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ARTICLE

Catheter-related *Corynebacterium* bacteremia: should the catheter be removed and vancomycin administered?

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Abstract The purpose of this study was to determine the need for central venous catheter removal in patients with corynebacterial catheter-related bloodstream infections and the impact of central venous catheter retention on response to systemic antibiotic therapy and relapse. We searched the microbiology laboratory database and patients' medical records at our institution between January 2000 and December 2006. We identified 98 patients with corynebacteria infection. Most of the episodes (94%) were catheter-related. Removing the catheter did not affect the outcome of treatment, particularly when an active non-glycopeptide antibiotic was used. All *Corynebacterium* species isolates were susceptible to vancomycin, 54/55 (98%) to linezolid, 80/95 (84%) to rifampin, and 69/85 (81%) to tetracycline. The median duration of antibiotic therapy was 12 days (range, 0–28), and vancomycin was the most commonly used antibiotic (64%). There was a trend toward earlier fever resolution in patients treated with non-glycopeptide antibiotics compared to vancomycin, particularly if the catheter was not removed. Central venous catheter removal might not be necessary in patients with corynebacterial catheter related bloodstream infection, particularly if systemic therapy consists of non-glycopeptide antibiotics. Treatment with a systemic active antibiotic over a 7-day period appears to be adequate for resolution of the infection.

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Introduction

Corynebacteria are known to cause a variety of serious infections and are frequently reported as contaminants of clinical specimens. When corynebacteria are isolated from blood cultures, they are primarily associated with central venous catheters [1, 2]. This organism is also known to form a biofilm matrix in which they embed themselves on the catheter [3, 4].

Corynebacterial species have been shown to be susceptible to vancomycin in most instances [5], although Williams et al. reported some vancomycin-resistant species [5]. Vancomycin is still considered the drug of choice for the treatment of corynebacterial infection. However, vancomycin is known to have poor ability to eradicate bacteria embedded in biofilm, which becomes a therapeutic challenge if the central venous catheter (CVC) is retained [6].

To date, there are no clear guidelines regarding the management of corynebacterial catheter-related bloodstream infections (CCRBSI). The current Infectious Diseases Society of America (IDSA) guidelines on the management of CCRBSI have remained relatively silent on this issue [7].

Patients and methods

Clinical characteristics

Through a search of the microbiology laboratory database and the patients' medical records at The University of Texas M. D. Anderson Cancer Center (Houston, Texas) between January 2000 and December 2006, we retrospectively identified 98 patients with corynebacteria infection.

This study was conducted under a waiver of informed consent and was approved by the M. D. Anderson Cancer Center Institutional Review Board.

Epidemiologic, clinical, and microbiologic data were collected for the patients. The APACHE II score had been calculated at the onset of bacteremia.

Definitions

A positive blood culture was defined as a quantitative culture using lysis-centrifugation with >30 colony-forming units (CFU)/mL. This definition was based on a recent study from our center that demonstrated that blood cultures with >15 CFU/mL of commensal skin organisms are highly suggestive of true bacteremia [8]. Definite or probable catheter-related bloodstream infections (CRBSI) were characterized as corynebacterial infections that were not related to an infection at another site.

CRBSI was classified as either definite or probable according to current IDSA criteria guideline. CRBSI was considered probable if the patient had an indwelling CVC with at least one positive blood culture with clinical manifestations of infections (i.e., fever, chills, and/or hypotension), and no apparent source for the bloodstream infection except the catheter.

CRBSI was considered definite if the patient fulfilled all the criteria for probable CRBSI plus at least one of the following: a positive semiquantitative (>15 CFU/catheter segment) or quantitative (>10^3 CFU/catheter segment catheter) culture whereby the same organism (species and antibiogram) was isolated from the catheter segment and peripheral blood; simultaneous quantitative blood cultures from the catheter and peripheral vein revealing a ratio >5:1 (CVC versus peripheral); indicative differential time to positivity (that is, the blood culture obtained through CVC became positive at least 2 hours earlier than a positive simultaneous blood culture obtained from a peripheral vein).

Corynebacterial bloodstream infections were defined as recurrent when blood cultures positive for *Corynebacterium* species occurred at least two weeks after an initial positive culture and after the patient had shown a clinical response to therapy with antibiotics with in vitro activity against the initial isolate.

Statistical methods

Chi-square or Fisher exact tests were used for categorical data analysis. Continuous variables were compared by Wilcoxon rank sum tests. The statistical significance was set at $p \leq 0.05$. All statistical analyses were performed using SAS version 9.1 (SAS Institute Inc., Cary, North Carolina, USA).

The analysis included 98 patients who met the criteria for *Corynebacterium* species bacteremia. The majority of the patients (66%) had hematologic malignancies, and almost half (47%) had neutropenia at the time of their first positive *Corynebacterium* species blood culture. Within a month before the first *Corynebacterium* species was isolated, 63% had received antibiotic treatment, 53% had transfusion of blood products, and 48% had been hospitalized.

