Nosocomial Outbreak of *Klebsiella pneumoniae* Carbapenemase-Producing *Klebsiella oxytoca* in Austria

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To date, no outbreak of carbapenemase-producing bacteria has been reported for Austria. While outbreaks of *Klebsiella pneumoniae* carbapenemase (KPC)-producing *K. pneumoniae* have been increasingly reported, no outbreak caused by KPC-producing *Klebsiella oxytoca* has been described yet, to the best of our knowledge. We report an outbreak of KPC-producing *K. oxytoca*.

In 5 months, 31 KPC-producing *Klebsiella oxytoca* strains were isolated from five patients. All patients were admitted to the same medical intensive care unit in Austria.

Carbapenems are considered the agents of choice for treatment of serious infections caused by resistant Gram-negative bacteria. Resistance to carbapenems is therefore the major threat for treatment of these infections, and production of carbapenemases is the most important molecular mechanism, both epidemiologically and clinically.

Carbapenemases in Enterobacteriaceae are represented by three molecular classes of beta-lactamase: A, B, and D (3). *Klebsiella pneumoniae* carbapenemase (KPC) is a class A beta-lactamase that poses a serious clinical challenge, as KPC-producing *Klebsiella pneumoniae* isolates are rapidly disseminating worldwide (1, 4).

KPC-type enzymes in carbapenem-resistant *Klebsiella pneumoniae* were first detected in 2001 in North Carolina and since then have spread all over the United States (14, 18, 24). Sizeable outbreaks of KPC-producing *K. pneumoniae* have also occurred in Israel, Greece, South America, and China (6, 12, 15, 22, 27, 28). The emergence of KPC-producing *K. pneumoniae*, often associated with smaller outbreaks, has recently been reported also from several European countries, including Germany, Italy, Poland, Switzerland, and France (9, 10, 13, 17, 23). In contrast, reports of KPC-producing *Klebsiella oxytoca* are rare (5, 11, 19, 25). Most of these reports cover one or two isolates and, to the best of our knowledge, no outbreak caused by KPC-producing *K. oxytoca* has been described yet. Even non-carbapenemase-producing *K. oxytoca* has rarely been reported as the cause of nosocomial outbreaks (7, 20).

![Dendrogram and similarity matrix for *K. oxytoca* for five patients. The *K. oxytoca* isolates of this outbreak were indistinguishable, with a similarity of between 98.6% and 99.4% (and no band difference) in the DiversiLab system.](http://aac.asm.org/FIG_1.png)
The three other patients in mid-October, making cross-transmission likely. Thereafter, the strain disappeared for 2 months. A fourth patient in mid-December 2010 at the division of hematology was horizontally transmitted to at least two additional patients in the same room of a medical intensive care unit (ICU).

A retrospective observational study of patients infected or colonized with KPC-producing *Klebsiella oxytoca* was conducted. Thirty-one strains (from five patients) were isolated within 5 months at the Medical University Hospital Graz, Austria, a hospital with a total of 1,600 beds. All strains had been identified (either the first colonizing or the first pathogenic isolate) was thawed and retested. Three of these strains had been previously published criteria were used (2). Treatment outcome was evaluated on day 7. Successful outcome was defined as cure or improvement (partial resolution of signs and symptoms and improvement of laboratory parameters) while on anti-infective therapy.

**TABLE 1** Clinical data, strains, and direct antimicrobial susceptibility in KPC-producing *Klebsiella oxytoca* Austria, 2010-2011

