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An outbreak of hemodialysis catheter-related bacteremia with sepsis caused by *Streptococcus agalactiae* in a hemodialysis unit

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ABSTRACT

Background: Rates of invasive group B Streptococcus (GBS; *Streptococcus agalactiae*) disease in adults are on the rise. Invasive GBS disease can be community- or healthcare-associated. We report an outbreak of GBS catheter-related bacteremia in a hemodialysis (HD) unit.

Materials and methods: Two patients undergoing HD at the same outpatient HD unit were admitted on the same day (within a few hours of each other) with catheter-related GBS bacteremia. A retrospective study was undertaken at the HD unit to address risk factors for febrile illness on the last HD session day. A detailed questionnaire was completed by all HD patients treated on the same day as the two GBS patients and by all members of the nursing and medical staff. Medical and nursing records of the HD unit were reviewed, as well as infection control and catheter care practices. Patients and staff members submitted swabs for culture.

Results: No rectal or vaginal culture of any HD patient or staff member was positive for GBS. The development of recent febrile disease was significantly associated with the presence of a hemodialysis catheter ($p = 0.028$) and care for more than 30 min by a specific nurse during the last two HD sessions ($p = 0.007$).

Conclusions: We speculate that the GBS strain was transmitted from one patient to the other through the hands of medical personnel. No such outbreak has ever been reported in HD patients. The importance of strict infection control practices in HD units and the avoidance of catheters for long-term HD should be emphasized.

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1. Introduction

Despite the successful prevention efforts targeting neonatal group B Streptococcus (GBS; *Streptococcus agalactiae*) disease, the rate of invasive GBS disease in adults continues to climb.[1] Given the decline in neonatal GBS disease, more than two-thirds of all invasive GBS disease in the USA now occurs in non-pregnant adults with a mean age of approximately 60 years, and has an associated mortality rate of 20–25%.[2–6]

GBS has been isolated from cultures of the human rectum, vagina, cervix, urethra, skin, and pharynx. Rates of colonization in healthy young men and women may be as high as 20% and 34%, respectively (twice as high in sexually active individuals).[7–9] Other studied groups include nursing home residents and staff (rectal colonization rates of 12% and 15%, respectively), male homosexuals (rectal carriage in 25%), and diabetics, who were reported to have a possibly lower carriage rate than matched non-diabetics, even though the incidence of invasive infection is substantially increased.[10–12]

The majority of invasive GBS disease occurs in adults with significant underlying conditions. Factors that have been associated with increased risk for community-acquired GBS infection, besides age, include cirrhosis, diabetes mellitus, stroke, breast or non-hematologic cancer, decubitus ulcer, and neurogenic bladder.[3–6] Nosocomial infection has been associated with age, placement of a central venous line, diabetes mellitus, congestive heart failure, and seizure disorder.[2,3] GBS has been associated with infection of intravenous catheters, arterial lines, polytetrafluoroethylene grafts, and an intravenous pacemaker wire.

In 2007, two patients with end-stage renal disease (ESRD) undergoing hemodialysis (HD) at the same outpatient HD unit, were admitted on the same day (patient A was brought to the

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Emergency Department 4–5 h before patient B) to the Nephrology Department of our hospital, with the same reason for admission: new-onset febrile illness with sepsis.

2. Case reports

2.1. Patient A

An 80-year-old white male with ESRD due to diabetes mellitus type II, on HD for the last three months, was admitted due to a febrile illness (up to 39 °C) of 3–4 days' duration, without an obvious focus. The highest level of fever was noted soon after the completion of his HD session on the day of admission. A subclavian cuffed HD catheter had been used since the beginning of his HD sessions and had never been changed. Two months previously, he had been hospitalized with *Staphylococcus epidermidis* catheter-associated bacteremia, which had responded to antibiotic therapy alone.

2.2. Patient B

A 65-year-old white male with ESRD due to amyloidosis diagnosed eight months ago, undergoing HD for the last 10 months, was admitted with a high fever of up to 40 °C, soon after the completion of his HD session on the day of admission. A subclavian cuffed HD catheter has been used since the beginning of his HD sessions and had been changed once eight months ago during a hospitalization for probable line sepsis. There was no history of more recent febrile illness or other new-onset symptoms.

