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Original article

Identification of causative organism in cardiac implantable electronic device infections

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ABSTRACT

Background: The causative organism in cardiovascular implantable electronic device (CIED) infection is usually diagnosed with the cultures from blood, removed leads, and/or infected pocket material. The cultured organism, however, is sometimes different among these samples.
Methods: Two hundred sixty patients with CIED infection, who underwent lead extraction between April 2005 and December 2014, were analyzed. More than two blood culture sets, all the extracted leads, and swab culture of the pocket were sent to the laboratory for culture. Among the patients all of whose microbiological examinations were available, we analyzed the causative organism defined as the species detected in at least two different sites.
Results: All the culture results were available in the 208 patients, showing 69 systemic infections (including 30 cases of infectious endocarditis) and 139 local infections. Blood culture, lead culture, and swab culture were positive in 57 (27%), 169 (81%), and 152 (73%), respectively. *Staphylococcus aureus* [37% including methicillin-resistant *S. aureus* (MRSA) (12%)] and coagulase-negative staphylococci (CoNS, 36%) were the most common causative organism, followed by non-staphylococci (23%), and polymicrobial infection (4%). The detection of *S. aureus* from pocket or removed leads rendered higher predictive value of a causative organism than that of CoNS. The detection of Gram-negative bacteria, fungi, and mycobacteria indicated that it was most likely a causative organism. Gram-positive bacteria excluding *Staphylococcus*, such as *Corynebacterium* spp., tended to coexist as a benign organism.
Conclusions: The causative organism is mostly *S. aureus* and CoNS. Detection of *S. aureus* or Gram-negative bacteria means that it is more likely a causative organism.

Introduction

Infection associated with cardiac implantable electrophysiological devices (CIEDs) is a serious complication with high morbidity and mortality. It showed in-hospital mortality of 2–5% and one-year mortality of approximately 20% [1–3]. To improve the outcome of CIED infection, the identification of the causative organism is a crucial issue.

The microbiology of CIED infection is generally confirmed based on positive cultures from blood, removed leads, and/or infected pocket material. The result of the cultures, however, can show different organisms among the samples. Recent studies have shown that nearly half of the patients who underwent de novo implantation or a replacement had positive results for bacterial swab cultures from the pacemaker pocket [4,5]. The cultures may

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show false positive due to contamination during an implanting operation rather than a bacterial colonization. Moreover, in the case of CIED infection, the interpretation of the causative organism is affected by some other factors such as: prescribed antibiotics before the procedure; previous debridement of the pocket tissue and secondary seeding of bacteremia or a distant site infection.

Therefore, we only analyzed positive cultures in patients available to all clinical samples including blood, extracted leads, and swab culture. The aim of this study was to describe the distribution of causative organisms based on the agreement with at least two different sites; and to examine the accuracy of each sample to contribute to the diagnosis.

Methods

Study subjects

This study included 260 consecutive patients (181 males; mean age 72 ± 14 years) with CIED infection, who underwent lead extraction in Kokura Memorial Hospital between April 2005 and December 2014. All patients with infective indications were based on class I or IIa in the 2000 NASPE (the North American Society of Pacing and Electrophysiology) policy statement or HRS (the Heart Rhythm Society) consensus at that time [6,7]. The details about the lead extraction procedure in our facility were previously reported [8]. New device replacement was performed on the contralateral side or intermuscular space after adequate days of antibiotic therapy. This was 7–14 days for pocket infection, at least 14 days for bacteremia, and more than 4 weeks for infectious endocarditis (IE). Written informed consent was obtained from all patients before the procedure. This study was approved by the ethical committee of Kokura Memorial Hospital.

Microbiology

Before the procedure, more than two blood culture sets were performed, even if no systemic infection signs were shown. All the removed leads (cut 5 cm from distal tip) and infected material (including a generator) from the pocket were cultured in Gifu anaerobic medium for cultivation. These were subsequently put on solid media (blood agar, chocolate agar, anaerobe isolation agar, and Sabouroud agar). The Bactec 9240 system (Becton Dickinson, Cockeysville, MD, USA) was used for blood culture and the Phoenix system (Becton Dickinson Diagnostic Systems, Sparks, MD, USA) was applied for identification of the species.

