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Concise Communication

Does marking as sterile mean really sterile? *Stenotrophomonas maltophilia* outbreak caused by a blood-gas injector containing liquid heparin

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Abstract

An outbreak investigation was initiated after detecting an increase in the number of patients with *Stenotrophomonas maltophilia* bloodstream infections (SM-BSIs) througout the hospital. *S. maltophilia* was isolated from the cultures of blood-gas ınjectors containing liquid heparin. The incidence density of SM-BSIs decreased significantly after prohibiting the use of those injectors.

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A hospital-wide increase in the incidence of *Stenotrophomonas maltophilia* bloodstream infections (SM-BSIs) was detected in the Hacettepe University adult and oncology hospitals, which serve as tertiary-care hospitals with ∼1,150 beds, including 150 beds in the intensive care units (ICUs). Herein, we summarize our outbreak investigation and highlight the impact of multimodal approaches to identify the source of the outbreak.

Material and methods

In April 2021, 10 patients with SM-BSIs were identified. The following month, 11 patients with SM-BSIs were identified. SM-BSIs were clustered mainly in the internal medicine intensive care unit (IM-ICU) and anesthesiology and reanimation ICU (AR-ICU). These findings triggered an outbreak investigation. Cultures of environmental surfaces and liquids (eg, saline, povidone iodine, chlorhexidine) were performed to identify potential sources from ICUs and emergency rooms (ERs) where the SM-BSIs were clustered (Table 1). This procedure was repeated 3 times when SM-BSIs peaked. A case–control study was planned to define the risk factors for SM-BSIs. Demographic and clinical characteristics of 50 consecutive patients with SM-BSIs were extracted from the electronic files. The strains that were isolated from those patients were sent to another academic center for arbitrarily primed polymerase chain reaction (AP-PCR) and pulsed-field gel electrophoresis (PFGE) to investigate molecular epidemiology as described previously.[1] Based on the similarity coefficients of the isolates, strains with >85% similarity were accepted as closely related. The Turkish Ministry of Health Advisory Board for Contagious Diseases was informed about the increasing number of patients with SM-BSIs.

During the study period, blood specimens were cultured using automated BACTEC FX (Becton Dickinson, Cockeysville, MD) at bedside. Matrix-assisted laser desorption–ionization time-of-flight, mass spectrometry (MALDI-TOF MS, Bruker, Germany) was used for species identification. Swabs were collected from possible contaminated areas. Swabs and liquid medical products were inoculated in broth thioglycolate broth containing a meropenem disc and incubated at 35°C in 5% CO_2 atmosphere for 24–48 hours then subcultured on MacConkey agar and 5% sheep blood agar plates. After 24-–48 hours of incubation, species identification of non–lactose-fermenting colonies was performed by MALDI-TOF MS.

The incidence density rates (IDRs) of SM-BSIs were calculated using OpenEpi (Open-Source Epidemiologic Statistics for Public Health) version 3.01 software (https://www.OpenEpi.com). The study was approved by the Hacettepe University Non-Interventional Clinical Research Ethics Committee, Ankara, Turkey.

Results

Stenotrophomonas maltophilia was isolated from 134 blood cultures from 98 patients between April 1, 2021, and December 8, 2021. Morover, 31 (31.6%) of 98 patients had simultaneous positive blood cultures obtained from the central venous catheter. Polymicrobial growth, including coagulase-negative staphylococci (CNS), Enterobacterales, nonfermenting gram-negative bacilli, and *Candida* spp, was detected in 39 blood cultures.

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Table.1. Incidence Densitiy Rate of *S. malthopilia* Bloodstream İnfections

Location	Incidence per 1,000 Patient Days (95% CI)					
	Jan–Mar 2021	Apr–May 2021	Jun–Jul 2021	Aug–Sep 2021	Oct–Nov 2021	Dec 2021–Apr 2022
Hospitalwide	0.29 (0.1556–0.5272)	0.86 (0.5634–1.316)	0.08 (0.02281–0.3033)	0.47 (0.2698–0.8241)	1.9 (1.444–2.508)	0.19 (0.1034–0.3315)
AR-ICU	2.93 (1.14–7.51)	3.09 (1.051–9.044)	2.27 (0.4013–12.76)	10.37 (5.465–19.59)	19.43 (12.47–30.14)	1.96 (0.6684–5.76)
IM-ICU	0.96 (0.2624–3.481)	4.08 (1.977–8.396)	1.1 (0.1947–6.218)	0.77 (0.1358–4.344)	6.64 (3.371–13.06)	0.91 (0.3108–2.683)
ER	1.87 (0.5123–6.783)	3.02 (1.029–8.853)	0	0	8.21 (4.168–16.12)	0.4 (0.07093–2.272)

Note. CI, confidence interval; AR-ICU, anesthesiology and reanimation ıntensive care unit; IM-ICU, ınternal medicine ıntensive care unit; ER, emergency room.

