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Note

Outbreak of Bloodstream Infections Associated with Dialysis Machine Waste Ports in a Hemodialysis Facility

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Abstract Eight cases of gram-negative bloodstream infection without a clinically evident source occurred at a hemodialysis unit in Jerusalem between February and September 1997. All infections could be traced to three of the 13 dialysis machines in use. Epidemiological investigation, including pulsed-field gel electrophoretic characterization of organisms isolated from the patients and dialysis machines, implicated the Waste Handling Option system of the machines as the source of the infections. Discontinuation of the Waste Handling Option system use was associated with prompt cessation of the outbreak.

Introduction

In August 1997, it became apparent that an outbreak of unexplained bloodstream infections (BSIs) was occurring at a hemodialysis facility in Jerusalem. From 30 July through 19 September 1997, five patients acquired six gram-negative BSIs (Figure 1, Table 1). Two BSIs had occurred previously, in February and April 1997. None of the patients had evidence of infection at the site of vascular access and no other potential source of BSI was indicated.

Initial epidemiological findings showed that all BSIs were due to gram-negative bacilli, that most cases were associated with the use of one dialysis machine (Table 1), and that there was no association with reuse of dialyzers. All BSIs had a very short incubation period after dialysis had begun. This observation led us to hypothesize that the BSIs were due to massive inocula of bacteria and prompted us to search for potential sources of infection in the dialysis procedure. A likely candidate was a port designed for disposal of dialyzer priming or rinse fluid, which is part of the Waste Handling Option (WHO) system, a complex fluid-filled system incorporating nonreturn valves. During priming, the tube that later carries the patient's blood is connected directly to this port using a short sterile disposable connector. Any contaminated fluid entering the tube by reflux from the port would have unhindered access to the patient's vascular system.

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Materials and Methods

A bloodstream infection was defined as a febrile reaction accompanied by positive blood cultures (bacteremia), for which no clinical source could be determined.

A febrile reaction was defined as the onset, during or shortly after dialysis, of shaking chills or elevation of body temperature to more than 38 °C in a patient who had no signs or symptoms of infection before starting the dialysis procedure [1].

The dialysis facility, located in central Jerusalem, provides hemodialysis services for approximately 70 ambulatory patients, carrying out about 830 dialyses per month. At the time of the outbreak, patients were dialyzed three times per week with Cobe Centrysystem 3 dialysis monitors (Gambro Healthcare, USA), equipped with the WHO port described above. Dialysis machines were rinsed daily before use with 6% sodium hypochlorite solution. Dialysate was produced from acid concentrate, bicarbonate solution in sealed single-use containers (Bicart; Gambro-Lundia, Sweden) and water deionized by reverse osmosis. High-flux dialyzers F60, F80 (Fresenius, Germany) and FB190u (Nipro, Japan) were processed for reuse on an Echo machine (Mesa Laboratories, USA) and a Renatron II Dialyzer Reprocessing Station (Renal Systems, USA) using Renalin Reprocessing Concentrate (Renal Systems, USA) and reverse osmosis water. Dialysate and reverse osmosis water were monitored frequently and cultured quantitatively on tryptic soy agar, as recommended by the Association for the Advancement of Medical Instrumentation [2]. Gram-negative bacilli were identified using routine laboratory procedures. Endotoxin was determined using a *Limulus polyphemus* amebocyte lysate assay (BioWhittaker, USA). All dialysis procedures were reviewed by the attending nephrologist, the nurse in charge of the facility, and nurse epidemiologists.

