Pacemaker lead endocarditis due to multi-drug resistant *Corynebacterium striatum* detected with sonication of the device

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Running title: Pacemaker endocarditis due to *Corynebacterium striatum* isolated through device sonication

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Abstract

*Corynebacterium striatum* is a commensal of human skin and has been recently recognized as an emerging pathogen. A case of nosocomial pacemaker lead endocarditis due to a multi-drug resistant *C. striatum* is described highlighting the role of sonication as a diagnostic tool in cardiac device infections (CDIs).

Keywords: Cardiac device infections (CDIs), pacemaker lead endocarditis, sonication, *Corynebacterium striatum*, diagnosis
Case report

A 71-year-old woman, who underwent pacemaker replacement two months before, was admitted with a 15-day history of fever and generator site pain. She was febrile (Tc 38.5°C), her blood pressure was 120/80 mmHg and pulse rate 76 beats/min. Erythema, warmth, tenderness and purulent drainage were observed at the pocket site. Respiratory, abdominal and neurological parameters were normal, examination of the heart showed a 2/6 systolic murmur. Laboratory analyses revealed a mild leucocytosis (11x10^9/L, with 85% of polymorphonuclear cells), and an erythrocyte sedimentation rate correspondent to 50mm/h. A markedly increased C-reactive protein (8UI/L) was observed.

Two separate sets of blood and swab cultures obtained from purulent secretion at the pocket site yielded coagulase negative Staphylococcus which showed resistance to methicillin and rifampicin and susceptibility to vancomycin, teicoplanin, linezolid and daptomycin.

A transthoracic echocardiogram revealed a mobile mass adherent to the intracardiac lead in the absence of valve vegetations. Treatment with daptomycin (6mg/kg once daily) was started leading to a rapid improvement on clinical and laboratory findings. Blood cultures and pocket swabs, performed 72 hours after the beginning of antimicrobial therapy, were sterile. Serum bactericidal activity was >1:16 (4). After seven days of daptomycin treatment, the patient developed renal failure (clearance of creatinine < 20ml/min) so that the antimicrobial therapy was switched to intravenous linezolid (600mg twice daily). Following this therapy, the patient became again febrile (Tc 39°C). Blood cultures and pocket site swabs resulted to be negative. The patient underwent device removal and a reimplantation of a new pacemaker was performed 8 days later. On macroscopic examination, the intracardiac portion of the electrode showed the presence of a mass adherent to the lead. Four samples of lead tips were collected: two of them were analyzed following the traditional microbiological procedures without sonication whereas the other two samples were submitted to device sonication and then cultured. Briefly, within 1 hour from the removal, two lead tips were inoculated in Trypticase Soy Broth (TSB) which was incubated for 24 hours and analyzed.
for bacterial growth. The other two lead tips were vortexed for 30 seconds, then sonicated in NaCl solution for 5 minutes at a frequency >20kHz and finally vortexed again for other 30 seconds. The Ultrasonik 300 bath (Ney, BarkMeyer Division, Yucaipa, CA) was used for sonication. The resulting sonication fluid was centrifuged at 3200 rpm for 15 minutes and the sediment was used for microbiological cultures. Anaerobic and aerobic sheep blood agar plates were incubated at 37°C for 5 days and the microorganisms were identified using conventional methods. The non sonicated cultures were sterile whereas the sonicated samples yielded small cream-colored non-hemolytic colonies. Gram-staining revealed club-shaped Gram-positive rods accounting for diphtheroids bacteria. Catalase test was positive and urease test was negative. The strain was identified as *Corynebacterium striatum* using the commercial system API 20 Coryne (bio-Mérieux, Marcy l’Etoile, France). Additional tests such as tyrosine hydrolysis, N-acetylglucosamine assimilation and phenylacetic acid assimilation were used to differentiate *C. striatum* from *C. amycolatum*. The isolate was confirmed to be *C. striatum* by PCR amplification of 16S rRNA gene using a new, commercial, universal 16S rRNA-based PCR assay (Sepsitest™, Molzym, Germany). Sequencing of the amplified product resulted to have 99% identity to *C. striatum* Genbank accession number X81910 and AY008302, and 97.2% identity to *C. striatum* Genbank accession number X84442. Microdilution broth method and E-test strips were used to assess the microorganism antimicrobial susceptibility pattern. E-test strips were only used for vancomycin, daptomycin and linezolid. All samples were cultured on cation-adjusted Mueller-Hinton agar and incubated at 37°C in ambient atmosphere for 24 hours. Mueller-Hinton agar supplemented to a final concentration of 50mg/L calcium was used to perform daptomycin susceptibility. CLSI breakpoints for *Corynebacterium spp* were used (7). Susceptibility to daptomycin was defined as MIC ≤ 1mcg/mL (8,14). A multi-drug resistant (MDR) *C. striatum* strain was observed (Table 1) with a resistance to more than 3 classes of drugs and susceptibility only to vancomycin, daptomycin and linezolid. Therapy with daptomycin was reintroduced and continued for 4 weeks after device removal in the absence of adverse events. A repeated echocardiogram was negative for the presence of lead or valve
vegetation. One month after the end of the therapy, the patient was afebrile and asymptomatic.

