First Identification of blaIMI-1 in an Enterobacter cloacae Clinical Isolate from France

Carbapenem resistance in Enterobacteriaceae is a growing concern worldwide (13). Resistance to carbapenems may be mediated by two mechanisms: hyperproduction of an AmpC-type cephalosporinase or extended-spectrum β-lactamase (ESBL) combined with decreased drug permeability through the outer membrane and carbapenem-hydrolyzing β-lactamas (4, 15). Carbapenemases belong to classes A, B, and D according to the Ambler classification (1, 12, 15). Class A carbapenemases have the ability to hydrolyze a broad variety of β-lactams, including carbapenems, and are usually inhibited by clavulanic and tazobactam (15). They can be chromosome-encoded like Nmc-A (9), SME (10), SFC-1 (6), and BIC-1 (5), plasmid-encoded like KPC (12) and GES (14, 15), or both, like IMI (2, 16). The chromosomborne IMI-1 enzyme was detected for the first time in Enterobacter cloacae strains isolated in 1984 from two patients in a California hospital (16). Since then, another plasmid-encoded variant, IMI-2, has been reported in Enterobacter asburiae from United States rivers (2) and in a single Enterobacter cloacae isolate from China (17).

In this study, we report on the first detection of IMI-1 in a clinical isolate of E. cloacae from Europe.

A 30-year-old patient was hospitalized in the neurosurgical ward of the hospital of Valenciennes, France, for frontal-parietal fracture subsequent to a severe motor vehicle traffic accident. After 4 days of hospitalization, he was transferred to the neurosurgical intensive care unit for severe ventilator-associated pneumonia. An imipenem-resistant E. cloacae Val-1 isolate was obtained from tracheal aspirate (10⁷ CFU/ml). The patient was treated with piperacillin-tazobactam and amikacin, and the infection was cured within 5 days. No other imipenem-resistant E. cloacae strain was isolated in the same hospital. E. cloacae was identified by using biochemical methods and 16S RNA and rpoB PCR/sequencing approaches (8). According to the CLSI guidelines, E. cloacae Val-1 was resistant to penicillins, co-amoxiclav, and narrow-, and expanded-spectrum cephalosporins and to carbapenems (3). It remained susceptible to expanded-spectrum cephalosporins, such as ceftaxime, ceftazidime, and cefepime (Table 1) and to non-β-lactam antibiotics (aminoglycosides, quinolones, and cyclines). The imipenem resistance trait could not be transferred by electroporation or by conjugation (14), and plasmid extraction was negative (7), suggesting a likely chromosomal origin of this resistance trait.

PCR and sequencing were used to detect carbapenemase genes and revealed the presence of blalMI-1 (2). Using primers of the genetic environment known for blalMI-1, a 2.2-kb fragment was amplified and corresponded to that described by Rasmussen et al. (16), including a blalMI-1 gene that is preceded by a gene encoding a protein identical to ImIR (16). The carbapenemase activity, determined by UV spectrophotometry with imipenem as a substrate (11), showed that IMI-1 was produced at a basal level and that expression was inducible by imipenem (10 μg/ml) or cefoxitin (50 μg/ml), as previously described (11).

IMI-1 enzymes have rarely been described in clinical settings. However, with the rapid diffusion of ESBL-producing enterobacterial species and the increased use of carbapenems, their isolation may increase. From a phenotypic point of view, IMI-producing E. cloacae resemble OXA-48-producing E. cloacae isolates (reduced susceptibility/resistance to carbapenems and susceptibility to expanded-spectrum cephalosporins) (13). Unlike OXA-48 producers, IMI-1 producers are inhibited by clavulanic acid. Evidence of a synergy image between carbapenems and clavulanate could be a way to differentiate them. This report underlines the diversity of spreading carbapenemases in Enterobacteriaceae, which are not limited only to KPC, VIM, IMP, NDM, and OXA-48.

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REFERENCES


### Table 1 β-Lactam MICs for E. cloacae VAL-1 and a wild-type isolate

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>MIC (μg/ml)</th>
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<tbody>
<tr>
<td>E. cloacae VAL-1</td>
<td>E. cloacae CIP7933</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>&gt;128</td>
</tr>
<tr>
<td>Ticarcillin</td>
<td>64</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>&gt;128</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>0.25</td>
</tr>
<tr>
<td>Imipenem</td>
<td>&gt;32</td>
</tr>
<tr>
<td>Imipenem + AC</td>
<td>32</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>2</td>
</tr>
<tr>
<td>Ertapenem + AC</td>
<td>0.38</td>
</tr>
<tr>
<td>Meropenem</td>
<td>1</td>
</tr>
<tr>
<td>Doripenem</td>
<td>0.5</td>
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</tbody>
</table>

* AC, clavulanate.

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