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Date of first detection</th>
<th>Comorbidities</th>
<th>Site of first detection</th>
<th>Site of infection caused by KPC</th>
<th>Treatment outcome (final outcome)</th>
<th>Antimicrobial therapy before isolation of KPC</th>
<th>Antimicrobial therapy for KPC</th>
<th>Susceptibility phenotype of KPC</th>
<th>MICs of KPC-Producing <em>Klebsiella oxytoca</em> (mg/liter)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>70</td>
<td>m</td>
<td>11 Dec 2010</td>
<td>DIC, ARF, AH</td>
<td>Urine</td>
<td>Tracheostoma, axilla</td>
<td>Death</td>
<td>Meropenem, levofloxacin</td>
<td>NA AMK (2.0), COL (0.125), FOS (4.0), TIG (0.5)</td>
<td>K. oxytoca (VAP; 15 days)</td>
<td>K. oxytoca (VAP; 15 days)</td>
</tr>
<tr>
<td>2</td>
<td>47</td>
<td>m</td>
<td>19 Dec 2010</td>
<td>ARF, DIC, AH</td>
<td>Tracheal aspirate, groin</td>
<td>VAP</td>
<td>Death</td>
<td>Meropenem, levofloxacin</td>
<td>NA AMK (2.0), COL (0.125), FOS (4.0), TIG (0.5)</td>
<td>K. oxytoca (VAP; 15 days)</td>
<td>K. oxytoca (VAP; 15 days)</td>
</tr>
<tr>
<td>3</td>
<td>82</td>
<td>m</td>
<td>28 Feb 2011</td>
<td>ARF, DIC, AH</td>
<td>None</td>
<td>Urine</td>
<td>NA (discharge)</td>
<td>Meropenem, levofloxacin</td>
<td>NA AMK (2.0), COL (0.125), FOS (4.0), TIG (0.5)</td>
<td>K. oxytoca (VAP; 15 days)</td>
<td>K. oxytoca (VAP; 15 days)</td>
</tr>
<tr>
<td>4</td>
<td>38</td>
<td>m</td>
<td>11 Dec 2010</td>
<td>DM, ARF</td>
<td>Sputum</td>
<td>Ventilator-associated pneumonia</td>
<td>Death</td>
<td>Meropenem, levofloxacin</td>
<td>NA AMK (2.0), COL (0.125), FOS (4.0), TIG (0.5)</td>
<td>K. oxytoca (VAP; 15 days)</td>
<td>K. oxytoca (VAP; 15 days)</td>
</tr>
<tr>
<td>5</td>
<td>43</td>
<td>m</td>
<td>27 Oct 2010</td>
<td>CAD, ARF, AH</td>
<td>BAL</td>
<td>CAP</td>
<td>NA (death)</td>
<td>Gentamicin, linezolid, moxifloxacin</td>
<td>NA AMK (2.0), COL (0.125), FOS (4.0), TIG (0.5)</td>
<td>K. oxytoca (VAP; 15 days)</td>
<td>K. oxytoca (VAP; 15 days)</td>
</tr>
</tbody>
</table>

**KPC-Producing *Klebsiella oxytoca* Outbreak, Austria, 2010-2011**

We recently reported the emergence of New Delhi metallo-beta-lactamase (NDM)-1 producing bacteria in Austria (26). To date, no outbreak of carbapenemase-producing bacteria has been reported for Austria. In this study, we describe an outbreak of *Klebsiella oxytoca* KPC-producing (KPC-4). While patient 2 died due to staphylococcal scalded skin syndrome before identification of the carbapenemase-producing KPC-Producing *Klebsiella oxytoca* (KPC). From October 2010 through February 2011, five patients were infected with KPC-producing *Klebsiella oxytoca* which affected five patients. All of them had stayed in the same room of a medical intensive care unit (ICU).
was ruled out, as environmental cultures of bronchoscopes and equipment used with them remained negative in repeated tests.

Rep-PCR with the DiversiLab instrument showed that all strains were indistinguishable from one another, with a similarity index of >98.5% (Fig. 1).

KPC-producing *K. oxytoca* was causative for infection in three patients (VAP in all three patients and also a urinary tract infection in one patient). Systemic anti-infective treatment for KPC-producing *K. oxytoca* infection was started for two of the patients and was successful for both. The third patient with VAP died before adequate anti-infective treatment could be started.

Travel history was unremarkable for all of the patients. Patients 1 and 2 had not even been outside Austria for the last 10 years. This is of particular interest, as carbapenem-resistant *K. pneumoniae* isolates have rarely been reported for Austria in the European Antimicrobial Resistance Surveillance Network (http://www.ecdc.europa.eu/en/activities/surveillance/EARS-Net/database/Pages/table_reports.aspx). All detected KPC-producing *K. oxytoca* strains were multiresistant, and they exhibited susceptibility to colistin, fosfomycin, tigecyclin, and amikacin only. Details of the outbreak are given in Table 1.

The emergent and worldwide spread of carbapenem-resistant Enterobacteriaceae is a challenge for both clinicians and clinical microbiologists. We report a clonal outbreak of KPC-producing *K. oxytoca* in Austria involving five patients and lasting for 5 months. While outbreaks of KPC-producing *K. pneumoniae* have been described frequently, no outbreak of KPC-producing *K. oxytoca* has yet been described, to the best of our knowledge.

Previous studies have identified poor functional status, ICU stay, transplantation, mechanical ventilation, prolonged hospitalization, and receipt of antibiotics as risk factors for acquisition of KPC-producing organisms (16, 21). The observational design of our study did not allow us to make any conclusions regarding risk factors for KPC-producing *K. oxytoca* acquisition at our institution. All of these risk factors except transplantation, however, were present in three or more of the patients described here.

The susceptibility profile of the isolates recovered during the present outbreak underscores the extremely limited therapeutic options available for the treatment of infected patients. Similar results have also been reported in previous studies (22). Surprisingly, fosfomycin was active in vitro in all of the isolated strains. *In vivo* efficacy of this bactericidal agent has not yet been evaluated. In our study, however, fosfomycin combination therapy with either tigecycline or colistin was associated with a successful outcome.

In conclusion, we describe a nosocomial outbreak of KPC-producing *K. oxytoca*. These observations provide some insight into the epidemiology and clinical importance of KPC carbapenemases that also pose a serious clinical threat when produced by *K. oxytoca*.

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**REFERENCES**