Two sets of blood cultures (one drawn through the central venous line and one from the periphery) were taken from both patients on admission. All cultures became positive at 24 h and all grew *S. agalactiae* sensitive to penicillin, ampicillin, erythromycin, clindamycin, aminoglycosides, and vancomycin.

Both patients were initially treated with intravenous (IV) vancomycin, which was subsequently changed after three days to IV ampicillin–sulbactam, when the culture results became available. In both cases, the bloodstream was promptly sterilized and the central venous HD catheter (CVHDC) was kept in place. Both were soon discharged and resumed their HD schedule. At that time, ampicillin–sulbactam was changed back to IV vancomycin to complete a total of 21 days of therapy (nephrologist's decision).

3. Materials and methods

We attempted an outbreak investigation by visiting the outpatient HD unit (referred to from this point on as the Unit). Our first visit occurred two weeks after the simultaneous GBS bacteremia (referred to from this point on as the main incident) that prompted admission of the two patients to the hospital.

A retrospective study was undertaken at the Unit to address risk factors for febrile illness on the last HD session day.

A detailed questionnaire addressing risk factors for invasive GBS disease was distributed to all HD patients present who had been treated on the same day as the two GBS patients (total of 12 HD patients). One patient (patient 3 in Figure 1) was absent at the time of our visit due to a recent hospitalization for pelvic fracture; her data were collected from medical records and from discussions

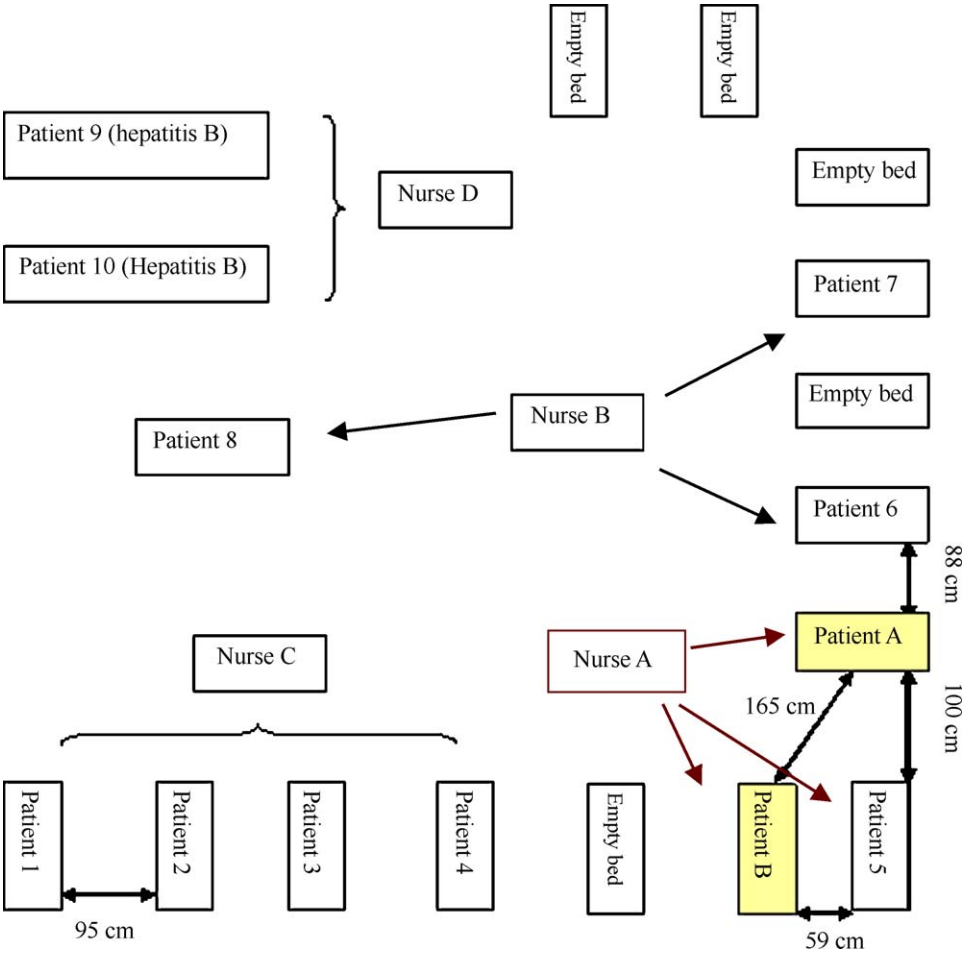

Figure 1. Bed and patient locations within the hemodialysis unit and standard assignment of nursing care (all bed-to-bed spaces are 95 cm unless marked otherwise).

with the medical staff. In addition, the medical and nursing staff completed a similar questionnaire.