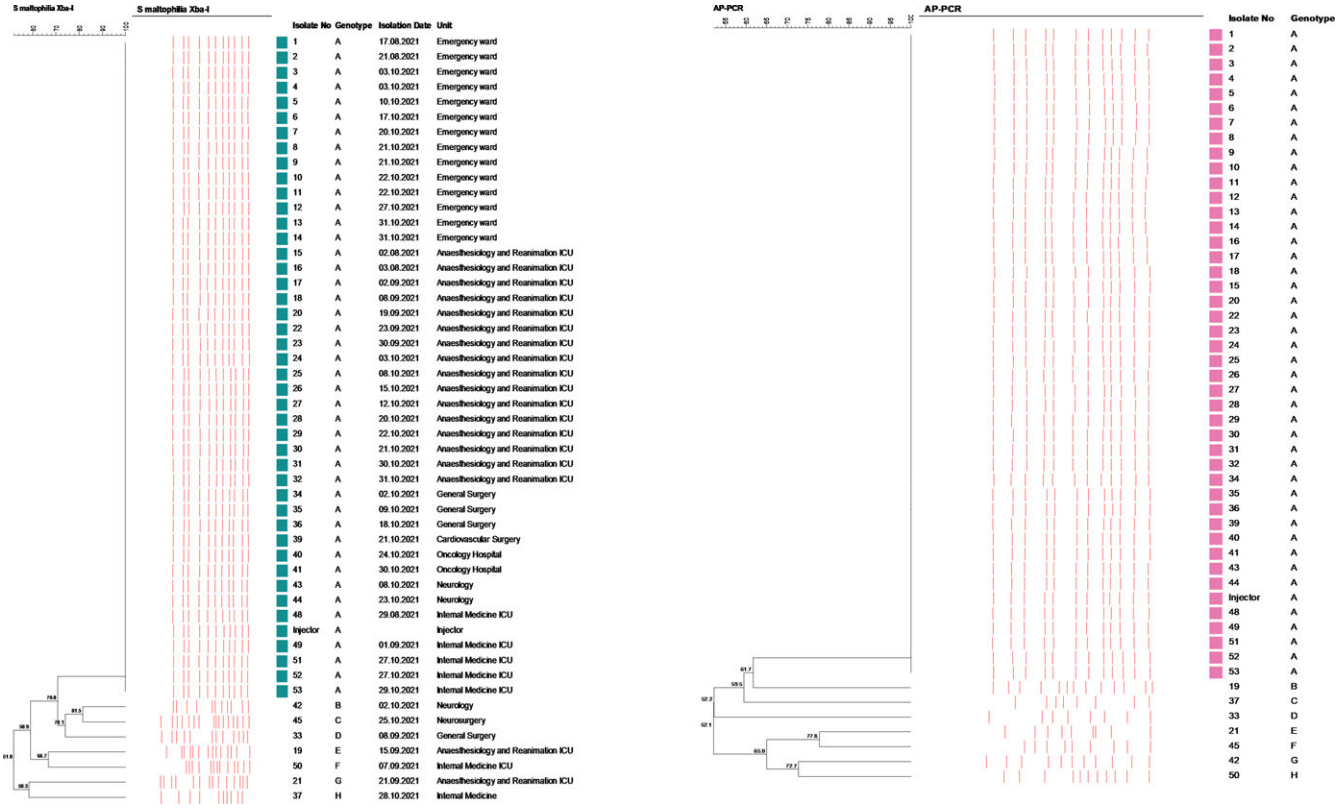

Fig. 1. Dendrogram of PFGE analysis of the *S.malthopilia* isolates.

At the beginning of the epidemiological investigation, the hospitalwide IDR of SM-BSIs in April and May increased to 0.86 (95% CI, 0.56–1.32) per 1,000 patient days, compared to 0.29 (95% CI, 0.16–0.52) during the previous 3 months (Table 1). After detecting no cases of SM-BSI in July, the number of the cases started to increase in August. This increase in IDR of SM-BSIs persisted in October, and the IDR of SM-BSIs reached 1.9 (95% CI, 1.44–2.51) per 1,000 patient days hospitalwide.

