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Original article

# *Propionibacterium acnes* endocarditis: a case series

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ABSTRACT

*Objectives:* *Propionibacterium acnes* remains a rare cause of infective endocarditis (IE). It is challenging to diagnose due to the organism's fastidious nature and the indolent presentation of the disease. The purpose of this study was to describe the clinical presentation and management of *P. acnes* IE with an emphasis on the methods of diagnosis.

*Methods:* We identified patients from the Cleveland Clinic Infective Endocarditis Registry who were admitted from 2007 to 2015 with definite IE by Duke Criteria. *Propionibacterium acnes* was defined as the causative pathogen if it was identified in at least two culture specimens, or identified with at least two different modalities: blood culture, valve culture, valve sequencing or histopathological demonstration of microorganisms.

*Results:* We identified 24 cases of *P. acnes* IE, 23 (96%) of which were either prosthetic valve endocarditis or IE on an annuloplasty ring. Invasive disease (71%) and embolic complications (29%) were common. All but one patient underwent surgery. *Propionibacterium acnes* was identified in 12.5% of routine blood cultures, 75% of blood cultures with extended incubation, 55% of valve cultures, and 95% of valve sequencing specimens. In 11 of 24 patients (46%), no causative pathogen would have been identified without valve sequencing.

*Conclusions:* *Propionibacterium acnes* almost exclusively causes prosthetic valve endocarditis and patients often present with advanced disease. The organism may not be readily cultured, and extended cultures appear to be necessary. In patients who have undergone surgery, valve sequencing is most reliable in establishing the diagnosis. **J.M. Banzon, CMI 2017;▪:1**



## Introduction

*Propionibacterium* spp. are anaerobic, Gram-positive bacilli that are ubiquitous members of the skin flora [1]. When identified in blood cultures, *Propionibacterium acnes* is frequently considered to be a contaminant. However, serious infections caused by *P. acnes* are increasingly reported, particularly in association with bioprosthetic material [2–4]. It is reported to be a rare cause of infective endocarditis (IE), causing ~0.3% of all cases [5]. The case reports and small case series published to date provide limited details regarding the diagnosis and management of *P. acnes* IE [3,5,6]. We therefore conducted this study to identify cases of *P. acnes* IE at our institution and describe their clinical presentation, methods of diagnosis, management and outcomes.

## Materials and methods

We reviewed the Cleveland Clinic Infective Endocarditis Registry for cases of *P. acnes* IE from 1 July 2007 to 30 September 2015. We reviewed patient records for demographic information, comorbid conditions, predisposing risk factors for IE, echocardiographic findings, microbiological data, histopathology, antibiotic treatment and IE complications. This study was approved by the Cleveland Clinic Institutional Review Board.

Since 2009, cardiac valve specimens from most patients undergoing surgery for endocarditis have been sent for molecular testing to the University of Washington Laboratories, Seattle, WA.

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This involves amplification by PCR followed by 16s rDNA sequencing (henceforth referred to as 'valve sequencing'). The testing, done at the request of the treating physicians, includes one or more of the following: universal bacterial PCR, universal fungal PCR, or mycobacterial PCR.

Similarly, most cardiac valve specimens are sent for histopathological examination. Cardiac pathologists and infectious disease clinicians hold weekly valve pathology rounds to review cases of suspected IE. Special staining for microorganisms is performed on all such valve specimens, which includes Gram, Periodic acid–Schiff, and Gomori methenamine silver stains. Visualization of Gram-positive bacilli or coccobacilli on valve specimens was defined as consistent with *P. acnes*.

### *Case definition*

Only cases that met the Duke Criteria for definite IE were included [7]. To discriminate between contamination and true infection when *P. acnes* was identified on microbiological testing, cases had to fulfil any of the following criteria to define *P. acnes* as the causative pathogen for endocarditis: (a) two or more blood cultures positive; (b) two or more valve cultures positive; (c) two or more valve sequencing results positive; or (d) at least two of the following: positive blood culture, positive valve culture, positive valve sequencing, or histopathological demonstration of microorganisms consistent with *P. acnes*.

## Results

There were 1325 episodes of definite IE included in the registry, and of these 606 were prosthetic valve endocarditis (PVE). We identified 24 patients with IE caused by *P. acnes* between 1 July 2007 and 30 September 2015. Median age at presentation was 64 years (range 38–84 years).

