Catheter-related Bacteremia Caused by *Agrobacterium radiobacter* in a Hemodialysis Patient

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Abstract

Agrobacterium radiobacter, a Gram-negative bacillus, is recognized as an emerging opportunistic human pathogen that has a propensity to cause infections in patients with indwelling foreign devices. Here, we describe the first reported case of catheter-related bacteremia caused by *A. radiobacter* in a hemodialysis patient with a long-term tunneled-cuffed hemodialysis catheter. This case shows that *A. radiobacter* should be included in the list of pathogens that can cause catheter-related bacteremia in hemodialysis patients.

Key words: *Agrobacterium radiobacter*, catheter-related bacteremia, hemodialysis, tunneled-cuffed catheter

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Introduction

The number of hemodialysis patients with a tunneled-cuffed hemodialysis catheter (TCHC) for long-term vascular access has increased in recent years, due to an increase in patients in whom construction of an arteriovenous fistula or graft is difficult because of exhausted vasculature or severely impaired cardiac function. Catheter-related bacteremia (CRB) is a serious complication of a TCHC that can lead to substantial morbidity and catheter removal, and may occasionally be fatal (1).

The causative organisms of CRB are Gram-positive cocci (*Staphylococcus* and *Enterococcus* species) in approximately 60% of hemodialysis patients with TCHCs, with a wide variety of Gram-negative bacilli accounting for about 30% of cases. Mixed infections and fungal organisms make up the remaining isolates (1, 2). The incidence of CRB due to Gram-negative bacilli in hemodialysis patients is increasing, reflecting trends in isolate patterns reported for patients with non-dialysis central venous catheters (3), and unusual organisms such as *Serratia*, *Acinetobacter* and *Citrobacter* are also emerging as opportunistic pathogens (1, 2). Here, we describe a unique case of CRB caused by one such uncommon Gram-negative bacillus, *Agrobacterium radiobacter*, in a patient receiving chronic hemodialysis with a TCHC.

Case Report

The patient was a 75-year-old Japanese woman who had received hemodialysis 3 times a week for 3 years due to end-stage kidney disease secondary to diabetic nephropathy. She was referred from an outpatient hemodialysis unit because of spiking fever with chills after hemodialysis sessions over 2 weeks. The hemodialysis was performed via a right subclavian TCHC (Soft-Cell™; C.R. Bard., 12.5 Fr, 19 cm) that had been inserted 2 years earlier for long-term vascular access, since she had no other options for vascular access due to markedly decreased cardiac function (LVEF 28%) caused by severe coronary disease and exhausted vasculature.

A physical examination failed to reveal a sign of infection, including in the tunnel tract and exit-site of the TCHC. The patient had severe symptoms of heart failure and showed marked weakening. Blood pressure was 84/38 mmHg, heart rate was 70 beats/min and regular, and body temperature was 36.6°C (18 hours after the hemodialysis session). Laboratory tests revealed a white blood cell (WBC) count of $6.2 \times 10^3/\mu\text{L}$ ($6.2 \times 10^9/\text{L}$) and a C-reactive protein (CRP) level of 6.44 mg/dL. All other data were unremarkable. A chest X-ray showed mild congestive heart failure. Gallium scintigraphy and computed tomography of

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the brain, chest and abdomen showed no evidence of infection or malignancy.

Empirical antibiotic therapy with parenteral ampicillin/sulbactam (1.5 g/day) was initiated, based on a suspected diagnosis of CRB from the symptom of spiking fever after the hemodialysis session. Two sets of blood cultures using samples from peripheral veins and one set based on samples taken through the lumen of the TCHC were obtained. All three sets yielded a Gram-negative bacillus, which was later identified as *A. radiobacter*. Therefore, the patient was diagnosed with CRB caused by *A. radiobacter*. The isolates were susceptible to ampicillin, cefotiam, cefmetazole, imipenem/cilastatin, meropenem, amikasin, minomycin and levofloxacin, but resistant to piperacillin, fosfomycin and ceftazidime.

The patient showed rapid abatement of fever, remained afebrile and showed clinical improvement. Thus, we continued to attempt to salvage the TCHC as long as the patient had a good clinical response to antibiotic therapy. Antibiotics were administered for 21 days and the infection seemed to have been resolved completely. However, spiking fever of 39°C developed again after a hemodialysis session 3 days after completion of antibiotic therapy. The same antibiotic therapy was reinitiated and two sets of blood cultures from peripheral veins both yielded *A. radiobacter*. In view of the relapsing nature of CRB, we decided to remove the catheter since we judged that salvage of the TCHC would be difficult. The period from TCHC insertion to removal was 736 days. Cultures of the cuff of the catheter and the catheter tip gave negative findings. The infection was controlled efficiently after removal of the TCHC, but the patient had difficulty with hemodialysis due to further exacerbation of cardiac function and died of heart failure 4 weeks after removal of the catheter. The death was not directly attributed to CRB.

