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Original article

Retrospective evaluation of the clinical characteristics associated with *Corynebacterium* species bacteremia

Mitsuru Yanai[a,*], *Maiko Ogasawasa*[a], *Yuta Hayashi*[a], *Kiyozumi Suzuki*[a], *Hiromichi Takahashi*[b], *Atsushi Satomura*[b]

[a] *Nihon University School of Medicine, Department of Internal Medicine, Division of General Medicine, Tokyo, Japan*
[b] *Nihon University School of Medicine, Department of Pathology and Mircobiology, Division of Laboratory Medicine, Tokyo, Japan*

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ABSTRACT

Objectives: *Corynebacterium* spp. are becoming recognized as pathogens that potentially cause various infections. We aimed to evaluate the clinical characteristics associated with *Corynebacterium* spp. bacteremia.

Patients and methods: We retrospectively reviewed the medical records of all adult patients who had positive blood cultures for *Corynebacterium* spp. in a single university hospital between January 2014 and December 2016. Patients were divided into a bacteremia group and a contamination group based on microbiological test results and clinical characteristics. Patients' characteristics, antimicrobial susceptibility of isolated species, antimicrobials administered, and patient outcomes were evaluated.

Results: *Corynebacterium* spp. were isolated from blood samples of 63 patients; *Corynebacterium striatum* was the predominant isolate. Twenty-eight patients were determined to have bacteremia. Younger age ($p = 0.023$), shorter time to positivity ($p = 0.006$), longer hospital stay ($p = 0.009$), and presence of an indwelling vascular catheter ($p = 0.002$) were observed more often in the bacteremia group compared to the contamination group. The source of infection in most patients with bacteremia was an intravenous catheter. All tested strains were susceptible to vancomycin. Four of the 27 patients with bacteremia died, despite administration of appropriate antimicrobial therapy.

Conclusions: We found that younger age, shorter time to positivity, and presence of an indwelling catheter were related to bacteremia caused by *Corynebacterium* spp. Appropriate antimicrobials should be administered once *Corynebacterium* spp. are isolated from the blood and bacteremia is suspected.

* *Corresponding author.*
E-mail address: yanai.mitsuru@nihon-u.ac.jp (M. Yanai).

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Introduction

Except for *Corynebacterium diphtheriae*, all *Corynebacterium* spp. are ubiquitous skin commensals and are usually considered to be blood culture contaminants.[1] However, some reports have highlighted the importance of *C. striatum* and *C. jeikeium* as causes of catheter-related bloodstream infections in immunocompromised patients, and as causes of various infections in immunocompetent patients, such as arthritis and endocarditis.[2–5] It is difficult to distinguish contamination from bacteremia when *Corynebacterium* spp. or coagulase-negative staphylococci are isolated from blood samples.[6–9] In clinical practice, it is important to distinguish contamination from bacteremia to prevent unnecessary prescription of antimicrobial agents, which can lead to selection of antimicrobial-resistant organisms, longer duration of hospitalization, and increased costs.[10]

There are few studies on *Corynebacterium* spp. infection, and the clinical significance of these organisms remains unclear. Thus, in this study, we aimed to evaluate the clinical characteristics of bloodstream infections caused by *Corynebacterium* spp. by analyzing clinical cases of blood cultures positive for *Corynebacterium* spp.

Patients and methods

Patient selection and study period

This retrospective cohort study was conducted at the Nihon University Itabashi Hospital (NUIH), a 1037-bed teaching hospital. The catchment area of NUIH encompasses the north part of Tokyo, Japan. We reviewed the medical records of all patients aged >18 years who had positive blood culture results for *Corynebacterium* spp. between January 2014 and December 2016. Only the first episode was considered in case of multiple episodes within a 4-week period.

Definitions

Blood specimens were cultured using a set of culture bottles (BACTEC 92F and 93F; BD Diagnostic Systems, Franklin Lakes, NJ, USA) and automated systems (BACTEC 9240 and 9120; BD Diagnostic Systems) with continuous agitation were used. Bacterial species were identified through several methods, including assessment of morphologic appearance and colonies, and assessment of biochemical characteristics using manual procedures or commercial kits (API series; bioMérieux, Marcy l'Etoile, France and N-ID test SP-18; Nissui Pharmaceutical Co., Ltd., Tokyo, Japan) or an automated identification system (RAISUS system, Nissui Pharmaceutical Co., Ltd.). Antimicrobial susceptibility tests were performed by broth microdilution using the Clinical and Laboratory Standards Institute's breakpoints.[11]

Patients were categorized as having bacteremia if at least two blood culture sets taken at the same time turned out positive for the same *Corynebacterium* spp., or when one blood culture specimen and another clinically relevant sample taken from another site (such as a catheter tip, sputum, or pus) yielded positive results. If only one set of blood cultures turned out positive and culture specimens taken from other sites were negative, or if another infection was more likely at the time, the case was deemed to be contamination. The final decision of bacteremia or contamination was determined by the authors, which includes certified infectious diseases specialists on the antimicrobial stewardship program team.

Evaluated parameters

We reviewed the medical records to extract data on each patient's background (age, sex, underlying disease, body temperature, clinical department, presence of a vascular catheter, laboratory data), clinical course (response to antimicrobial therapy), and outcome. In addition, we analyzed microbiological data, including time from admission to collection of blood culture samples and time to positivity; antimicrobial susceptibility test results; and isolation of bacteria from sites other than blood.

Statistical analysis

Continuous data were expressed as the median and interquartile range (IQR), and categorical variables as percentages or absolute values. Statistical significance was calculated using the chi-square test for categorical variables and the Mann–Whitney *U* test for continuous variables. A p-value <0.05 was considered statistically significant. Statistical analyses were performed using StatMate V software (ATMS Co., Ltd., Tokyo, Japan).

Ethical considerations

The Clinical Research Judging Committee at NUIH approved the study protocol and waived the need for informed consent given the retrospective nature of the study.

Results

During the study period, 66 patients had positive blood cultures for *Corynebacterium* spp. Three patients were excluded because of a second episode of serial infection. Of the remaining 63 patients, 28 (44%) met the criteria for bacteremia and 35 (56%) met the criteria for contamination. Patients' baseline characteristics are summarized in Table 1. The overall median age was 73 years, and the contamination group was significantly older than the bacteremia group ($p = 0.023$). Men constituted 74.6% of cases. Fourteen cases were identified in the emergency department and critical care medicine; this department had a significantly higher proportion of contamination cases than did the other departments ($p = 0.049$). Overall, 39 patients had a central venous catheter in place, five had a peripheral venous catheter in place, and 19 did not have a venous catheter; bacteremia was diagnosed more frequently in patients who had peripheral or central venous inserted catheters ($p = 0.002$). The median interval from admission to blood culture sampling was 25 days (IQR, 6–49); this interval was significantly longer in the bacteremia group than in the contamination group ($p = 0.006$). The median time to culture positivity was significantly shorter in the bacteremia group

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