Data regarding all febrile episodes had been collected prospectively since March 1996. These included a detailed record of the patient's symptoms, timing of symptom onset, dialysis machine

Table 1 Characteristics of seven cases of bloodstream infection (BSI) associated with dialysis machine waste ports

Date of BSI onset	Machine no.	Patient no.	Age (years)	Diagnosis	Day/shift	Vascular access	Blood isolates
9 February	3	1	46	familial nephropathy	Sunday/evening	graft	*E. cloacae*, *P. aeruginosa*
15 April	7	2	32	sclerosis after streptococcal glomerulonephritis	Monday/morning	fistula	*E. coli*
30 July	7	3	53	obstructive uropathy	Wednesday/noon	fistula	*E. coli*, *P. aeruginosa*
30 July	7	4	36	diabetes mellitus	Wednesday/evening	graft	*E. coli*
10 August	7	5	45	familial renoretinal syndrome	Friday/morning	graft	*S. maltophilia*
2 September	2	6	60	focal sclerosis	Tuesday/noon	graft	*P. aeruginosa*
10 September	7	4	36	diabetes mellitus	Wednesday/evening	graft	*E. coli*
19 September	3	7	31	sclerosis after unilateral nephrectomy	Friday/morning	graft	*E. cloacae*

used, type and reuse status of the dialyzer, connecting nurse, bacteriologic test results, and patient's antibiotic treatment. Reverse osmosis water and dialysate samples were collected for culture from each machine used at the time of febrile reactions; on three occasions the entire tubing sets and dialyzers were submitted for culture.

Blood cultures were performed according to routine clinical practice, using the BacTAlert system (Organon Teknika, Belgium). In our facility, significant isolates are routinely preserved at –80 °C, so bacteria grown from the BSIs were available for study. Pulsed-field gel electrophoresis characterization of the BSI and machine isolates was carried out using a CHEF DR-II instrument (BioRad, Israel) on DNA extracts digested with *Not-I* (Stratagene, USA).

Results and Discussion

The clinical presentation consisted of shaking chills that occurred 30 min to 4 h after the start of dialysis (mean 1.5 h, median 1 h). Cessation of dialysis was associated with gradual waning of the chills in all patients. Only one patient (no. 7) developed clinical shock requiring treatment beyond discontinuation of dialysis. All patients affected received antibiotic therapy; this was administered immediately in five episodes and only after culture results became available in the rest. All patients survived without apparent sequelae.

Four patients had BSIs with *Escherichia coli*, three with *Pseudomonas aeruginosa*, two with *Enterobacter cloacae*, and one with *Stenotrophomonas maltophilia* (2 patients had mixed infection with *Pseudomonas aeruginosa*). All BSIs were associated with three of the 13 machines in use at the time (Table 1). Five cases of bacteremia, including all four due to *Escherichia coli*, were associated with one machine (machine 7), and the two cases caused by *Enterobacter cloacae* were associated with another (machine 3). The single case of infection associated with machine 2 was due to *Pseudomonas aeruginosa*. Infections were not associated with nursing shift, day of the week, connecting nurse, dialyzer type, new or reused dialyzer, type of vascular access, or underlying diagnosis.

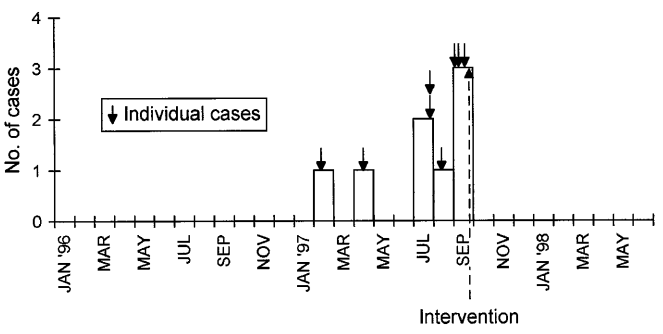

Figure 1 Cases of bacteremia and result of intervention during the outbreak

A review of the dialysis procedures used revealed that most aspects were performed adequately, including cross-infection prevention and machine disinfection protocols. An enhanced disinfection procedure failed to end the outbreak.

