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Clinical management of dialysis catheter-related bacteremia with concurrent exit site infection

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Abstract

Dialysis catheter-related bacteremia (CRB) can frequently be treated with systemic antibiotics, in conjunction with an antibiotic lock, in an attempt to salvage the catheter. It is unknown whether CRB associated with an exit site infection can be treated with such an approach. We retrospectively queried a prospective, computerized vascular access database, and identified 1436 episodes of CRB, of which 64 cases had a concurrent exit site. The frequency of concurrent exit site infection was 9.6% with *Staphylococcus epidermidis*, 6.1% with *Staphylococcus aureus*, and only 0.7% with Gram negative CRB ($p < 0.001$ for *Staphylococcus* vs Gram negative rods). Five serious complications (4 major sepsis, 1 endocarditis) occurred in 24 patients with *Staphylococcus aureus* infection, but none in 32 episodes of *Staphylococcus epidermidis* infection. Catheter survival was significantly shorter in patients with *Staphylococcus aureus* infections. The median catheter survival (without infection or dysfunction) was 14 days with *Staphylococcus aureus* vs 30 days with *Staphylococcus epidermidis* infection. In conclusion, concurrent exit site infection is seen most commonly in association with *Staphylococcal* CRB. When the infecting organism is *Staphylococcus epidermidis*, attempted salvage with systemic antibiotics and an antibiotic lock is reasonable. However, prompt catheter removal is indicated when the pathogen is *Staphylococcus aureus*.

Introduction

Catheters are used for vascular access in about 25% of U.S. hemodialysis patients (1). Their infectious complications include exit site infections and catheter-related bacteremia (2). Exit site infections can be treated with local antiseptics and oral or intravenous antibiotics. When conservative management is inadequate to resolve an exit site infection, the infected catheter is removed, and a new one placed through a different subcutaneous tunnel. Catheter-related bacteremia always requires administration of intravenous antibiotics. There are three options for management of the infected catheter: removal of the catheter with delayed placement of a new tunneled dialysis catheter; guidewire exchange of the infected catheter for a new one after a few days, if the symptoms and bacteremia have resolved with antibiotics; or instillation of an antibiotic lock into the catheter lumen, in conjunction with systemic antibiotics, in an attempt to salvage the catheter (3-13).

A subgroup of patients develops catheter-related bacteremia with a concurrent exit site infection. Such patients accounted for 24% of the total in a series of 114 patients with catheter-related bacteremia (4). The optimal medical management of such patients remains uncertain. One study suggested that if the patient's symptoms were mild, a cure could be achieved in 75% of cases by exchanging the infected catheter over a guidewire with creation of a new subcutaneous tunnel (4). The goal of the present study was to determine whether the dialysis catheter could be salvaged in such patients by treatment with systemic antibiotics and an antibiotic lock.

To evaluate this question, we retrospectively queried a prospective computerized database to identify all patients diagnosed with a concurrent catheter-related bacteremia and an exit site infection. We determined the frequency of this occurrence, the type of pathogen, and the clinical outcomes of the patients.

Methods

Study population

The University of Alabama at Birmingham (UAB) provides medical care to approximately 500 in-center hemodialysis patients at 5 hemodialysis units in metropolitan Birmingham. UAB nephrologists supervise the medical care of these patients. At any time, approximately 25% of these patients are catheter-dependent. Two full-time access coordinators schedule all vascular access procedures, monitor for complications, and maintain a prospective, computerized database of all procedures and outcomes (14).

Management of hemodialysis catheters

UAB interventional radiologists or nephrologists placed the tunneled hemodialysis catheters. Catheters were connected and disconnected to the dialysis tubing using aseptic technique. The catheter lumens were instilled with heparin after each dialysis session. Catheters with suspected dysfunction were instilled with tissue plasminogen activator (tPA). If this measure was unsuccessful in restoring patency, the catheters were exchanged for a new one over a guidewire. Catheter exit site infection was diagnosed in patients with purulent drainage from the exit site with positive wound cultures.

Catheter-related bacteremia was suspected in patients with fever or rigors. After obtaining blood cultures from the catheter lumen and the dialysis bloodline, the patients were initiated on empiric broad-spectrum antibiotics (vancomycin and ceftazidime), in conjunction with an antibiotic lock (8). The antibiotics were discontinued in patients with negative blood cultures. Patients with positive blood cultures and uncomplicated infection received a three-week course of systemic antibiotics (tailored to the reported sensitivities), along with an antibiotic lock. The duration of antibiotics was prolonged to 6 weeks in patients with evidence of metastatic infection. The dialysis catheter was removed in patients with persistent fever and rigors after 48 hours of antibiotics or in those with recurrent bacteremia after discontinuation of the antibiotic regimen.

Data and statistical analysis

The dialysis nurses reported each suspected infection to the access coordinators, and filled out a standardized form with the relevant information. The access coordinators maintained a computerized record of all suspected catheter infections, verified whether the patient's symptoms resolved, monitored the culture results, and scheduled subsequent catheter procedures in patients with persistent symptoms or recurrent bacteremia. Our local Institutional Review Board provided approval for retrospective review of existing medical records of patients with access complications. We retrospectively queried the computerized database to identify all (N=2061) episodes of suspected catheter-related bacteremia during a 5-year period (6/4/04 to 6/3/09). The UAB electronic medical records were used to obtain patient information, hospitalizations, and clinical outcomes.

