Management and investigation of a large carbapenemase producing enterobacteriaceae OXA-48 outbreak in a French university hospital

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Introduction
In June 2013, a strain of Citrobacter freundii producing OXA-48 carbapenemase was isolated from a urinary clinical sample in a patient already hospitalized for more than one month in the medicine Department at the Nantes university hospital. This index case had no recent hospitalization in a foreign country. We report the investigation and the management of a 11-month outbreak period.

Materials and Methods
Setting. The University of Nantes Hospital is a 3,000-bed, tertiary-care institution.

Epidemiological investigation. Cases were defined as patients hospitalized during the outbreak period harboring a clinical sample or a positive rectal screening swab for OXA-48 CPE. A patient was defined as exposed when his stay had overlapped with a case patient, and healthcare workers shared. The outbreak period was defined as the time between the presentation of the first case (defined as case index) and the last isolation of OXA-48 CPE strain.

Microbiology. All exposed patients were screened weekly with rectal swabs. Selective chromogenic mediums were used for the screening. All OXA-48 CPE isolates were further characterized by pulsed-field gel electrophoresis (PFGE). PFGE profiles were analyzed using BioNumerics software (Applied Maths, Sint-Martens-Latem, Belgium ), and the strains were then compared by use of a dendrogram.

Infection control measures. The implementation of national guidelines consisted of: isolation or cohorting of colonized/infected patients with dedicated healthcare workers; strict contact precautions; improvement of healthcare workers behaviors, in particular reinforcement of hand hygiene; active surveillance of contact patients by rectal swab cultures; management of contact patients transferred to another service (screening and contact isolation).

References

Results
From May 2013 to April 2014, 54 OXA-48 CPE cases were isolated in our institution (Figure 1). During the outbreak period, 7 patients died but none of the death was related to the CPE infection. Most OXA-48 CPE isolates were Klebsiella pneumoniae and Escherichia coli strains (Figure 2).

Table 1. characteristics of patients infected or colonized by OXA-48 positive Enterobacteriaceae, Nantes, 2013-2014 (n=54 cases)

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>N=54</th>
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<tbody>
<tr>
<td>Median age, years (min-max)</td>
<td>75 (20-102)</td>
</tr>
<tr>
<td>Infections/Colonizations, n</td>
<td>5/49</td>
</tr>
<tr>
<td>Median time between hospital admission and the first CPE isolation, days (min-max)</td>
<td>17 (2-63)</td>
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<tr>
<td>Number of contact patients screened</td>
<td>2,008</td>
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<td>Number of rectal swabs done during the outbreak period</td>
<td>3,921</td>
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</table>

The first epidemic episode occurred from May 2013 to October 2014. Firstly, Internal Medicine and Infectious Diseases Departments were involved (both units are located on the same floor). Since July 2013, secondary cases were detected in the Nephrology Department after the transfer of a contact patient from the Infectious Diseases Department. Cohorting areas including three distinct zones with dedicated staff was then performed in those units and allowed to control the spread of the epidemic strain at the end of October. The second epidemic episode occurred from November 2013 to April 2014, after readmission of a case patient in the Infectious Diseases Department. A new cohorting was performed to limit the spread of the epidemic strain.

Conclusions
Initial control measures have failed to control the spread of blaOXA-48-positive plasmids and/or strains due to the fortuitous and late detection of the index case. The implementation of cohort units was the key measure to control the outbreak despite the large spread. The economic impact of this large OXA-48 CPE outbreak is ongoing.

Figure 1. Epidemic curve of detection date of first OXA-48 positive isolate per patient during an outbreak of OXA-48 positive Enterobacteriaceae, Nantes, 2013-2014 (n=54 cases)

Figure 2. Dendrogram to show the relatedness of PFGE profiles for Klebsiella pneumoniae isolates with OXA-48 carbapenemase from patients during the outbreak, Nantes, 2013-2014