A prolonged multispecies outbreak of carbapenemase-producing Enterobacteriaceae due to transmissible plasmid with carbapenemase gene

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Background

- In Japan, metallo-β-lactamase, especially IMP type, is a predominant carbapenemase in Enterobacteriaceae
- Bacteria harboring blaIMP-4 are often susceptible to imipenem in vitro (MIC<2µg/ml)
- IMP producer is resistant to cefazidime-avibactam
- In July 2010, a patient with CRE with blaIMP-4 was found at Osaka National Hospital (ONH), an acute-care hospital with about 700 beds
- The number of cases reached to more than 100 cases despite control measures by the hospital, and investigation was conducted as a public health response on March 2014

Objectives

- To describe the feature of this event and to identify risk factor of its acquisition among patients with abdominal surgery in the hospital

Methods

- A case was defined as a hospitalized patient with blaIMP-4 positive Enterobacteriaceae (IMP-6 CPE) identified at ONH between Jun 2013-Mar 2014
- Case control study: To identify risk factors of acquiring IMP-6 CPE among patients who had abdominal surgery at ONH
  - Case: Above cases with IMP-6 CPE from abdominal wound or abdominal drain discharge after abdominal surgery
  - Control: Inpatients who were positive for meropenem-susceptible Enterobacteriaceae at abd. wound or abd. drain discharge after abd. surgery
- Pulsed-field gel electrophoresis (PFGE) was conducted using XbaI for Klebsiella oxytoca, K. pneumoniae and E. coli. Speil for Enterobacter cloacae
- To obtain the draft genome sequence of chromosome and plasmid separately, PFGE with S1 nuclease was performed and DNA bands were cut out, followed by WGS using illumina MiSeq and de novo assembly using A5-miseq ver.
- In 20140604. Multi-locus sequence typing, plasmid replicon typing and detection of antibiotic resistance genes were performed by in silico analysis against public database (PubMLST, PlasmidFinder and ResFinder)

Results

Figure 1. Basic characteristics of IMP-6 CPE cases and its isolates, Osaka, Japan, June 2013-March 2014, and the timeline of its detection

Figure 2. Dendrogram of PFGE profiles, MLST data and plasmid type for 22 isolates from IMP-6 CPE cases

Figure 3. Plasmid types in 22 isolates from IMP-6 CPE cases

Table 1. Risk factors of acquiring IMP-6 CPE among cases with abdominal surgery, Osaka, Japan

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<tr>
<th>Factors</th>
<th>Odds Ratio (95% CI)</th>
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<td>Male gender</td>
<td>1.5 (1.0-2.4)</td>
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<td>ASA score (IQR)</td>
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Conclusions

- Pancreato-duodenectomy, changing drains at fluoroscopy room and enteric fistula were associated with IMP-6 CPE acquisition among patients with abdominal surgery
- Plasmid analysis under the following-link of those under complicated IMP-6 CPE outbreak, and facilitates understanding those links with further careful epidemiological investigations, (e.g. case 1, 2, and 5 were considered to have epidemiological link (stayed in the same ward and facilitates understanding those links with further careful epidemiological investigations, (e.g. case 1, 2, and 5 were considered to have epidemiological link (stayed in the same ward)
- With a bundled infection control with Osaka City Public Health Office (OCPHO), the outbreak was contained in July 2016

Acknowledgements & Funding

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Strict standard precautions, stop sharing plastic containers for fluid collection and strict indication of continuous peritoneal lavage

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Pancreato-duodenectomy, changing drains at fluoroscopy room and enteric fistula were associated with IMP-6 CPE acquisition among patients with abdominal surgery

Plasmid analysis under the following-link of those under complicated IMP-6 CPE outbreak, and facilitates understanding those links with further careful epidemiological investigations, (e.g. case 1, 2, and 5 were considered to have epidemiological link (stayed in the same ward at least a day), but the species of the isolates from them were different — A1 plasmid

It may be possible to control prolonged CPE outbreak through coordinated response with hospital and local/national public health sectors

Table 1. Risk factors of acquiring IMP-6 CPE among cases with abdominal surgery, Osaka, Japan

Adjusted by days of hospitalization, | Based on crude date, | American Society of Anesthesiology

Asterisks indicate cases in a case-control study, and all isolates had blaIMP-4 and IncR M

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