Discussion

Members of the genus *Agrobacterium* are aerobic, motile, oxidase-positive, and non-spore-forming Gram-negative bacilli. These organisms are found chiefly in soils worldwide and are primarily known to cause tumorigenic plant disease. *A. radiobacter* is the most common species of the genus known to cause human disease. This organism is found only infrequently in clinical specimens, but is emerging as a rare opportunistic pathogen that causes infections in chronically debilitated patients. *A. radiobacter* infection can be resolved in the majority of patients and is rarely fatal, indicating that this organism has low virulence (4).

Mastroianni et al (5) summarized 34 cases of *A. radiobacter* infections from 1980 to 1996, and thereafter Paphitou and Rolston (6) described 8 additional cases from 1996 to 2002. Of the combined 42 cases, 81% (34/42) were associated with the presence of foreign devices (e.g., indwelling intravascular devices, peritoneal dialysis catheters, nephrostomy tubes) and 93% (39/42) had underlying conditions in-

cluding an immunocompromised state (cancer, hematologic malignancy, AIDS) or debilitation due to a chronic disease such as end-stage kidney disease requiring peritoneal dialysis. These data indicate that *A. radiobacter* is an opportunistic organism that has the propensity to cause infection in patients with indwelling foreign devices. CRB, peritonitis that is usually associated with peritoneal dialysis, urinary infections in the presence of nephrostomy tubes, and pneumonia are the most common clinical conditions associated with *A. radiobacter* infection (5-7). The strong correlation between *A. radiobacter* and indwelling foreign devices may be explained by the finding of Alnor et al that this organism showed marked adhesion to silicone tubes, comparable to *Staphylococcus* species, in an experimental model (8).

The mechanism of acquisition of *A. radiobacter* has yet to become clear. Although the organism is found in soil, only one case report has mentioned probable central venous catheter contamination from exposure to soil before development of *A. radiobacter* infection (9). The patient in the current case was not exposed to soil or plant material as an explanation for inoculation, and the source of bacteria and the route of bacterial entry to the bloodstream are unknown.

Diagnosis of CRB in a hemodialysis patient is definite when the same organism is cultured from the catheter tip and from a peripheral or catheter blood sample in a symptomatic patient with no other apparent source of infection. The catheter tip culture gave a negative finding in this case, but we believe that CRB caused by *A. radiobacter* was the appropriate diagnosis because two samples from peripheral blood and a sample from catheter blood all yielded *A. radiobacter* without another evident source and the infection was efficiently controlled after removal of the TCHC. In addition, spiking fever after hemodialysis indicated that bacteria or pyrogens sequestered in or around the TCHC had been released by blood flow through the TCHC. The negative finding for the catheter tip culture may have reflected the use of antibiotics delivered through the TCHC.

This case showed typical characteristics of *A. radiobacter* infection, since the patient had an indwelling intravascular device and was a chronically debilitated host due to underlying end-stage kidney disease, impaired cardiac function, and diabetes mellitus. We believe that this is the first reported case of CRB caused by *A. radiobacter* in a hemodialysis patient. The case indicates that *A. radiobacter* should now be viewed as an emerging pathogen of opportunistic infections in hemodialysis patients, particularly given the increasing number of patients with indwelling foreign devices who are chronically debilitated due to diabetes mellitus, cardiovascular disease or complications related to chronic hemodialysis.

The clinical practice guidelines for vascular access published by the Kidney Disease Outcomes Quality Initiative of the National Kidney Foundation (NKF-K/DOQI) (10, 11) indicate that the TCHC should be removed in a clinically unstable CRB patient regardless of the causal organism. In addition, these guidelines recommend treatment of stable CRB patients without exit-site or catheter tunnel tract in-

volvement who become afebrile after initial antibiotic therapy by exchanging the catheter over a guidewire plus a minimum of 3 weeks of systemic antibiotics or catheter salvage with systemic antibiotics in conjunction with antibiotic locks. Parenteral antibiotic therapy alone is not recommended due to its low success rate (25-32%) (1, 2, 12). However, a lack of clinical evidence makes it unclear whether these guidelines are applicable in cases caused by *A. radiobacter*.

There is no consensus regarding the need for removal of indwelling foreign devices in treatment of *A. radiobacter* infections. The guidelines for management of intravascular catheter-related infections published by the Infectious Diseases Society of America (IDSA) (13) lists the *Agrobacterium* species among the Gram-negative organisms for which "serious consideration should be given to catheter removal, especially if bacteremia continues despite appropriate antibiotics or if the patient becomes unstable." Of the combined

42 cases described above, 48% of CRB cases (10/21) were treated successfully without catheter removal and this success rate was higher than that of other organisms. Therefore, we initially attempted to salvage the TCHC based on the prior evidence of an effect of antibiotic therapy.

Based on literature data and our experience, antibiotic therapy for salvage of an intravascular catheter in CRB caused by *A. radiobacter* is a good initial choice, but caution must be exercised since the infection can relapse after therapy, even in cases in which the antibiotic therapy appears to have sufficiently suppressed *A. radiobacter*, as in the current case. The catheter should be removed immediately for a better outcome upon relapse of the infection. In conclusion, we suggest that *A. radiobacter* should be included in the list of pathogens that cause CRB in hemodialysis patients with a TCHC, and that the course of treatment should be determined on a case-by-case basis and may involve catheter removal.

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