Journal of Hospital Infection xxx (2015) 1–6

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevierhealth.com/journals/jhin

Challenges of controlling a large outbreak of OXA-48 carbapenemase-producing *Klebsiella pneumoniae* in a French university hospital☆

B. Semin-Pelletier [a], L. Cazet [a], C. Bourigault [a], M.E. Juvin [a], D. Boutoille [b,c], F. Raffi [b], M. Hourmant [d], G. Blancho [d], C. Agard [e], J. Connault [d], S. Corvec [a,c], J. Caillon [a,c], E. Batard [c,f], D. Lepelletier [a,c,*]

[a] *Bacteriology and Hygiene Department, Nantes University Hospital, Nantes, France*
[b] *Infectious Diseases Department, Nantes University Hospital, Nantes, France*
[c] *University of Nantes, EA 3826, UFR Medicine School, Nantes, France*
[d] *Renal Transplant Department, Nantes University Hospital, Nantes, France*
[e] *Internal Medicine Department, Nantes University Hospital, Nantes, France*
[f] *Emergency Department, Nantes University Hospital, Nantes, France*

ARTICLE INFO

Article history:
Received 31 October 2014
Accepted 17 November 2014
Available online xxx

Keywords:
Carbapenemase-producing *Klebsiella pneumoniae*
Infection prevention and control
Outbreak
OXA-48

SUMMARY

A large outbreak of OXA-48 carbapenemase-producing *Klebsiella pneumoniae* at Nantes University Hospital was investigated. The index case had no history of travel or hospitalization abroad and had been hospitalized in the internal medicine department for more than one month when the epidemic strain was isolated from a urine sample in June 2013. Seventy-two secondary cases were detected by weekly screening for gastrointestinal colonization during the two phases of the outbreak from June to October 2013 (33 cases) and from November 2013 to August 2014 (39 cases). Spread of the epidemic strain was attributed to the proximity of, and staff movement between, the infectious diseases (32 cases) and the internal medicine (26 cases) departments; 14 secondary cases were also observed in the renal transplant department following the transfer of an exposed patient from the infectious diseases department. Most of the patients (90%) were colonized and no death was linked to the epidemic strain. More than 3000 contact patients were reviewed and 6000 rectal swabs were performed. Initial control measures failed to control the outbreak owing to the late detection of the index case. The late implementation of three successive cohort units, the large number of transfers between wards, and the frequent readmission of cases contributed to the incomplete success of control measures.

Introduction

Over the last decade, carbapenemase-producing Enterobacteriaceae (CPE) have emerged as a significant public health threat worldwide.[1] Although CPE infections have been reported in France since 2004, it is not yet endemic as in other

☆ The results of this investigation were presented in part at ECCMID, Barcelona, Spain, 10–13 May 2014.

* Corresponding author. Address: Bacteriology and Hygiene Department, Nantes University Hospital, 44000 Nantes, France.
E-mail address: didier.lepelletier@univ-nantes.fr (D. Lepelletier).

http://dx.doi.org/10.1016/j.jhin.2014.11.018
0195-6701/

countries in Europe.[2] However, several sporadic cases and outbreaks in France have been traced to patients with a recent stay or hospitalization abroad.[3–6] National recommendations to limit the spread of highly resistant bacteria were published in 2010 and 2013.[7,8] A recent investigation at a large French institution showed that a co-ordinated CPE control programme greatly reduced secondary cases, in spite of a rise in the number of index cases who had recently been hospitalized or who had stayed abroad.[9]

In June 2013, a strain of *Citrobacter freundii* that produced OXA-48 carbapenemase was isolated from the urine of a patient who had been admitted to the internal medicine department at Nantes University Hospital more than a month earlier. The index case had not recently been hospitalized in, or travelled to, a foreign country. An outbreak followed of colonization and infection by *Klebsiella pneumoniae* that produced the same OXA-48 carbapenemase. We report here the investigation of this outbreak and the challenges faced in controlling it during the 14 months from June 2013 to August 2014.

Methods

Setting

The outbreak occurred at Nantes University Hospital (France), a 3000-bed University-affiliated tertiary care centre serving an urban area with 800,000 inhabitants. Nantes University Hospital admits ~90,000 patients per year and employs 2000 physicians, 5000 nurses, and 2000 assistant nurses. The epidemic CPE spread over three departments: internal medicine (IMD) with 10 beds, infectious diseases (IDD) with 22 beds, and renal transplant (RTD) with 39 beds. IMD and IDD are located on the same floor and shared healthcare workers (HCWs) except medical staff.

