rosco Diagnostica, Taastrup, Denmark) were not consistent with a KPC enzyme or metallo-β-lactamase. PCR and sequencing confirmed that *E. coli* 110833-1 harbored *bla*<sub>OXA-48</sub>, *bla*<sub>TEM</sub>-1, and *bla*<sub>OXA-1</sub> (7, 17, 18) and belonged to the ST131 clonal group (4). *E. coli* 110833-1 harbored 2 plasmids of 61 kb and 4 kb (1). All 7 *K. pneumoniae* isolates were indistinguishable by pulsed-field gel electrophoresis (PFGE), and a 61-kb plasmid was detected in all cases (15). Multilocus sequence typing (MLST) was performed according to the method of Diancourt et al. (6) and indicated that all *K. pneumoniae* isolates belonged to ST913. Mero- penem and ertapenem MICs for *E. coli* 110833-1 were 0.25 μg/ml and 1.0 μg/ml, respectively, as determined by Etest (AB Biodisk, Solna, Sweden), and the isolate was susceptible to ceftazidime, cefotaxime, cefpodoxime, aztreonam, cefoxitin, amikacin, kana-

---

TABLE 1 Microbiological and molecular analyses of all OXA-48-producing *Enterobacteriaceae*

<table>
<thead>
<tr>
<th>Isolate no.</th>
<th>Patient no.</th>
<th>Species</th>
<th>Isolate source</th>
<th>MIC (μg/ml)</th>
<th>Antibiogram&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Genes harbored&lt;sup&gt;b&lt;/sup&gt;</th>
<th>PFP&lt;sup&gt;c&lt;/sup&gt;</th>
<th>MLST result</th>
<th>Plasmid size(s) (kb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>31779</td>
<td>1</td>
<td><em>K. pneumoniae</em></td>
<td>Urine</td>
<td>0.5</td>
<td>AAugPtz</td>
<td><em>bla</em>&lt;sub&gt;OXA-48&lt;/sub&gt;, <em>bla</em>&lt;sub&gt;TEM&lt;/sub&gt;-1, <em>bla</em>&lt;sub&gt;OXA-1&lt;/sub&gt;</td>
<td>KpN</td>
<td>ST913</td>
<td>61</td>
</tr>
<tr>
<td>110833-1</td>
<td>2</td>
<td><em>E. coli</em></td>
<td>Rectal swab</td>
<td>0.25</td>
<td>AAugPtz</td>
<td><em>bla</em>&lt;sub&gt;OXA-48&lt;/sub&gt;, <em>bla</em>&lt;sub&gt;TEM&lt;/sub&gt;-1, <em>bla</em>&lt;sub&gt;OXA-1&lt;/sub&gt;</td>
<td>EcJ</td>
<td>ST131</td>
<td>61, 4</td>
</tr>
<tr>
<td>110833-3</td>
<td>2</td>
<td><em>K. pneumoniae</em></td>
<td>Rectal swab</td>
<td>1.5</td>
<td>AAugPtz</td>
<td><em>bla</em>&lt;sub&gt;OXA-48&lt;/sub&gt;, <em>bla</em>&lt;sub&gt;TEM&lt;/sub&gt;-1, <em>bla</em>&lt;sub&gt;OXA-1&lt;/sub&gt;</td>
<td>KpN</td>
<td>ST913</td>
<td>61</td>
</tr>
<tr>
<td>110758</td>
<td>3</td>
<td><em>K. pneumoniae</em></td>
<td>Rectal swab</td>
<td>1.5</td>
<td>AAugPtz</td>
<td><em>bla</em>&lt;sub&gt;OXA-48&lt;/sub&gt;, <em>bla</em>&lt;sub&gt;TEM&lt;/sub&gt;-1, <em>bla</em>&lt;sub&gt;OXA-1&lt;/sub&gt;</td>
<td>KpN</td>
<td>ST913</td>
<td>61</td>
</tr>
<tr>
<td>110856</td>
<td>4</td>
<td><em>K. pneumoniae</em></td>
<td>Rectal swab</td>
<td>1.5</td>
<td>AAugPtz</td>
<td><em>bla</em>&lt;sub&gt;OXA-48&lt;/sub&gt;, <em>bla</em>&lt;sub&gt;TEM&lt;/sub&gt;-1, <em>bla</em>&lt;sub&gt;OXA-1&lt;/sub&gt;</td>
<td>KpN</td>
<td>ST913</td>
<td>61</td>
</tr>
<tr>
<td>111385</td>
<td>5</td>
<td><em>K. pneumoniae</em></td>
<td>Rectal swab</td>
<td>1.5</td>
<td>AAugPtz</td>
<td><em>bla</em>&lt;sub&gt;OXA-48&lt;/sub&gt;, <em>bla</em>&lt;sub&gt;TEM&lt;/sub&gt;-1, <em>bla</em>&lt;sub&gt;OXA-1&lt;/sub&gt;</td>
<td>KpN</td>
<td>ST913</td>
<td>61</td>
</tr>
<tr>
<td>111518</td>
<td>6</td>
<td><em>K. pneumoniae</em></td>
<td>Rectal swab</td>
<td>12</td>
<td>AAugPtz</td>
<td><em>bla</em>&lt;sub&gt;OXA-48&lt;/sub&gt;, <em>bla</em>&lt;sub&gt;TEM&lt;/sub&gt;-1, <em>bla</em>&lt;sub&gt;OXA-1&lt;/sub&gt;</td>
<td>KpN</td>
<td>ST913</td>
<td>61</td>
</tr>
<tr>
<td>101101</td>
<td>7</td>
<td><em>K. pneumoniae</em></td>
<td>Rectal swab</td>
<td>4</td>
<td>AAugPtz</td>
<td><em>bla</em>&lt;sub&gt;OXA-48&lt;/sub&gt;, <em>bla</em>&lt;sub&gt;TEM&lt;/sub&gt;-1, <em>bla</em>&lt;sub&gt;OXA-1&lt;/sub&gt;</td>
<td>KpN</td>
<td>ST913</td>
<td>61</td>
</tr>
</tbody>
</table>

