SERRATIA MARCESCENS OUTBEAK ASSOCIATED WITH CARDIO-THORACIC SURGERY

BACKGROUND

Serratia marcescens is an aerobic Gram-negative bacillus that thrives in moist environments. This species of bacteria has been shown to contaminate solutions and hospital equipment and has been documented in a number of common source outbreaks [1]. In the US, *Serratia* species cause 1.4% of nosocomial bloodstream infections (BSI) [2].

On January 14, 2005, ACDC received a call from an acute care hospital reporting seven post-operative cardio-thoracic (CT) surgery patients with symptoms of systemic infection occurring within 24 hours after surgery over a 10-day period. At that time, blood cultures from three patients were positive for *S. marcescens*. The California Department of Health Services (CADHS) and CDC were consulted. Elective cardiac surgery was canceled by the hospital.

After extensive environmental cleaning and staff education, CT surgery resumed on January 24 with preliminary recommendations—this included appropriate environmental cleaning, medication management, hand hygiene, and antibiotic coverage. Despite compliance, four of the seven patients (57%) operated on after surgery resumed developed post-operative fever. CT surgery was cancelled again. According to the prior agreement of infection control implemented when reinstating this surgical procedure, all patients received prophylactic antibiotics during surgery to cover for *Serratia* infection. Blood cultures on all of these febrile patients were negative for bacterial infection. At this time, ACDC requested the assistance of the CDC Division of Healthcare Quality Promotion Epidemic Intelligence Service (EIS). And on January 25, the officer accepted the invitation to assist with the investigation.

Since no ongoing transmission of *S. marcescens* was demonstrated, CT surgery was resumed January 28 with the usual surgical prophylaxis regimen. Surveillance blood cultures were obtained from all CT surgery patients for a total of 5 weekdays to assist in early detection of *S. marcescens* bacteremia.

No additional cases of *S. marcescens* BSI among CT surgery patients were identified after five days. At that time, usual methods of post-operative infection surveillance were resumed. No further cases were identified.

METHODS/RESULTS

Observational and Environmental Studies: The day following receiving the report of illness (January 15), ACDC conducted a site inspection. This included reviewing policies and procedures; interviewing representatives of the operating room (OR), Cardiac Surgical Unit (CSU), and pharmacy; inspecting the OR and CSU; and obtaining numerous environmental specimens for bacterial culture by the hospital laboratory, hospital reference laboratory, and Los Angeles County Public Health Laboratory. Specimens included open vials of medication including multidose medication and drips, medication tubing, gel for echo sonogram, water samples from faucets and ice machine in the surgical unit, swabs from OR equipment, scrub sinks, and the ice machine filter. The bags that transported many of the specimens (one for each OR room) were also cultured.

Review of infection control procedures identified no major breaches. No *S. marcescens* was cultured from samples collected from the environment and open medications (Table 1).

Background *S. marcescens* Rate: Microbiology records at the hospital were reviewed for *S. marcescens* cultures from January 2004 to January 2005 and compared the rate of *S. marcescens* BSI prior to the

outbreak period (January 2004 to December 2004) to the rate during the outbreak period (January 2005) to determine if it had significantly increased.

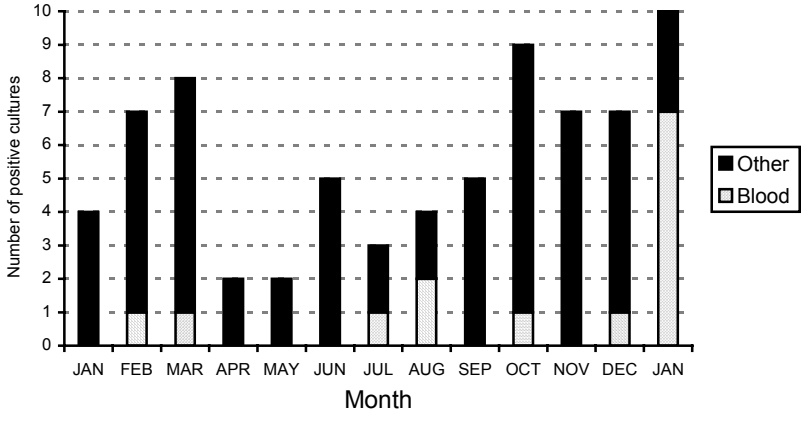
Table 1. Environment Specimen Results

Source	Number of Specimens	Results
Open medication vials	51	No Serratia marcescens isolated
Medication tubing	1	No Serratia marcescens isolated
Echosonogram gel	4	No Serratia marcescens isolated
Water samples	3	No Serratia marcescens isolated
Equipment	22	No Serratia marcescens isolated
Scrub sink soaps and lotions	21	No Serratia marcescens isolated
Ice machine filter	1	No Serratia marcescens isolated
Transport bags	4	No Serratia marcescens isolated

The rate of *S. marcescens* BSI cultures to total S. marcescens cultures during the outbreak period in January 2005 was 60% (6 of 10), which was significantly higher than the year before the outbreak period, which had a rate of 11% (7 of 63), $p<0.001$.