Medical and nursing records of the Unit were reviewed, as well as infection control and catheter care practices. A review of medical and nursing records was undertaken for the two months prior to the hospitalization of the two patients, and included all patients receiving HD at the unit. Several discussions took place with the HD staff, both individually and also as a group, at each of the study team visits to the Unit, to better clarify the specific conditions and sequence of events during the last HD sessions (especially the last two) that most likely led to the two patient hospitalizations.

All patients and staff members were asked to submit rectal swabs for culture (in addition, women submitted vaginal swabs). Samples from patient 3 were not available due to her absence, while patient 4 refused to submit samples. All swabs were collected on the following day (second study team visit day) and were promptly transported to the Microbiology Department of Evaggelismos General Hospital. All swabs were incubated in brain heart broth at 35 °C and, after 24 h, the broths were subcultured on blood, MacConkey, and Sabouraud agar plates. A 5% CO_2-containing atmosphere was used for the blood agar plates. Species identification results were confirmed using the Vitek II Automated Microbiology System with ID card GP (bioMérieux). No serotyping or molecular typing was performed on the two isolates.

We visited the Unit once more, three weeks later, to obtain follow-up information on the status of all the patients. The level of cooperation between our study team and the Unit medical staff rose above any expectation.

3.1. Statistical analysis

Collected data were entered into a Microsoft Excel spreadsheet, and SPSS v.13 software was used for data processing (SPSS Inc., Chicago, USA). We used the Student's *t*-test for independent samples for the comparison of continuous variables and Fisher's exact test for categorical variables. A *p*-value of 0.05 or less was considered clinically significant.

4. Results

4.1. Organization of the hemodialysis unit, protocols used for patient care, and infection control practices

The Unit served a total of 28 patients at the time of the main incident. All these patients received care exclusively at this specific Unit. Twelve patients (including the two case patients) received care every Monday, Wednesday and Friday and 16 patients every Tuesday, Thursday and Saturday. The staff of the Unit included four female registered nurses (RNs) specialized in nephrology and three male physicians, two specialized nephrologists and an internal medicine resident on nephrology rotation. Every RN was responsible for two to four patients on a rotating schedule. Two beds of the Unit were reserved for patients with chronic hepatitis B and were served exclusively by one of the nurses. The locations of the beds and patients within the Unit, along with nursing assignments are shown in Figure 1.

The RN responsibilities when dealing with a patient included accessing the patient's device for HD (fistula, graft or CVHDC), connection of the patient to the HD equipment and machine, monitoring during HD, disconnection from the HD equipment, and final care of the HD device. A single brand of double-lumen cuffed HD catheter was in use in the Unit. The RNs applied the following aseptic techniques when handling the CVHDC: they initially used regular gloves to expose the device, then sterile gloves to release the CVHDC ports and cleanse at the CVHDC skin entry site with povidone–iodine solution; this was then covered again with sterile gauze. The ports and proximal parts of the CVHDC were subsequently cleansed with ethyl alcohol solution and povidone–iodine solution and then placed on sterile drapes. After changing sterile gloves, the ports were connected to the HD machine. After disconnection, the ports were flushed with heparinized saline, the openings were cleansed again with ethyl alcohol solution and povidone–iodine solution, and new caps were used to close the ports. The CVHDC skin entry site was then reopened for new cleansing with povidone–iodine solution, subsequent povidone–iodine ointment application and the CVHDC was finally covered and wrapped with sterile gauze. As a general rule, the RNs used a new pair of sterile gloves for every manipulation of the CVHDC and disposable gloves for equipment preparation.

4.2. Clinical characteristics of the remaining patients

The remaining patients did not differ from the two case patients in terms of age, sex, Hellenic or non-Hellenic ethnicity, rates of diabetes mellitus, hypertension, congestive heart failure, chronic liver disease, neurologic disease, or peripheral vascular disease (Table 1). Of the four female members of the group, three were over the age of 65 years and sexually inactive, while the fourth (age 47 years) reported menstrual irregularities, no vaginal complaints or known infections, and a single sexual partner. No individual had a known malignancy or was receiving any kind of immunosuppressive therapy. Additionally, no one had received any kind of antibiotic during the last two weeks before the main incident.