### *Clinical features*

The clinical features are outlined in Table 1. Notably, all patients were male. All had left-sided endocarditis, 16 (67%) aortic, five (21%) mitral and two (8%) double valve. Presence of a prosthetic valve (22 patients) or annuloplasty ring (one patient) was the most commonly identified predisposing factor, together seen in 23 patients (96%). The time from prosthetic valve or ring placement to diagnosis of IE ranged from 4 months to 12 years. Four (17%) patients had a cardiac implantable device (implantable cardioverter defibrillator or permanent pacemaker).

Patients usually had advanced disease on presentation. Seven (29%) patients developed embolic complications. This included splenic and kidney infarcts in two patients, acute peripheral arterial thromboembolism in two patients, and central nervous system involvement in four patients. Thirty-three per cent had evidence of valvular dehiscence on echocardiography, and 46% had echocardiographic evidence of perivalvular abscess. Seventy-one per cent (17/24) had invasive disease, defined as extension of disease beyond the annulus. This was suggested preoperatively by evidence of valve dehiscence or perivalvular abscess on imaging, and determined definitively at the time of surgery.

### *Diagnosis*

During the study period blood cultures were not necessarily held for extended incubation (i.e. longer than 5 days). Among the 24 patients, blood cultures were positive for *P. acnes* in six (75%) of eight patients who had one or more blood cultures held for extended incubation versus two (12.5%) of 16 patients whose blood cultures were not held for extended incubation (OR 21, 95% CI 2.4–185.9, p 0.005, Fig. 1). The median time to blood culture positivity was 7 days (range 3–9). Valve cultures were sent for 22 of the 23 patients who underwent surgery, and were positive in 12 (55%). The median time to valve culture positivity was 5.5 days (range 3–28). There were no mixed blood or valve cultures. The distribution of diagnostic criteria fulfilled by each patient is shown in Table 2. Six patients (25%) had negative blood and valve cultures. Valve sequencing (bacterial 16S rDNA PCR), on the other hand, was positive in 20 of the 21 patients (95%) who had samples sent. The number of specimens sent for sequencing for each patient ranged from one to three (median 1.5). Valve histopathology was performed in all patients who underwent surgery, which showed evidence of inflammation for all patients. Microorganisms consistent with *P. acnes* were visualized in 16 (70%).

**Table 1**
Demographic and clinical features of patients with *Propionibacterium acnes* endocarditis

| Characteristics | *n* (%) |
|---|---|
| Male | 24 (100) |
| Age, years, median (range) | 63 (38–78) |
| Co-morbid conditions | |
| Coronary artery disease | 11 (46) |
| Chronic renal disease | 3 (13) |
| Diabetes mellitus | 4 (17) |
| Malignancy | 1 (4) |
| Immunosuppression | 0 (0) |
| Predisposing factors | |
| Prosthetic valve or ring | 23 (96) |
| Cardiac implantable device | 4 (17) |
| Indwelling vascular catheter | 0 (0) |
| Haemodialysis | 0 (0) |
| Injection drug use | 0 (0) |
| Prior history of endocarditis | 3 (13) |
| Valve(s) infected | |
| Aortic valve | 16 (67) |
| Aortic + tricuspid valves | 1 (4) |
| Aortic + mitral valves | 2 (8) |
| Mitral valve | 5 (21) |
| Clinical presentation | |
| Acute onset of symptoms[a] | 9 (38) |
| Fever and chills | 21 (88) |
| Malaise | 21 (88) |
| Embolic complication as presentation | 4 (17) |
| Echocardiogram findings | |
| Vegetation >1 cm | 3 (13) |
| Severe valvular regurgitation[b] | 8 (33) |
| Valvular dehiscence | 8 (33) |
| Perivalvular abscess | 11 (46) |

[a] Defined as onset of symptoms <3 weeks before admission.
[b] Valvular regurgitation of 3+ or greater.

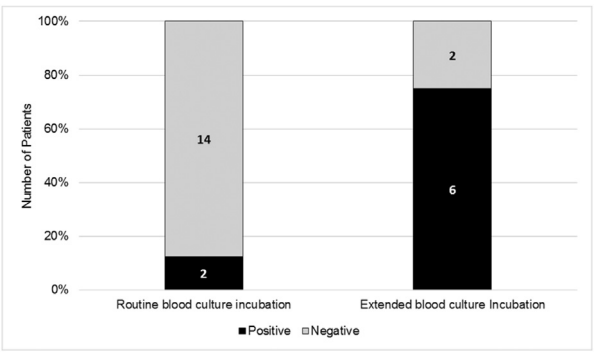


**Fig. 1.** Proportion of positive blood cultures with routine versus extended incubation.

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