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Brief Report

Serratia marcescens sepsis outbreak caused by contaminated propofol

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We presented a sepsis outbreak caused by *Serratia marcescens* from contaminated propofol to raise awareness. Three patients had sepsis syndrome after chest surgery. Isolation of *S marcescens* from patients' respiratory and blood samples alerted us to a possible outbreak. Four syringes filled with propofol and 1 saline solution yielded *S marcescens.* Nine of 10 isolates from samples of patients and environment genotyped by pulsed-field gel electrophoresis were the same. Disobeying aseptic injection rules of propofol is still causing outbreaks.

Propofol is a lipid-based general anesthetic. Propofol vials have no preservative or antimicrobial content, and bacterial and fungal pathogens can grow freely in case of contamination.[1] Despite improvement of infection control practices and several warnings by the US Food and Drug Administration,[2] outbreaks are still a problem.[3-6] *Serratia marcescens* is a common Gram-negative bacteria causing several outbreaks from propofol-based sources.[3] Here, we present a sepsis outbreak caused by *S marcescens* from contaminated propofol to a chest surgery department to raise awareness.

METHODS

Hospital setting and patients

The setting for this study was a 1,800-bed university hospital. The chest surgery department performed 249 surgeries in 2014. On April 10, 2014, 3 patients who were operated on consecutive days (April 7, 2014, April 8, 2014, and April 9, 2014) had sepsis syndrome in the intensive care unit. (Table 1). Patients' respiratory, blood and urine samples were taken. On April 11, 2014, S *marcescens* was isolated from patients' respiratory and blood samples. Since *S marcescens* was a rare pathogen in chest surgery ICU, microbiology laboratory and Chest Surgery Clinic alerted the Infection Control Team for a possible outbreak.

Outbreak investigation

On April 11, 2014, we learned that 3 patients had surgery in the same operating room by different surgeons. All 3 surgeries were performed under general anesthesia. One additional patient who had surgery in the same operating room with spinal anesthesia showed no sign of infection. The operating theater was closed on April 11, 2014, and samples were taken from the environment (oxygen tubes, suction systems, ventilation devices, disinfectants, opened and unopened general anesthetic medications, saline solutions, laryngoscopes, and from the rest of the used medications in the trash) and from the staff (throat, nose nares, and hands).

Microbiology

Fourty-nine samples from the environment and 15 samples from the staff were cultured. Bacterial identification was performed via matrix-assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF MS, Bio Merieux, France). Antibiotic susceptibility tests were performed by VITEK 2 automated system (Bio Merieux, France), and the results were evaluated according to

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Table 1
Demographic characteristics of patients

Case No.	Age	Sex	Diagnosis	Operation	Operation date	Samples that *S marcescens* isolated	Treatment
1	60 y	F	Thymoma, Myasthenia gravis	Mass excision	07/04/2014	Deep tracheal aspirate	Ceftriaxone
2	48 y	F	Bronchiectasis	Lobectomy	08/04/2014	Blood	Levofloxacin
3	53 y	M	Lung cancer	Lobectomy	09/04/2014	Deep tracheal aspirate, pleural fluid, blood	Meropenem

F, female; *M*, male.

CLSI criteria.[7] For genotypic analysis, pulsed-field gel electrophoresis was performed as described previously.[8]

RESULTS

Patients

All patients had a fever on the same day. However, they were on different antibiotics (Table 1). After antimicrobial susceptibility test results, treatment of patient 2 and 3 was changed to ceftriaxone. Fortunately, no deaths occurred.

Microbial investigation

We cultured 64 samples from the environment and the staff. Five of the samples yielded *S marcescens*: an opened propofol vial, 3 different sized-syringes filled with propofol, and the rest of the used saline solution placed in the trash. There was no bacterial growth on samples of unopened syringes or vials with the same and different lot numbers even after they stayed at room temperature for 24 hours. All isolates from clinical samples of patients and contaminated medications had the same antimicrobial susceptibility (resistant to ampicillin, amoxicillin clavulanic acid, and cefuroxime; sensitive to ceftriaxone, cefepime, imipenem, meropenem, ertapenem, amikacin, gentamicin, ciprofloxacin, and trimethoprim sulfamethoxazole).

When we checked the laboratory records in the previous months, we saw a *S marcescens* growth in both the pleural fluid and intravenous catheter tip of a patient who had chest surgery on April 1, 2014. This isolate had the same antimicrobial resistance pattern as with the previous ones.

Five isolates from respiratory and blood samples of 3 patients[1-5] and 5 isolates from opened propofol vials, different syringes filled with propofol, and other opened saline solution[6-10] were genotyped by pulsed-field gel electrophoresis (Fig 1). We could not include the isolate from patient who was operated on in the same room 1 week before. Nine of 10 isolates were the same, but the isolate from the deep tracheal aspirate of patient 1 was not relevant (Fig 1).