Duration of catheter survival was calculated from catheter infection to non-elective catheter removal or exchange (due to infection or dysfunction). Kaplan-Meier survival curves were generated for catheter survival, with patient follow-up censored at the time of death or elective catheter removal due to a mature arteriovenous access. The differences between survival curves were analyzed using the log rank test. A p-value <0.05 was considered statistically significant.

Results

During the five-year period included in our study analysis, there were 2061 episodes of suspected catheter-related bacteremia. Of these, 1436 (70%) had positive blood cultures. Polymicrobial bacteremia was present in 81 cases (~6%). The remaining cases of catheter-related bacteremia included 919 with a Gram positive coccus and 436 with a Gram negative rod. Thus, 68% of episodes were caused by a Gram positive coccus. The breakdown of specific pathogens is summarized in **Table 1**.

Overall, a concurrent exit site infection was present in 64 cases of catheter-related bacteremia, or 4.4% of the total (Table 1). However, the frequency of concurrent exit site infection varied greatly among organisms, being 9.6% with *Staphylococcus epidermidis* infections, 6.1% with *Staphylococcus aureus* infections, and only 0.7% with Gram-negative infections (p=0.08 for *Staphylococcus epidermidis* vs *Staphylococcus aureus*, and p<0.001 for *Staphylococcus epidermidis* vs Gram negative rods). Thus, infections with *Staphylococcus aureus* or *Staphylococcus epidermidis* accounted for 88% of all cases of concurrent catheter-related bacteremia and exit site infection.

The *Staphylococcal* infections with concurrent bacteremia and exit site infection were analyzed further in terms of patient outcomes. Among the 24 patients with *Staphylococcus aureus* infection, there were 5 major complications, including severe sepsis in 4 and endocarditis in 1. Three of these patients died of their infection. In contrast, among 32 patients with *Staphylococcus epidermidis* infection, none had a serious complication. Thus, major complications were significantly more common with *Staphylococcus aureus* than with *Staphylococcus epidermidis* infections (20% vs 0%, p=0.01 by Fisher's exact test).

We also examined catheter survival from the time of infection for these two patient subgroups (Figure 2). Catheter replacement within 4 days of the infection occurred in 33% of patients with *Staphylococcus aureus*, but only 12.5% of patients with *Staphylococcus epidermidis* infection. The median catheter survival (without infection or dysfunction) was 14 days with *Staphylococcus aureus* vs 30 days with *Staphylococcus epidermidis* infection. The hazard ratio for catheter failure for infections with *Staphylococcus aureus* was 1.81 (95% confidence interval, 1.05-3.58; $p=0.035$).

Discussion

We observed a relatively high (6.1 to 9.6%) frequency of concurrent exit site infection in patients with hemodialysis catheter-related *Staphylococcus aureus* or *epidermidis* bacteremia, and a much lower rate (<1%) in patients with Gram negative bacteremia. This difference suggests that *Staphylococcus* species are much more likely than Gram-negative rods to colonize the skin. The frequency of concurrent exit site infection observed in the current study was substantially lower than the 24% rate reported by Beathard et al (4). It should be noted, however, that we used a more stringent definition of exit site infection, requiring a purulent exudate with positive cultures. In contrast, Beathard et al defined exit site infection as “some combination of erythema, swelling, tenderness and purulent drainage surrounding the catheter exit site” (4). In addition, the proportion of catheter-related bacteremias due to Gram positive cocci was lower in the present study (~68%), as compared with the 84.5% rate reported by Beathard.

On the basis of their observations, Beathard et al recommended that catheter-related bacteremia associated with an exit site infection be treated by guidewire exchange with creation of a new subcutaneous tunnel (4). The present study suggests that in a subset of such patients (those with *Staphylococcal epidermidis* bacteremia), systemic antibiotics in conjunction with an antibiotic lock can frequently permit catheter salvage while curing the infection. In contrast, patients with *Staphylococcus aureus* infections had a high rate of metastatic infection, death, and treatment failures. The higher morbidity associated with *Staphylococcus aureus* infections is consistent with previous reports (8, 15, 16).

The current study has some limitations. First, the data analysis was retrospective. However, the information was collected and recorded prospectively, suggesting that it was complete and accurate. Second, the results represent a single center experience, and may not generalize to all dialysis centers.

In summary, exit site infection is relatively often associated with *Staphylococcal* dialysis catheter-related bacteremia, but rarely seen in conjunction with Gram negative infection. When the infecting organism is *Staphylococcus epidermidis*, attempted catheter salvage with systemic antibiotics and an antibiotic lock is a viable approach. However, when the infecting organism is *Staphylococcus aureus*, prompt catheter removal is the preferred medical management

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Fig 1. Catheter survival after infection in patients with concurrent catheter-related bacteremia and exit site infection. The endpoint was catheter removal or exchange due to infection or dysfunction. $p=0.035$).

Table 1

Microbiologic features of patients with catheter-related bacteremia

Bacteria	ALL CRB's	CRB + concurrent exit site inf, N (%)
All	1436	
Single organism	1355	62 (4.6%)
Gram positive coccus	919	
<i>Staph epi</i>	335	32 (9.6%)
<i>Staph aureus</i>	393	24 (6.1%)
<i>Enterococcus</i>	191	3 (1.6%)
Gram neg rods	436	3 (0.7%)
<i>Enterobacter</i>	129	
<i>Klebsiella</i>	92	
<i>Pseudomonas</i>	62	
<i>E. coli</i>	44	
<i>Proteus</i>	42	
<i>Acinetobacter</i>	40	
<i>Serratia</i>	27	

CRB, catheter-related bacteremia