There was no growth in the environmental cultures performed on 3 occasions during the surge of SM-BSIs. The infection control team did not detect any change in hand hygiene, environmental cleaning practices, or invasive-device care bundles. The Ministry of Health Advisory Board for Contagious Diseases was informed about the situation. Then, another tertiary-care university hospital reported *S. maltophilia* isolation from sterile, needleless, blood-gas injectors containing liquid heparin. The Turkish Ministry of Health Pharmaceuticals and Medical Devices Agency (MH-PMDA) issued a warning to stop the use of these injectors. The use of this product was immediately discontinued in our hospital and several ready-to-use sterile products, including the blood gas injectors from the same manufacturer, were cultured in our microbiology laboratory. *S. maltophilia* was isolated from the cultures of blood-gas injectors containing liquid heparin. Based on AP-PCR and PFGE analysis, 1 dominant cluster included 45 *S. maltophilia* strains isolated from patients and the injector (Fig. 1). A significant decrease was observed in the IDR of SM-BSIs after use of the blood-as injectors was discontinued (Table 1).

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The median age of the 50 patients in the representative cohort was 74.5 years, and 54% of the patients were female. In addition, 22 patients (44%) had central venous catheters, and 80% of the patients had symptoms consistent with sepsis when blood cultures were performed. The 30-day overall mortality rate among patients with SM-BSI was 24%. Because we were able to identify the source of SM-BSIs, we canceled the case–control study to define the risk factors.

Discussion

Informing the Ministry of Health Advisory Board combined the efforts of several institutions and resulted in the identification of contaminated blood-gas injectors containing liquid heparin as the source of SM-BSIs. A molecular epidemiological investigation demonstrated that the strain isolated from the injector was identical to those isolated from 45 patients and identified the injector as the source of the outbreak.

Environmental sampling is an essential part of the investigation process. We were not able to isolate *S. maltophilia* in the cultures of any liquids such as saline solutions, povidone-iodine, or chlorhexidine. Because *S. maltophilia* was isolated concomitantly in 31.6% of the blood cultures obtained from CVCs, samples were taken from all materials that were used during the care of central and peripheral catheters, including several injectors of different sizes. Blood-gas injectors were excluded because they were purchased for use only for blood-gas collection. Also, during inquiries made after notification of growth of *S. maltophilia* from blood gas injectors at another tertiary-care center, ICU staff stated that these products were not used outside their intended purpose. However, the infection control team observed that these injectors were used for peripheral- and central-catheter care just before the MHPMDA issued a notice to discontinue use of these injectors. This situation highlights the importance of sharing such information with other centers and health authorities.

Notably, sterile products can be the source of an outbreak. A previous study from Brazil reported an outbreak of bloodstream infections due to *Pseudomonas putida* and *S. maltophilia* associated with a contaminated heparin catheter-lock solution.[2]

Because these commercial blood-gas injectors are used in many centers around the country, SM-BSIs became nationwide problem. A center from Istanbul, Turkey, reported 131 patients with *S. maltophilia* infections between January 1, 2021, and December 10, 2021.[3] The molecular epidemiological investigation showed genotypically identical strains from respiratory samples, blood, ECMO water, and blood-gas injectors as well as nonidentical strains from ECMO water.[3] Some other routes of transmission might exist that are difficult to identfy. In our investigation, ECMO was not used in any of the cases.

We recognized that ethylene oxide was used to sterilize the blood-gas injectors with liquid heparin that were associated with the outbreak. Ethylene oxide gas sterilization is not commonly recommended for liquid products like heparin because of the limited penetration.[4]

Our study had several limitations. The molecular epidemiology of the strains, demographic and clinical characteristics of the patients, and the impact of SM-BSIs on the outcome were analyzed only after the second peak of SM-BSIs in the representative cohort. We collected clinical information for only 40% of the patients with SM-BSIs, so the impact of SM-BSIs on the outcome of all patients could not be analyzed.

In conclusion, careful observations, multidisciplinary work, and communication both within and between institutions are important components to identify outbreaks and find the source. Strict regulations regarding the sterilization of liquids, such as heparin locks, are essential to prevent future outbreaks.

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