Corynebacterium species are aerobic, non-sporulating, pleomorphic, Gram-positive bacilli that are commonly found in animals and in the normal human skin (18). Among the 73 recognized species in the genus Corynebacterium, C. striatum is distinguished from other Corynebacteria by reduction of nitrates, utilization of glucose and sucrose but not maltose, failure to produce propionic acid and decomposition of tyrosine (8). Most of C. striatum strains are susceptible to a variety of antimicrobial agents including beta-lactams, vancomycin, gentamicin and rifampicin; however, reports of MDR C. striatum have been recently described (8,14). Among the most recent drugs, daptomycin showed a marked in vitro activity against C. striatum (14). Our strain was only susceptible to vancomycin, daptomycin and linezolid, indicating a MDR phenotype.

Although frequently regarded as a contaminant when isolated in biological samples, C. striatum has been increasingly identified as the causative agent of serious infections including meningitis, arthritis and infective endocarditis both in immunocompetent and immunocompromised subjects (5). C. striatum is mainly a nosocomial acquired bacterium and it is strongly associated with the presence of medical devices (9). A literature search in the Medline PubMed database only revealed 17 cases of infective endocarditis due to C. striatum (5,6) whereas just one report of C. striatum pacemaker lead infection has been described (Table 2) (11). The patient under study herein had several risk factors for C. striatum infection, such as the elderly age and the presence of cardiac device.

Microbiological diagnosis is crucial for the appropriate treatment of cardiac device infections (CDIs), whose incidence has increased over the last ten years (15). Although cultures of generator pocket site tissue and lead tips are useful in identifying the causative organisms of CDIs (1), no bacterial detection occurs in about 30% of cases (2,17). Sonication, which is a simple and rapid method for detection of microbial biofilms in foreign bodies, has been recently validated for orthopaedic devices (12,16) whereas its application in the settings of CDIs is still limited (10).
Sonication of the device before culture could be an useful technique to improve microbiological diagnosis in CDIs (13). A recent study comparing traditional swab cultures with sonication of intracardiac devices showed that bacterial detection through sonication resulted to be more sensitive than traditional cultures especially in infected devices (13). Thus, conventional cultures of intracardiac devices might be unable to detect the causative organisms of CDIs as it occurred in our case where *C. striatum* only grew after device sonication. Whether the detection of bacteria on devices represents a true colonization, a subclinical infection or a contamination, remains an area of active investigation (3). Our case should be considered a real device infection rather than a colonization; in fact, the patient developed fever during antimicrobial therapy and her impaired conditions probably allowed low-virulence colonizer such as *C. striatum* to assume a pathogenic role. Non-diphteriae MDR *Corynebacteria* should be considered as emerging nosocomial pathogens in the settings of CDIs. Sonication of removed devices could be crucial for microbiological diagnosis in CDIs especially when patients are already receiving antibiotic therapy.

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**References**


Table 1. Broth dilution method and E-test MICs for *C. striatum* isolated from sonicated intracardiac device

<table>
<thead>
<tr>
<th>Antimicrobial drugs</th>
<th>Broth dilution method</th>
<th>E-test</th>
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<tbody>
<tr>
<td></td>
<td>MICs (mcg/mL)*</td>
<td>MICs (mcg/mL)*</td>
</tr>
<tr>
<td>Penicillin</td>
<td>R 128 mcg/mL</td>
<td></td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>R 32 mcg/mL</td>
<td></td>
</tr>
<tr>
<td>Gentamicin</td>
<td>R 32 mcg/mL</td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td>R 32 mcg/mL</td>
<td></td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>R 128 mcg/mL</td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td>R 64 mcg/mL</td>
<td></td>
</tr>
<tr>
<td>Vancomycin</td>
<td>S 0.5 mcg/mL</td>
<td></td>
</tr>
<tr>
<td>Linezolid</td>
<td>S 0.25 mcg/mL</td>
<td></td>
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<tr>
<td>Daptomycin</td>
<td>S 0.125 mcg/mL</td>
<td></td>
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* Based on CLSI breakpoints of *Corynebacterium spp* (7)

MICs: Minimal Inhibitory Concentrations (mcg/ml)
<table>
<thead>
<tr>
<th>Reference</th>
<th>Sex</th>
<th>Age</th>
<th>Underlying diseases</th>
<th>Prosthetic valve</th>
<th>Valve involvement</th>
<th>Clinical presentation</th>
<th>Medical Therapy</th>
<th>Surgical intervention</th>
<th>Dosage of antibiotic therapy</th>
<th>Outcome</th>
<th>C. striatum isolation</th>
</tr>
</thead>
<tbody>
<tr>
<td>(II) M 73</td>
<td>Pacemaker battery replacement</td>
<td>No</td>
<td>Yes (tricuspid)</td>
<td>Fever</td>
<td>Vancomycin</td>
<td>Pacemaker removal</td>
<td>Not reported</td>
<td>Survived</td>
<td>Blood, drainage pus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present case F 71</td>
<td>Pacemaker battery replacement, Yes (mitralic)</td>
<td>No</td>
<td>Fever, pocket infection</td>
<td>Daptomycin</td>
<td>Pacemaker removal</td>
<td>6 mg/kg once daily</td>
<td>Survived</td>
<td>Device sonication</td>
<td></td>
<td></td>
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</tbody>
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