<sup>a</sup>A, ampicillin; Cpd, cefpodoxime; Ctx, cefotaxime; Car, cefazidime; Fox, cefoxitin; Azt, aztreonam; Aug, amoxicillin-clavulanic acid; Ptz, piperacillin-tazobactam; Na, nalidixic acid; Cip, ciprofloxacin; Gn, gentamicin; K, kanamycin; Amk, amikacin; C, chloramphenicol; S, streptomycin; Su, sulfonamides; T, tetracycline; Tm, trimethoprim; Mn, minocycline.

<sup>b</sup>Based on PCR results.

<sup>c</sup>PFP, pulsed-field profile.
mycin, and streptomycin by the Clinical and Laboratory Standards Institute (CLSI) disk diffusion method (Table 1) (5).

This is the first report of an isolate belonging to the pandemic E. coli clonal group O25b:H4-ST131 that produces an OXA-48 carbapenemase, although KPC-2, NDM-1, and VIM-1 carbapenemases have recently been reported in this group (8, 10, 11, 13). In general, OXA-48 does not confer frank resistance to the carbapenems as defined by current interpretive standards. It is likely that many OXA-48-producing Enterobacteriaceae may go unrecognized given the low MIC compound by the lack of an enzyme inhibitor to facilitate phenotypic detection. The worldwide dissemination of CTX-M-15 is attributed in part to its association with E. coli O25b:H4-ST131. As carbapenems are vital therapeutic agents for treatment of severe infection, the introduction of OXA-48 and other carbapenemases into this clonal group is of major concern.

ACKNOWLEDGMENTS

We are grateful to all the staff of the diagnostic laboratories and the clinical areas of the hospital.

REFERENCES


Dearbháile Morris
Edel McGarry
Antimicrobial Resistance and Microbial Ecology (ARME) Group
School of Medicine
National University of Ireland Galway
Galway, Ireland

Meaghan Cotter
Department of Microbiology
Mater Misericordiae University Hospital
Dublin, Ireland

Virginie Passet
Institut Pasteur
Genotyping of Pathogens and Public Health
Paris, France

Maureen Lynch
Department of Microbiology
Mater Misericordiae University Hospital
Dublin, Ireland

Catherine Ludden
Antimicrobial Resistance and Microbial Ecology (ARME) Group
School of Medicine
National University of Ireland Galway
Galway, Ireland

Margaret M. Hannan
Department of Microbiology
Mater Misericordiae University Hospital
Dublin, Ireland

Sylvain Brisse
Institut Pasteur
Genotyping of Pathogens and Public Health
Paris, France

Martin Cormican
Antimicrobial Resistance and Microbial Ecology (ARME) Group
School of Medicine
National University of Ireland Galway
Galway, Ireland