Definition of cases and outbreak period

A case was defined as any patient infected or colonized with CPE. A contact patient was defined as a patient for whom either of the following applied: (i) during their current hospitalization care had involved sharing (with a case) paramedical or medical HCWs anywhere in the hospital during at least one day or night shift; (ii) during previous hospitalizations had been strongly suspected of exposure to a CPE carrier. The outbreak period was defined as beginning on 2 May 2013 (the day of admission of the index case) and ending on 31 August 2014. All patients with the epidemic strain of CPE who had been inpatients in the hospital during the outbreak period were included.

Infection control programme

Patients who had stayed or been hospitalized in a foreign country during the previous year were systematically detected at hospital admission. Reinforcement of both contact precautions and room surface disinfection was implemented for CPE patients. Systematic rectal screening of contact patients to detect asymptomatic carriage was performed weekly in the three departments until one week after the discharge of CPE patient. Contact precautions were applied to any patient discharged to another ward or hospital until they had negative screens for three consecutive weeks after discharge. Contact patients who had not had three negative screens after discharge (for example because they had gone home or to a long-term care facility) were screened at readmission. Readmission of CPE cases was automatically detected during registration. Readmitted cases were assigned dedicated HCWs to encourage compliance with contact precautions. When case patients were discharged, their rooms were disinfected according to a specific protocol. Dedicated bags were used for the collection and disposal of faeces and urine. An evaluation of hand hygiene compliance was conducted during the outbreak. Weekly meetings were held with ward staff, infection control professionals, microbiologists, and administrative and health directors during the whole of the outbreak period to evaluate the infection control programme. A weekly report of the progress of the outbreak (number and location of secondary cases) was submitted to the regional ICT and the National Health Institute.

Microbiological methods

To screen patients for CPE carriage, rectal swabs were cultured on chromogenic agar targeting OXA-48 carbapenemase-producing Enterobacteriaceae (Gélose chromID® OXA-48, bioMérieux, Marcy l'Etoile, France). Relatedness among all carbapenemase-producing *K. pneumoniae* clinical isolates was investigated by pulsed-field gel electrophoresis (PFGE), performed according to the manufacturer's instructions (BioRad, Marnes-la-coquette, France). Whole-cell DNA was digested with the *Spe*I restriction enzyme overnight at 37°C. Electrophoresis was performed with a CHEF DRII apparatus (BioRad) through a 1% agarose gel in 0.5 × Tris–borate–EDTA buffer. Migration conditions were as follows: temperature, 14°C; voltage, 6 V/cm; switch angle, 120° with one linear switch ramps of 2–20 s for 20 h. After migration, gels were stained in a 0.5 μg/mL ethidium bromide solution. Pulsed-field gel electrophoresis profiles were analysed using Bionumerics software (Applied Maths, Sint-Martens-Latem, Belgium) and PFGE results were analysed according to the criteria of Tenover *et al.*[10]

Results

The index case had no recent history of hospitalization or travel in a foreign country. He had been in the IMD since admission on 2 May 2013. *Citrobacter freundii* that produced an OXA-48 carbapenemase was isolated from his urine in June 2013. The infection control team retrospectively identified 290 contact patients among those who had been inpatients between 2 May and 13 June 2013. Fifteen contacts were still in various wards in our hospital, 19 patients had been transferred to other hospitals and 256 had been discharged home. Only those contacts still in our or other hospitals were screened for CPE colonization: three out of 15 and four out of 19 contacts were colonized, respectively.

From 13 June, systematic screening for CPE by culture of rectal swabs was established. In late June, two 'secondary' cases with *K. pneumoniae* that produced OXA-48 carbapenemase were identified in the IMD. A further case was then discovered incidentally by the isolation of OXA-48 carbapenemase-

Please cite this article in press as: Semin-Pelletier B, et al., Challenges of controlling a large outbreak of OXA-48 carbapenemase-producing *Klebsiella pneumoniae* in a French university hospital, Journal of Hospital Infection (2015), http://dx.doi.org/10.1016/j.jhin.2014.11.018