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Brief Report

Outbreak of CTX-M-15–producing *Enterobacter cloacae* associated with therapeutic beds and syphons in an intensive care unit

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An outbreak of extended-spectrum β-lactamase–producing *Enterobacter cloacae* (ESBL-ECL) occurred in our intensive care unit (ICU) and involved 18 patients (8 infected and 10 colonized). The mean age of patients was 69 years, and all infected patients had underlying medical conditions. Within hours' recognition of the spread of ESBL-ECL, the infection control team requested for staff education, reinforcement of infection control measures, and environmental screening. New transmissions were observed in the institution after weeks of enhanced infection control measures. Microbial swabbing revealed bacterial contamination of some mattresses and syphons with epidemiologic links between environmental, screening, and clinical isolates. This outbreak resulted in the temporary closure of the ICU for complete biocleaning.

In the intensive care unit (ICU), *Enterobacteriaceae* as *Enterobacter cloacae* are frequently involved in nosocomial infections.[1,2] The reservoir for these bacteria is the gastrointestinal tract, and cross-transmission mainly occurs via contaminated hands or environmental contamination.[3] This article describes a 4-month outbreak of extended-spectrum β-lactamase–producing *E cloacae* (ESBL-ECL) between July and November 2013 in an ICU. Eighteen patients were involved (8 infected and 10 colonized). We also describe the investigation and control measures that have been necessary to control the epidemic phenomenon.

MATERIALS AND METHODS

Clinical setting

The outbreak occurred in the ICU of the Begin Military Teaching Hospital, which consists of 10 inpatient beds for both medical and surgical patients. The ICU has 2 different sectors: one comprising 4 individual rooms with a large airlock, and a second sector with 6 individual rooms, grouped by sets of 2 with a common airlock. Each room has a single sink used for handwashing and disposal of body fluid, and the distance between the sink and the patient is <1 m. The policy for preventing hospital-acquired infections in this ICU relies on hand hygiene with alcohol-based handrub, daily biocleaning, and respect of standard precautions. Active surveillance of cultures of rectal and nasal swabs is performed routinely for multidrug-resistant organisms screening: detection of carriage of methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, and ESBL-producing *Enterobacteriaceae* (ESBLE) is performed in all patients on admission to the ICU and once a week throughout their stay. Contact precautions are implemented for suspicious or confirmed multidrug-resistant organism–infected or –colonized patients.

Clinical and epidemiologic data

Patients hospitalized in the ICU and having an ESBL-ECL–positive microbiologic specimen (clinical specimens or routine screening swabs) between June and December 2013 were recorded (n = 19). Only patients with the clonal ESBL-ECL strain were finally considered (n = 18), of which 17 were in the ICU and 1 had been transferred to the surgical ward. For each case, demographic

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data, cause of ICU admission, underlying diseases, length of stay, and clinical outcome were recorded.

Bacterial isolates and antibiotic susceptibility testing

To search for ESBLE, rectal swabs, clinical isolates, and environment isolates were plated onto chromID ESBL agar plates (bioMérieux, Marcy l'Etoile, France). The isolates were identified by mass spectrometry (Microflex; Brüker, Germany), and the antimicrobial susceptibility was determined by the disk diffusion method on Mueller-Hinton agar plates (Bio-Rad, Marnes-la-coquette, France). The results were interpreted according to the guidelines of the Antibiogram Committee of the French Society of Microbiology. ESBL production was detected by double-disk synergy testing.

Environmental investigation

Environmental screening was performed on 3 occasions. The screening was carried out on equipment shared by patients (bronchial fiberscope, electrocardiogram, echograph, radiography equipment, stethoscopes, glucometers, phones, and keyboards) and environmental sources (water, hand disinfectant vials, sinks, syphons, and therapeutic beds).

Molecular study

ESBL characterization was performed with polymerase chain reaction (PCR) and sequencing. Bacterial DNA isolation was performed from a single colony on Mueller-Hinton agar plates using the QIAamp DNA mini kit (Qiagen, Courtaboeuf, France). The oligonucleotide primer sets specific for amplification of $bla_{\text{CTX-M-1}}$, $bla_{\text{CTX-M-2}}$, $bla_{\text{CTX-M-9}}$, bla_{SHV}, and bla_{TEM} were taken from the literature.[4] PCR products were purified using the QIAquick PCR purification kit (Qiagen) and subjected to DNA sequencing using the BigDye terminator v3.1 cycle sequencing kit (Applied Biosystems, Foster City, CA) and an 3730 XL capillary sequencer (Applied Biosystems). Sequence analysis was carried out using a Sequence Scanner (Applied Biosystems) compared with published sequences in the GenBank BLAST software (The National Center for Biotechnology Information [NCBI], Bethesda, MD).