Ninety-two patients (94%) met the criteria for CRBSI (32% definite and 62% probable). Seventy-six patients (78%) were admitted to the hospital, with a median hospital stay of 7 days (range, 1–70 days). Most patients had fever (93%) and sepsis (84%), but few (4%) had septic shock. One (1%) death was attributable to *Corynebacterium* infection, with only 2 (2%) recurrences and no complications due to disseminated disease were noted within 3 months of follow-up. The median APACHE II score on the date of infection was 14 (range, 3–23). All *Corynebacterium* species

Table 1 Effects of treatment with vancomycin on outcome[a]

Outcomes	All cases			Patients whose catheters were not removed		
	Vancomycin (n=63)	Non-glycopeptide[b] antibiotics (n=35)	P	Vancomycin (n=33)	Non-glycopeptide[b] antibiotics (n=17)	P
Time to fever resolution in days for patients with CRBSI, median (range)	2 (0–53)	1 (0–11)	0.11	2 (1–53)	1 (0–4)	0.06
Length of hospital stay in days for all patients with CRBSI, median (range)	9 (2–57)	4 (1–21)	0.0002	10 (2–57)	4 (1–8)	0.006
Length of hospital stay in days for patients who were admitted because of CRBSI, median (range)	7 (1–57)	4.5 (2–40)	0.04	6 (2–57)	4 (2–6)	0.046

CRBSI catheter-related bloodstream infection

[a] For patients whose catheters were removed within 72 hours, there was no significant difference in the outcomes outlined above (vancomycin therapy versus other antibiotics)

[b] The nonglycopeptide antibiotics used were: imipenem, meropenem, piperacillin/tazobactam, cefepime and levofloxicin

isolates were susceptible to vancomycin, 54/55 (98%) to linezolid, 80/95 (84%) to rifampin, and 69/85 (81%) to tetracycline. The median duration of antibiotic therapy was 12 days (range, 0–28), and vancomycin was the most commonly used antibiotic (64%).

There was a trend toward earlier fever resolution in patients treated with non-glycopeptide antibiotics compared to vancomycin, particularly if the CVC was not removed ($p=0.06$, Table 1). In a subanalysis of these patients, the median duration of hospital stay with which vancomycin therapy was associated relative to treatment with non-glycopeptide antibiotics was significantly prolonged only when the CVC was retained longer than 72 hours, with median stays of 10 days (range, 2–57) for the former group and 4 days (range, 1–8) for the latter ($p=0.006$). This difference was not noted when the catheter was removed within 72 hours.

This study is the largest case series of *Corynebacterium* bacteremia in cancer patients. Our data show that *Corynebacterium* bacteremia is largely (98%) associated with indwelling intravascular catheters [1, 2]. In addition, the use of vancomycin was significantly associated with longer hospital stay when the CVC was not removed within the first 72 hours. However, removal of the CVC may not be necessary in the management of all CCRBSI, particularly if a nonglycopeptide antibiotic is used.

Our patients had all the traditional risk factors for corynebacterial infections [2, 9–11], and like others, we found a preponderance of infections in men [12]. Recipients of blood products are also known to be at increased risk of *Corynebacterium* bacteremia [9], and in our study over 50% of the patients had received blood products.

Vancomycin has been considered the drug of choice for the treatment of *Corynebacterium* infections [9, 11, 12] primarily because many of the commonly isolated *Corynebacterium* species, such as *C. jeikeium*, are known to be susceptible to vancomycin but resistant to other antibiotics. Furthermore, several studies reported that *Corynebacterium* species can form a biofilm on catheter surfaces [3, 4], and vancomycin has been shown to have poor activity in eradicating bacteria embedded in biofilm [4, 6]. Therefore, it is not surprising to note longer durations of hospitalization and a trend towards an increased number of days to fever resolution in patients treated with vancomycin when the indwelling CVC is not removed.

The management of vascular access catheters has been controversial. Most publications, including the current IDSA guidelines for management of intravascular catheter-related infections, suggest catheter removal when the infection is due to *C. jeikeium* [7] and antibiotic therapy without catheter removal for infections caused by other species of corynebacteria [2, 7]. However, Wang et al. [11] demonstrated that *C. jeikeium* bacteremia may be treated successfully without catheter removal. In our study, retaining the CVC neither increased the risk of relapse nor prolonged the number of days to fever resolution or the length of hospital stay. This is important because cancer patients depend immensely on the vascular access device, and removal and reinsertion of the CVC might not be feasible and may be associated with complications and increased cost.

Consistent with the study by Wang et al. [11], we did not find any deep-seated complications as a result of invasiveness or dissemination of the *Corynebacterium* species, such as infective endocarditis, septic phlebitis, or any deep soft tissue infections. In addition, patient mortality attributable to *Corynebacterium* infection was only 1%.

The limitations of the study include its retrospective design, the lack of identification of *Corynebacterium* species, and the lack of routine follow-up blood cultures, necessitating the use of clinical signs to assess response.

In conclusion, CVC removal might not be necessary in patients with CCRBSI, particularly if systemic therapy consists of non-glycopeptide antibiotics. In addition, treatment with a systemic active antibiotic over a 7-day period appears to be adequate for resolution of the infection.

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