Table 1
Demographic and clinical characteristics of the two patients with group B streptococcal bacteremia and the other patients in the hemodialysis unit

Characteristic	Patients with group B streptococcal bacteremia ($n=2$)	Other hemodialysis patients ($n=10$)	*p*-Value
Age	73.5 ± 9.2	68.4 ± 11.7	0.58
Male sex	2/2	5/10	0.19
Hellenic ethnicity	2/2	8/10	0.49
Diabetes mellitus	1/2	5/10	1.00
Hypertension	0/2	6/10	0.45
Congestive heart failure	0/2	5/10	0.47
Chronic renal failure >6 months	2/2	9/10	0.64
Central venous catheter use for hemodialysis	2/2	2/10	0.028
Duration of hemodialysis >2 months	2/2	8/10	0.49
Hospitalization last 6 months	0/2	2/10	0.32
Febrile illness last 2 months	1/2	4/10	1.0
Care by nurse A for >30 min during last two hemodialysis sessions	2/2	1/9	0.007
Care by nurse B for >30 min during last two hemodialysis sessions	1/2	3/10	0.58
Care by nurse C for >30 min during last two hemodialysis sessions	0/2	3/10	0.37
Care by nurse D for >30 min during last two hemodialysis sessions	0/2	2/10	0.48

There were no significant differences between the remaining patients and the case patients in terms of duration of renal failure or hemodialysis. Usage of a CVHDC for HD was significantly less in the remaining patients (2/10, $p = 0.028$; patient 3 and patient 9 in Figure 1), with 7/10 using a fistula and 1/10 having an arteriovenous graft in place.

There was no prior incident of documented GBS bacteremia in any of the HD patients up to one year before the main incident. Additionally, the two groups did not differ in rates of hospitalization during the last six months ($p = 0.32$) or any febrile illness during the two-month period before the main incident ($p = 1.0$).

4.3. Pertinent characteristics of the Unit personnel

The age of the four female nurses ranged from 26 to 52 years, with three of them (nurses A, B and D) below the age of 35 years. Nurses A and D were at the first part of their menstrual cycle at the time of the main incident and nurse B at the second part (nurse C was post-menopausal). All four were sexually active, between one and five times per week, with a single stable partner. Only one out of the four (nurse D) reported regular condom use and there was no use of intrauterine devices. None reported symptoms or signs of vaginitis or a history of sexually transmitted diseases. None of the medical or nursing staff was suffering from a chronic medical condition or was receiving immunosuppressive therapy.

4.4. Detailed description of clinical events during the last two hemodialysis sessions

There were many lines of evidence, from staff recollection and written notes, that nurse A had been extremely busy with patient A during the last two HD sessions. Patient A was already febrile when he came for the previous HD session. The session had been repeatedly interrupted due to the patient's dizziness and generalized weakness. Since no significant hypotension was noted, the session was completed. No blood cultures were sent or antibiotic therapy administered at that time. At the last session, patient A presented with similar complaints and the session was terminated after 50 min due to hypotension, prompting admission to the hospital. Nurse A repeatedly used the help of nurse B in taking care of patient A during the last two HD sessions, but was much more involved with patient A than was nurse B. In addition, nurse B definitely did not take care of patient B at any time during the last two HD sessions. Patient B did not have any significant problems during any HD session (he had an abrupt onset of fever a few hours later). Nurse A could not rule out a possible breach in aseptic technique practices during CVHDC care of the two patients during the last two HD sessions.

4.5. Microbiology results

No rectal or vaginal culture of any HD patient or staff member was positive for GBS. All other samples and all vaginal samples from patients revealed only normal flora. All rectal swabs from the Unit personnel grew normal flora. Three out of the four vaginal samples from the Unit nurses revealed normal flora with concurrent presence of *Escherichia coli*, while the sample from nurse D grew *Streptococcus dysgalactiae* subsp *equisimilis* along with normal flora.

4.6. Further analysis

From patient records and interviews with nurses, we quantified the time each patient received care by one or more of the RNs during the last two HD sessions. The development of a recent febrile disease among the HD patients was significantly associated with the presence of a CVHDC ($p = 0.028$) and care for more than 30 min by nurse A during the last two HD sessions ($p = 0.007$).