To assess clonal spread of the ESBLE into the ICU, all isolates were typed by randomly amplified polymorphic DNA analysis (RAPD) using primers opam7, p208, and p272.[5] The interpretation of random amplification of polymorphic DNA findings was based on differences in banding patterns.

Infection control measures

After recognition of the outbreak, a series of strategies were implemented to control the infections and colonization as follows: informing the hospital infection committee and all health care workers of the ICU, daily education on infection control measures (hand hygiene, standard precautions, contact precautions, and body fluids management), enhanced environmental biocleaning, and rational using of antimicrobial therapy. Then, separating patient cases into cohorts was instituted. Finally, the temporary closure of the ICU with the transfer of hospitalized patients to a new ward in the hospital was undertaken to conduct extensive renovation and large environmental biocleaning.

RESULTS

Before this outbreak, isolation of ESBL-ECL had been uncommon in this ICU: during the first 5 months of 2013, no ESBL-ECL had been isolated in this unit. By contrast, the number of patients with ESBL-ECL had noticeably increased during the second half of 2013. In the ICU, the annual incidence rate of ESBL-ECL has gone from 0.25% (1/400 admissions) in the year 2012 to 4.8% (20/417 admissions) in 2013 (Fig 1).

From June 9, 2013 to October 6, 2013, 18 patients hospitalized in the ICU (including 1 transferred in surgical ward) developed ESBL-ECL colonization (n = 10) or infection (n = 8).

Of these, 11 (61.1%) were women and 7 (38.9%) were men. The mean age of patients was 69 years. The mean length of ICU stay was 18.7 days. Two of the infected patients were also colonized. The clinical diagnoses were lower respiratory tract infection for all infected patients. Of these, all had underlying medical conditions, including chronic obstructive pulmonary disease (n = 2), respiratory distress syndrome (n = 5), chronic renal failure (n = 1), obesity (n = 2), diabetes (n = 4), cardiac failure (n = 3), and HIV infection with pneumocystis pneumonia (n = 1). All infected patients had received mechanical ventilation. Seven were treated with piperacillin-tazobactam associated or not with amikacin. One patient with ESBL-ECL in a respiratory specimen did not receive any specific antibiotic treatment because an alternative diagnosis was confirmed (pneumocystis pneumonia); the patient was finally considered as pulmonary colonization of ESBL-ECL. Four patients were cured, and 4 patients died. Characteristics of the patients are summarized in Table 1.

Our investigations started at the beginning of July after the isolation of 3 ESBL-ECL isolates within the same week in the ICU (cases B1, B2, and B3) and 1 isolate (case B4) in a patient from the surgery unit but initially hospitalized in the ICU. Adherence to infection control measures, especially regarding hand hygiene with alcohol-based products after handling of urine- and feces-contaminated disposals, was reiterated by a member of the infection control team of our hospital. In addition, cleaning of rooms was reinforced. However, 3 additional isolates were grown from rectal swabs (cases B5, B6, and B7) 3 weeks after the first detections. Subsequently, the infection control team conducted a hand hygiene observational audit and a search for potential environmental sources by a visit of the ICU. During this period, use of alcohol-based handrubs was only 50% of the target defined by the national guidelines for the ICU. The audit showed that the gold standard technique to perform hand hygiene (by rubbing with an alcohol-based formulation) was not exhaustive. Handwashing with soap and water was still used when hands were not visibly dirty or visibly soiled with blood or other body fluids. Moreover, when handrubbing was performed, the duration of the entire procedure was not strictly applied. Consequently, education programs and sensitization on handwashing were conducted in the ICU.

On August, 3 new ESBL-ECL isolates were grown from bronchoalveolar fluid and 2 rectal swabs (cases B8, B9, and B10). Forty-eight samples were obtained from potential environmental reservoirs. None of the samples were found positive for ESBL-ECL. One week after, a new campaign of 41 samples from the environment were analyzed: all specimens obtained from sink drains and syphons were positive for ESBL-ECL.

Clinical and environmental ESBL-ECL isolates exhibited the same antibiotic resistance profile. They were resistant to cefotaxime, ceftazidime, ceftriaxone, cefepime, ciprofloxacin, tobramycin, gentamicin, and trimethoprim-sulfamethoxazole. The isolates remained susceptible to piperacillin-tazobactam, imipenem, ertapenem, and amikacin and had a positive double-disk synergy test. PCR and Sanger sequencing identified the $bla_{\text{CTX-M-15}}$ gene. Molecular typing of the ESBL-ECL isolates using RAPD revealed that all isolates except 1 had the same RAPD profile and therefore were considered likely clonally related. This epidemic strain was suspected of belonging to the same epidemic clone as the clone found in several northern hospitals in France. The remaining isolate from case B9 yielded distinct RAPD profiles.