Infection control and observation

We learned that anesthesia technicians had the responsibility of preparing all medications before surgery. They had 2 years of education in anesthesia practices after college. During our investigation, we also learned that anesthesia technicians sometimes gave single-use propofol vials to multiple patients. Propofol was drawn into syringes before the procedure, and the syringes were kept at room temperature for long hours. In addition, they used a common syringe (50 mL) to prepare medications.

An educational program (including hand hygiene and sterile injection practices) for anesthesia technicians was performed on April 16, 2014. We prepared a written protocol for the preparation, storage, and use of general anesthetics. This educational program was repeated every 3 months. The operation room was cleaned and disinfected under observation of infection control nurses on April 17, 2014, and the operations started on April 18, 2014. There was only 1 additional case of nosocomial *S marcescens* (in August 2014) empyema until October 8, 2018.

DISCUSSION

To our knowledge, this is the first propofol-based outbreak reported from Turkey. Propofol has been on the market in Turkey since 1990, but clinicians reported no outbreaks. Outbreaks might have been undiagnosed because they were considered to be surgical complications.

The first outbreak caused by contaminated propofol was surgical-site infection with *S aureus* in 1992 in the United States.[4] Twenty propofol-related outbreaks were reported with different infectious organisms between 1989 and 2014. A total of 144 people were affected, and 10 deaths occurred in these outbreaks.[3] *S marcescens* caused 4 outbreaks.[3] Recently, there was an *S marcescens* meningitis outbreak after spinal anesthesia due to contaminated medications and a wound and soft tissue infection outbreak due to contaminated saline bottles reported from Turkey.[9,10]

In our report, the microbiology lab alerted us to the outbreak on the same day of *S marcescens* isolation. We defined the source of the outbreak and closed the operating room the next day. In 2 days, we learned that isolates were genotypically related. By early source detection, further cases were prevented.

We presumed that in this outbreak propofol was extrinsically contaminated since unopened ampoules were sterile. It is probable that

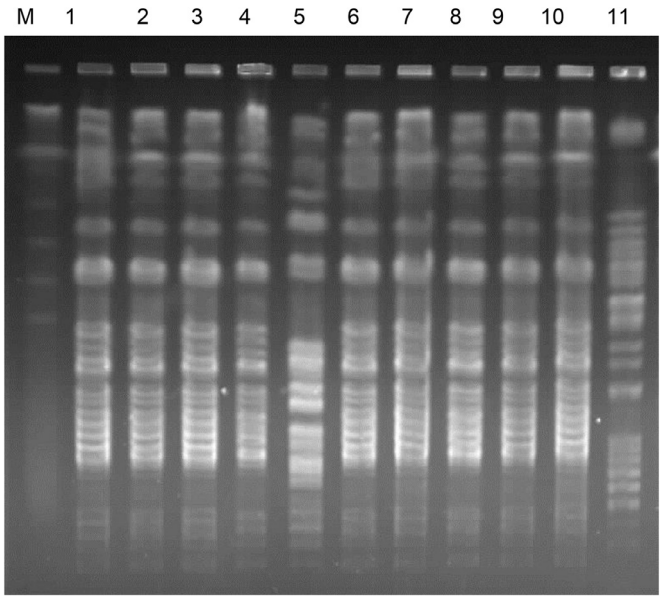

Fig 1. Pulsed-field gel electrophoresis of *Serratia marcescens* isolates from samples of patients and the operating room. (M) Marker. (1) Blood (patient 2). (2) Central venous catheter (patient 2). (3-4) Blood (patient 3). (5) Deep tracheal aspirate (patient 1). (6) Propofol in the syringe. (7) Saline solution in the trash. (8-10) Propofol in the different syringes in the trash. (11) *Eschericia coli* anhydrotetracycline.

main problems were caused by disobeying aseptic injection rules, reusing single-use ampules for multiple patients, using a common needle/syringe, and/or using prepared propofol after 12 hours. In Turkey, surgeons are supposed to operate on more patients for higher scores in a performance-based payment system. Anesthesia technicians might have found little time to prepare medications between patients and might have disobeyed basic infection control measures because of the speedy turnover. Furthermore, it was not possible to use single propofol vials as single use due to the economic problems of the hospital.

The limitations of our study are: (1) we could not include the sample of the patient who had surgery in the same operating room and had *S marcescens* bacteremia before we detected the outbreak and (2) we could not explain the source of a different clone in the patient. We suggest that the patient might have acquired the *S marcescens* via cross-contamination from the environment.

In conclusion, outbreaks caused by contaminated propofol still occur. In the presented outbreak, *S marcescens* was isolated from 1 opened propofol vial, different syringes filled with propofol, and opened saline solution in the trash, but unopened propofol ampules were sterile. Our data suggest that they were contaminated extrinsically. This study emphasizes the importance of continuous microbiological data analysis, quick interventions, and strictly obeying aseptic injection rules to prevent more outbreaks and possible deaths.

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