Definitions

The definition of the causative organism was defined as the consisted species detected from at least two different sites. Each blood culture and removed lead was counted as a different material. Pocket material was considered as a single site. The agreement of each material with the causative organism was regarded as positive concordance. Systemic infection was defined as the evidence of bacteremia, sepsis, or endocarditis; local infection was defined as only local signs inside of a pocket. The time from the most recent replacement was defined as early when the infection had occurred within 6 months; as late when it had occurred after 6 months [9]. The definition of the procedural outcomes was classified as complete procedural success, clinical success, and failure based on the consensus statement [7].

Statistical analysis

Parametric data are reported as the mean and standard deviation (SD). Non-parametric data are reported as the median and range. Categorical factors are summarized as percentages, and differences between groups were determined using Pearson's x^2 test. Statistical significance was defined at $p < 0.05$. Statistics were calculated with JMP® 10.0.0 software (SAS Institute Inc., Cary, NC, USA).

Results

Patients' characteristics

The clinical characteristics of the 208 study patients, who were available for all of the microbiological examinations, are listed in Table 1. Of the study patients, the mean age was 73 ± 14 years, males were 144 (70%) and body mass index (BMI) was 22.0 ± 3.7. As for type of infection, 139 (67%) were diagnosed as local infection and 69 (33%) as systemic infection [including 30 (14%) IE]. The time from implantation to extraction was on average 87 ± 70 months (range 1–418 months). The time from last replacement to extraction was on average 27 ± 26 months (range 1–102 months). Antibiotics had been prescribed in 144 (69%) and debridement of the pocket had been performed in 85 (41%) before the extraction procedures. Lead extraction was performed transvenously in all but five surgical hybrid cases, which resulted in 194 (93%) instances of complete procedural success, 9 (4%) instances of clinical success, and 5 (2%) instances of failure.

Microbiology

Blood culture, lead culture, and swab culture were positive in 57 (27%), 169 (81%), and 152 (73%), respectively among 208 patients. Based on the definition, causative organism was identified in 157 (75%) (Fig. 1A). The diagnostic yield was higher in patients with systemic infection (93% vs. 67%; $p < 0.01$). Prescribed antibiotics tended to render the lower diagnostic yield (72% vs. 84%; $p = 0.055$). The variation of causative organism based on the above definition is shown in Fig. 1B. *Staphylococcus aureus* [37% including methicillin-resistant *S. aureus* (MRSA) (12%)] and coagulase-negative staphylococci (CoNS) (36%) were the most common causative organisms, followed by non-staphylococci (23%), and

Table 1
Clinical characteristics of the patients.

Characteristic	Value
Age, years, mean ± SD	73 ± 14
Male, *n* (%)	144 (69%)
Body mass index, kg/m^2, mean ± SD	22.0 ± 3.7
Patient comorbidities, *n* (%)	
Hypertension	120 (58%)
Coronary artery disease	30 (14%)
Valvular heart disease	10 (5%)
Diabetes	30 (14%)
Chronic kidney disease	37 (18%)
Hemodialysis	4 (2%)
APT or OAC use	89 (43%)
Reduced ejection fraction (<40%)	37 (18%)
Type of infection, *n* (%)	
Local infection	139 (67%)
Systemic infection	69 (33%)
Infective endocarditis	30 (14%)
Prescribed antibiotics, *n* (%)	144 (69%)
Previous debridement, *n* (%)	85 (41%)
Mean time from implantation to extraction	87 ± 80 months (range 1–418)
Mean time from last replacement to extraction	27 ± 26 months (range 1–102)
Early (<6 months)	51 (25%)
Late (>6 months)	157 (75%)

APT, antiplatelet therapy; OAC, oral anticoagulant.

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