The protocol for dialyzer reprocessing was strictly adhered to, and particular attention was paid to membrane integrity checks. After febrile episodes, dialyzers were checked for ruptures, and all were found to be intact. Samples taken from dialyzers after reprocessing and after dialysis showed no bacterial growth. Dialysate samples generally yielded bacterial counts of less than 1000 cfu/ml. Interpretation of reverse osmosis cultures was difficult, being complicated by inadequate techniques for sampling from the distribution system. This resulted in sporadic high counts, which were unexplained and followed no logical pattern. Counts from samples taken from the supply tanks fell within acceptable limits (<200 cfu/ml). Endotoxin determinations in reverse osmosis water and dialysate were all less than 5 endotoxin units/ml.

Cultures of the WHO ports of all 13 machines were positive at least once, with most isolates being nonfermentative gram-negative bacilli. *Escherichia coli* and *Pseudomonas aeruginosa* were recovered from machine 7, which had been used for all patients with *Escherichia coli* BSIs. *Enterobacter cloacae* and *Pseudomonas aeruginosa* were cultured from two machines, including the

one associated with the two *Enterobacter cloacae* BSIs, and *Pseudomonas aeruginosa* and other nonfermentative gram-negative bacilli grew from three additional machines.

All of the *Escherichia coli* isolates obtained from the WHO port of machine 7 and from the BSIs were nonlactose fermenting, which is an unusual characteristic. Pulsed-field gel electrophoresis performed on the *Escherichia coli* blood isolates obtained in April, July, and September 1997 and from the WHO port showed that all organisms were identical. This finding, together with the demonstrated incompetence of the check valves (see below), provided solid evidence that bacteria from the WHO ports were gaining direct access to the vascular systems of the patients who developed BSIs. Of note is the fact that a single *Escherichia coli* strain was isolated from the BSIs and the associated machine port for over 5 months, despite enhanced cleaning regimens and even direct injection of sodium hypochlorite into the WHO port. *Enterobacter cloacae* isolates obtained from patients' blood and the WHO port of machine number 3 were untypable by pulsed-field gel electrophoresis but had identical antibiograms.

The nonreturn valves of the WHO ports on the three implicated machines were shown to be malfunctioning, especially that of machine 7, from which large volumes could be aspirated, and machine 3, in which fluid backed up spontaneously. It was discovered that the manufacturer's recommendations regarding daily testing and disinfection of the WHO system were not being followed. This was due to differences between the operating instructions provided in Hebrew by the local agent and the English original, which was not available in the unit. The operator's manual for the dialysis machines (in English) did not include procedures for the WHO system.

Use of the WHO ports was discontinued on 24 September 1997, 5 days after the last episode of BSI, when results of the WHO cultures became available. In place of the WHO system, priming fluid was drained into sterile plastic bags. Figure 1 demonstrates the cessation of BSIs in the 9 months following the intervention. By June 1999, no further cases had been observed.

Bacteremia is a well-recognized cause of morbidity and mortality in hemodialysis patients [1]. This complication has been attributed to several causes, such as vascular access infection [1, 3], inadequate reprocessing of dialyzers [4, 5], poor water quality and inadequate disinfection of dialysis machines [6], and even cross-infection due to inattention to basic infection control measures [5].

Recently, priming-fluid drain ports in Centrysystem 3 dialysis machines (the WHOs) have been independently implicated as a probable source of bacteremia in hemodialysis patients in other centers [7, 8]. The outbreak reported here provides strong evidence that these drain devices may be contaminated by the same bacteria over a very long period. Such contaminating organisms have physical access to fluid and tubing that comes into contact with the patient's blood.

In the outbreak reported here, several departures from the recommended maintenance and disinfection procedures were discovered, almost all of which were due to inadequacies in the instructions provided with the unit. Users should be aware of such potential pitfalls and ensure that dialysis staff are fully familiar with and proficient at carrying out the detailed instructions covering all aspects of quality assurance, maintenance, and disinfection of the complex equipment on which their patients depend.

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