4.7. Outcome of the two case patients and the remaining Unit patients

At the follow-up visit and in phone conversations with the Unit staff, it was determined that there was neither any recurrence of GBS bacteremia in the two case patients nor any other episode of documented GBS bacteremia or any febrile syndrome necessitating hospital admission in any of the Unit patients for up to eight weeks from the main incident date. The exception was patient B, who later (three weeks after completing treatment for GBS bacteremia) had a new episode of CVHDC-related sepsis with *S. epidermidis*.

During every single visit, our team tried to reinforce in every possible way the routine application of standard of care infection control practices in the Unit and also addressed the issue of vascular access in dialysis patients. We especially encouraged the initiation of routine surveillance for colonization by multi-resistant organisms and the maintenance of appropriate nurse-to-patient ratios at all times. The above were repeatedly and thoroughly discussed with both the Unit personnel and the administration.

5. Discussion

Within the limitations of our study effort, we speculate that the GBS strain was transmitted from patient A to patient B through the hands of medical personnel (most likely nurse A, who functioned as a transient carrier). The infection in patient A had arisen two to three days before, explaining his difficulties with his last two HD sessions. The primary responsibility of nurse A for both patients, in conjunction with conditions of emergency patient care during the last two HD sessions and localized patient and caregiver crowding (Figure 1), most likely led to one or more episodes of breaching in aseptic technique practices during CVHDC care of patients A and B, which resulted in bacteremia and sepsis in patient B after only a few hours. The isolates from the two patients had exactly the same susceptibility pattern to antibiotics. No serotyping was available and no molecular typing was performed to document clonality and horizontal transfer between the two patients.

No similar outbreak has ever been reported in HD patients. Gram-positive organisms are responsible for the majority of HD catheter-related infections, mainly coagulase-negative staphylococci and *Staphylococcus aureus* (40–81% of cases in reported studies). Risk factors for tunneled catheter infection include skin and nasal colonization with Staphylococcus, catheter hub colonization, prolonged duration of usage, thrombosis, a history of previous catheter-related bacteremia, frequency of catheter manipulation, diabetes mellitus, iron overload, immuno-incompetency, and the conditions of catheter placement.[13]

GBS can cause several types of urogenital syndromes and bacteremia in pregnant women, and also early- and late-onset neonatal sepsis.[14,15] Nosocomial transmission has been documented in newborn nursery outbreaks, implicating the hospital personnel as the vehicle for cross-infection.[16,17] The only existing report of a clinically overt GBS outbreak in adults in the English literature is that of a respiratory infection outbreak in an oncology unit with evidence of co-existent cross-infection with *Streptococcus pneumoniae* serotype 14 and GBS type Ia. The presumed route of transmission was patient-to-patient spread by droplets.[18] There is another report of epidemic GBS carriage only in a kindergarten, involving children and female staff members, where droplet spread along with other upper respiratory pathogens was also implicated.[19]

The importance of strict infection control practices in HD units and the avoidance of central venous catheters for long-term HD

cannot be overemphasized. The combination of a borderline ratio of nurse-to-HD patients, along with the use of a more infection-prone device for HD in comparison to fistulas or grafts, especially within the context of busy and emergency patient care, could have serious consequences for otherwise stable outpatients.

There are several limitations in our study. During the brief hospital stay of the two index patients, we were not able to do colonization studies, in part due to the rather late notification to the infectious diseases team. Also, serotyping and molecular typing was not available for the two isolates. The outbreak study took place relatively late and, although almost nothing is known about the duration of GBS carriage in HD patients, that delay may have accounted for the uniformly negative results from surveillance specimens. Due to limited resources in specimen handling and processing, no surveillance cultures were obtained from other body sites of the Unit patients and personnel. Thus, we cannot be certain about the way in which the sequence of events was initiated. Due to the same restrictions and the initial negative microbiology results, we did not screen the rest of the Unit patients. However, we carefully reviewed the medical records and discussed with the house staff the status of all patients several weeks before and after the main incident, and there was no suggestion of GBS disease.

In conclusion, we have presented a probable outbreak of hemodialysis catheter-related GBS bacteremia with sepsis in a small HD unit. Attention to proper infection control practices, avoidance of central venous catheters for long-term HD, along with prompt and complete evaluation of febrile episodes, are of the utmost importance for better care of these patients and better recognition of emerging pathogens posing a threat to their wellbeing.

Conflict of interest

No conflict of interest to declare.

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