Cohort Study Analysis: Two initial cohort studies of operational risk factors were conducted on all patients with CT surgery from January 10 to 15, 2005. In the first study, a case was defined as a patient with a positive blood culture for *S. marcescens*. In the second study the case definition was expanded to include patients with a positive blood culture for *S. marcescens* or a fever spike noted within 72 hours after surgery. In both cohorts, a non-case was a patient with no fever spike noted within 72 hours after surgery. Patient charts were reviewed for risk factors including personnel, equipment, medications, procedures, locations, and patient characteristics. All data were collected on standard forms, entered into Microsoft Access 2000, and analyzed by SAS 9.1.

Figure 1
Laboratory-reported postive inpatient *S. marcescens* culture
by month and culture site
January 2004–January 2005



The initial cohort and environmental studies of OR risk factors conducted by ACDC did not show any significant associations between OR risk factors (e.g., personnel, equipment, medications, procedures, locations, patient characteristics) and cases. No environmental or medication contamination was identified.

Molecular Epidemiological Analysis: The Los Angeles County Public Health Laboratory performed and interpreted pulsed-field gel electrophoresis (PFGE), using standard methods and criteria, on *S. marcescens* isolates from all seven post-operative CT surgery patients as well as many reference samples from 2004 and 2005. A case was

subsequently defined as a patient with a *S. marcescens* blood isolate indistinguishable by PFGE banding pattern.

Using PFGE, six case-patients were infected with an indistinguishable strain of *S. marcescens*.

Baseline Temperature Study: To establish a baseline for the proportion of post-operative CT surgery patients with temperature spikes, a random sample of 29 CT patients operated from January 2004 to November 2004 (a non-outbreak period) was analyzed. Post-operative temperatures were analyzed as greater than or equal to 38.0ºC, 38.2ºC, and 38.5ºC respectively.

Results showed 58% of post-op patients developed temperatures >38°C (Table 2). These data indicated that the rate of post-operative fevers in patients since resuming elective surgery (57%) remained at baseline.

Table 2. Tmax Data among Cardiac Surgical Patients ≤72 Hours Post-Operation, January–November 2004 (N=29)

Temperature	No. of Cases	% of Total	% of Fever Cases
≥ 38.0°C	14	58%	100%
≥ 38.2°C	10	42%	71%
≥ 38.5°C	5	2%	36%

Case-Control and Retrospective Cohort Study Analyses: A matched case-control study and a retrospective cohort study were also enacted. The case-control study compared case patients to randomly selected controls (1:3) who were present in the CSU within four hours of the case patients. The cohort study involved all patients in the cohort period (January 10, 2005 at 6:01am to January 16, 2005 at 3:00am) or until the patient was discharged from the CSU. All data were collected on standard forms, entered into Excel 2000 spreadsheets and analyzed using SAS software, version 8e.

Results from the matched case-control study showed the only risk factor of significance was magnesium sulfate [odds ratio (OR) 6.4, confidence interval (CI) 1.1-38.3]. Intravenous magnesium sulfate was administered within 24 hours to 100% (6 of 6) of the cases and 39% (7 of 18) of the controls. The cohort study showed significant associations between receipt of amiodarone (OR 4.9, CI 1.1-22.7), propranolol (OR 10.3, CI 4.1-26), calcium chloride (OR 10.3, CI 4.1-26), cell saver (OR 10.3, CI 4.1-26), or fresh frozen plasma (OR 10.3, CI 4.1-26) with *S. marcescens* infection.

Observational Studies: To identify potential sources and risk factors for transmission, several observational studies were performed. CSU and OR staff were interviewed regarding daily procedures, staff member roles, and infection control practices. Practices of cleaning, disinfection and sterilization of equipment were also assessed. Several patients were followed from the OR through the initial pre-operative and induction procedures in the CSU. Additional environmental samples were collected from the CSU to complement a complete environmental study of the OR that had been done previously by the ICP and DHS investigators.

Review of infection control procedures again identified no major breaches. No *S. marcescens* was cultured from over 36 samples from the environment and open medications.

Three case isolates were sent to the CDC Division of Healthcare Quality Promotion laboratory where they were confirmed to be *S. marcescens* with PFGE banding patterns indistinguishable from one another and matching a strain of *S. marcescens* cultured from an unopened bag of magnesium sulfate solution compounded by a single common pharmacy and from the blood of five patients in New Jersey.

DISCUSSION

Both the epidemiologic and microbiologic evidence support contaminated magnesium sulfate solution as the cause of this outbreak. In this outbreak, a major CT surgery center was closed and the situation was made public at the onset by a press release created and disseminated by the hospital. Given the nature of the outbreak (e.g., the severity of disease, rapid onset post-surgery, and complexity of the surgeries) a direct intravenous bolus of bacteria was suspected. ACDC focused attention in its initial investigation on procedures and personnel in the OR. For this reason, the initial studies conducted by ACDC failed to implicate the magnesium sulfate—since it was administered post-operatively in the CSU.

Though both the matched case-control and retrospective cohort studies included the CSU, only the matched case-control study implicated magnesium sulfate. This is probably due to the small sample size and the fact that the cohort study included a broader period of risk.

This investigation led to the eventual discovery of a multi-state outbreak caused by the same product that was compounded and nationally distributed by single common pharmacy in Texas. The US Food and Drug Administration issued an alert on one lot of the company's magnesium sulfate solution on March 18, 2005 [3]. The implicated common pharmacy initiated a nationwide magnesium sulfate solution recall of all 50 ml admixtures of $MgSO_4$ in 5% dextrose on April 8, 2005 [4]. As a result of this outbreak several public health concerns associated with compounding have been noted by FDA and CDC and will be explored.

REFERENCES

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