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Case Report

Late-onset native valve endocarditis caused by *Corynebacterium kroppenstedtii*

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ABSTRACT

Corynebacterium kroppenstedtii is an emerging cause of granulomatous mastitis and recurrent breast abscesses in women, but data on its clinical relevance in nongynecological disease conditions are limited. Here, we report the first case of a late-onset endocarditis of a native aortic valve in a 73-year-old male patient who presented with symptomatic aortic insufficiency. Echocardiography and cardiac computed tomography revealed the perforation of the noncoronary cusp and a large perivalvular abscess cavity. Hence, the surgical replacement of the aortic valve and aortic root were performed. Intraoperatively obtained tissue specimens grew *C. kroppenstedtii* and the patient made a full recovery after a 6-week course of antibiotic treatment. We briefly review the literature pertaining to antimicrobial susceptibility patterns of *C. kroppenstedtii* and available treatment recommendations. Our report calls for further studies to assess the role of this bacterium as a causative agent of infections other than granulomatous mastitis.

Introduction

Corynebacteria comprise a heterogeneous group of gram-positive, aerobic, rod-shaped bacteria, which have a characteristic curved, palisade-like morphology on microscopy. While some species such as *Corynebacterium diphtheriae*, the causative agent of diphtheria, are of high clinical significance, many other *Corynebacterium* spp. are mere colonizers of the human body. Hence, it is a major challenge to judge the actual relevance of these bacteria when they are detected in clinical specimens. *Corynebacterium kroppenstedtii* was first described in the late 1990s, and was subsequently recognized as an emerging pathogen of cystic neutrophilic granulomatous mastitis and breast abscesses in women (Bernard et al., 2002; Paviour et al., 2002; Riegel et al., 2004; Le Flèche-Matéos et al., 2012; Dobinson et al., 2015). However, infections at other body sites are rare, and only a single case of early prosthetic valve endocarditis due to *C. kroppenstedtii* was reported thus far (Hagemann et al., 2015). Here, we describe the first case of late-onset infective endocarditis of a native valve caused by this bacterium, and briefly review the available literature.

Case report

A 73-year-old male patient was referred to our hospital in Germany for severe and symptomatic aortic insufficiency. Two years ago, the patient had undergone valve-sparing aortic root replacement for aortic valve insufficiency and root dilatation. At presentation, the patient was afebrile and blood parameters were not suggestive of an acute infection (no leukocytosis and normal C-reactive protein). However, the patient had a severe, symptomatic aortic regurgitation, and echocardiography on admission showed chronic aortic insufficiency with changes suggestive of endocarditis, i.e., perforation of the noncoronary cusp and a large perivalvular abscess cavity (Figure 1), which was also seen on cardiac computed tomography (Figure 2). Hence, repeated surgery was performed.

After connection to the cardiopulmonary bypass and under cardioplegic arrest, we found a perforation of the noncoronary cusp and a large chronic cavity in the aortomitral continuity. The aortic valve and root were replaced with a stentless bioprosthesis. The postoperative course was unremarkable.

As no pathogen had been detected in blood cultures sampled before surgery, an empirical antibiotic treatment regimen with daptomycin and ampicillin-sulbactam was started. In total, six samples of surgically removed cardiac tissue were sent for microbiological diagnostics. The tissue specimens were homogenized and independently subjected to the following diagnostics: (i)

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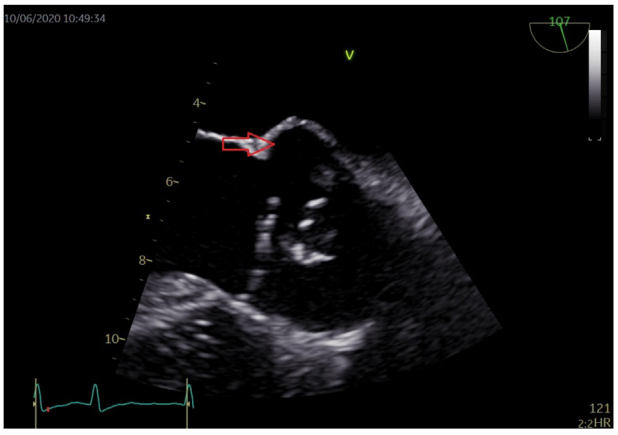

Figure 1. Transesophageal echocardiography of a patient with *Corynebacterium kroppenstedtii* endocarditis, demonstrating a large perivalvular abscess cavity (red arrow) suggestive of an endocarditis.

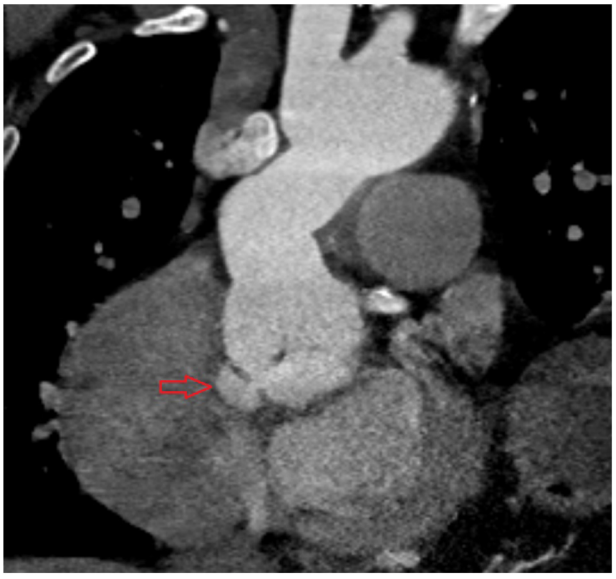

Figure 2. Cardiac computed tomography (CT) showing the same large (2 × 2.1 cm) perivalvular abscess in the aortomitral continuity (red arrow).

microbiological culture methods (incubation on tryptic soy blood agar, chocolate agar, Schaedler agar as well as aerobic and anerobic liquid broths), (ii) broad-range bacterial 16S rRNA gene polymerase chain reaction (PCR), and (iii) a set of specific PCRs targeting *Staphylococcus aureus*, coagulase-negative staphylococci, *Streptococcus* spp., *Enterococcus* spp., *Bartonella* spp., *Brucella* spp., *Coxiella burnetii*, *Tropheryma whipplei,* and mycobacteria. The bacterial 16S PCR yielded a positive result in one of the tissue samples, and subsequent DNA sequencing and analysis using a BLAST search based on the NCBI genome database showed a sequence homology of 98% to *C. kroppenstedtii*. No bacteria were detected on the corresponding solid agar media, but after one week of incubation, small bacterial colonies were grown from a brain–heart infusion enrichment broth. The bacterial colonies were nonhemolytic and nonpigmented to grayish, with a rather smooth appearance. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (Bruker Daltonics; Bremen, Germany) identified the colonies as *C. kroppenstedtii* with a score >2.0, thus indicating reliable species identification. Antimicrobial susceptibility testing was carried out using an Epsilometer test (E-test), a method to determine minimal inhibitory concentrations by placing a plastic strip, which contains specified antibiotic substances on inoculated agar media, e.g., Mueller-Hinton agar with 5% defibrinated horse blood. The method was carried out according to the validated recommendations put forth by the European Committee on Antimicrobial Susceptibility Testing (EUCAST; http://www.eucast.org/), and clinical breakpoints for coryneform organisms were used. The isolated *C. kroppenstedtii* strain was susceptible to penicillin, ciprofloxacin, vancomycin, and linezolid, but resistant to clindamycin.

Of note, all blood cultures remained negative. In one of six tissue samples obtained during cardiac surgery, *Staphylococcus epidermidis* was also grown. As the corresponding broad-range 16S PCR and staphylococcal-specific PCRs of the same sample remained negative, contamination could not be ruled out. However, to cover for both pathogens, the patient's empirical antimicrobial treatment was switched to intravenous vancomycin for a total duration of six weeks. The further clinical course was uneventful and without complications.

Discussion

Corynebacteria are rare pathogens of endocarditis (Brouqui and Raoult, 2001; Belmares et al., 2007). In recent years, some cases of endocarditis due to corynebacteria have been reported (Belmares et al., 2007; Hagemann et al., 2015), mainly in patients with early-onset prosthetic valve endocarditis (Belmares et al., 2007; Hagemann et al., 2015). While nontoxigenic *C. diphtheriae* is the most frequently isolated *Corynebacterium* species from heart valves (Belmares et al., 2007), *C. kroppenstedtii* has been reported only once in a German patient with prosthetic valve endocarditis (Hagemann et al., 2015). In our case, *C. kroppenstedtii* was isolated from a native aortic valve. Interestingly, our patient had previously undergone partial prosthetic replacement of the aortic root and aortic arch, which might have augmented the risk of later infection due to the known ability of certain bacteria to attach to nonnative vascular surfaces (Knox and Holmes, 2002; Belmares et al., 2007).

C. kroppenstedtii was described for the first time in 1998 by Collins and colleagues (Collins et al., 1988) in a sputum sample of an 82-year-old female patient with lung disease. Besides the lack of mycolic acids (Collins et al., 1988), one distinguishing characteristic of *C. kroppenstedtii* is its lipophilism, which is partially responsible for the difficulty to grow the bacterium on microbiological standard culture (e.g., tryptic soy agar) (Riegel et al., 2004).

Thus far, *C. kroppenstedtii* has almost exclusively been described in association with cystic neutrophilic granulomatous mastitis and breast abscesses (Bernard et al., 2002; Paviour et al., 2002; Riegel et al., 2004; Le Flèche-Matéos et al., 2012; Dobinson et al., 2015), whereas only five case reports from nongynecological compartments have been reported in the literature, i.e., two sputum samples (Collins et al., 1988; Bernard et al., 2002), one isolate each in a blood culture and a lung biopsy from Canada (Bernard et al., 2002), and the aforementioned prosthetic valve endocarditis in a German patient (Hagemann et al., 2015).

International guidelines do not provide distinct treatment recommendations for endocarditis caused by corynebacteria, and there are only few studies on antimicrobial susceptibility patterns of *C. kroppenstedtii*. Resistance to clindamycin is rare and only single cases have been reported (Fernández-Natal et al., 2016). Of note, *C. kroppenstedtii* usually remains susceptible to most other antibiotic classes (Riegel et al., 2004; Le Flèche-Matéos et al., 2012; Hagemann et al., 2015). However, researchers from New Zealand recently observed an increasing resistance to beta-lactam antibiotics (Dobinson et al., 2015).

In conclusion, we report a case of endocarditis due to *C. kroppenstedtii*, an emerging pathogen that is difficult to grow in culture and for which recommendations on appropriate antimicrobial treatment have not yet been established. Our report calls for further studies to assess the role of *C. kroppenstedtii* as a causative agent of infections other than granulomatous mastitis.

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Transparency declarations

All authors have nothing to disclose.

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