

Characteristics and Treatment Outcomes of *Propionibacterium acnes* Prosthetic Shoulder Infections in Adults

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Background. Prosthetic joint infections (PJIs) significantly complicate joint arthroplasties. *Propionibacterium acnes* is an increasingly recognized PJI pathogen, yet limited clinical and therapeutic data exist. We sought to examine characteristics of *P. acnes* shoulder PJIs and compare surgical and nonsurgical management outcomes.

Methods. A retrospective analysis of *P. acnes* shoulder PJIs was conducted at an academic center in Baltimore, Maryland from 2000 to 2013.

Results. Of 24 cases of *P. acnes* shoulder PJIs, 92% were diagnosed after extended culture implementation; 42% in the delayed and 46% in the late postsurgical period. Joint pain and diminished function were the predominant presenting clinical signs. Erythrocyte sedimentation rate and C-reactive protein elevations occurred in 47% and 44%, respectively. All tested isolates were susceptible to β -lactams, moxifloxacin, vancomycin, and rifampin. Clindamycin resistance was identified in 6%. Of the antibiotic-only treated cases, 67% had a favorable clinical outcome compared with 71% ($P = 1.0$) of cases with a combined antibiotic-surgical approach. Favorable outcome with and without rifampin therapy was 73% and 60% ($P = .61$), respectively.

Conclusions. *Propionibacterium acnes* PJI diagnoses increased with extended culture. Inflammatory markers were elevated in a minority of cases. Isolates maintained broad antimicrobial susceptibility. Compared to combined antibiotic-surgical approaches, antibiotic-only approaches were similarly successful in selected cases.

Keywords. antimicrobial susceptibility; *Propionibacterium acnes*; prosthetic joint infection; shoulder prosthesis.

Over 1 million prosthetic joints are placed in the United States each year. With an aging population, this number is projected to increase 4-fold over the next 2 decades [1–3]. A notable proportion of these joints subsequently fail. Prosthetic joint infections (PJIs) have been considered to be the most serious cause of subsequent joint failure, occurring in up to an estimated 2% of arthroplasties [1, 4–6]. In addition to the clinical impact, the economic burden of PJIs is markedly high, with an estimated cost in the United States approaching 1 billion dollars annually [5, 7].

Propionibacterium acnes is a Gram-positive anaerobic bacillus. It is a human commensal organism, primarily found in skin and superficial mucosal sites, with a predilection for pilosebaceous follicles that exist in the upper body such as the shoulder

region [8–10]. Initially considered an important agent in the pathogenesis of acne vulgaris, *P. acnes* has been more recently implicated in serious deep-seated postoperative and medical device-related infections, particularly PJIs [11–13]. With improved diagnostics, including extended culture protocols, *P. acnes* has been specifically recognized as a dominant organism in infections involving shoulder prostheses [14–23]. Yet, there has been a paucity of data on the clinical and microbiologic characteristics of such infections.

Treatment of PJIs beyond the acute postoperative period has traditionally relied on an appropriate antimicrobial regimen, combined with a surgical approach dependent on stability of the prosthesis, state of the periprosthetic tissue, patient comorbidity, and characteristics of the infecting organism [1, 3, 6]. Surgical options include debridement with implant retention or antibiotic spacer implantation with no subsequent arthroplasty, a 1-stage revision with immediate reimplantation of a new prosthesis, a 2-stage revision with reimplantation several months after prosthesis removal, permanent prosthesis removal, and amputation. Medical management options have been manifold, largely because antimicrobial activity against *P. acnes* has been reported for a wide spectrum of agents [24]. However, with the increasing use of antimicrobial agents for acne vulgaris, advancing resistance of *P. acnes* isolates has been reported, particularly

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in refractory cases of acne [25–27]. The susceptibility patterns of *P. acnes* isolates implicated in deep-seated infections have been less well characterized.

Medical management of PJIs without surgical intervention has been considered to result in poorer clinical outcomes [1, 28]. Such a limited approach has typically been reserved for patients with inoperable status [1, 6]. Occasionally, this strategy has been considered in clinical practice for low virulence organisms, although with limited supporting data. *Propionibacterium acnes* has been considered a low virulence organism, but little data exists on the comparative advantage of combined medical and surgical management to that of medical management alone for infections involving this organism.

We performed a retrospective analysis to describe clinical and laboratory characteristics of *P. acnes* prosthetic shoulder joint infections and antimicrobial susceptibility patterns of the associated isolates over a 14-year period. We further describe short-term treatment outcomes for surgical and alternative medical approaches to the management of these infections.

PATIENTS AND METHODS

Hospital Setting and Study Population

This study was conducted at the Johns Hopkins Hospital and Clinics in Baltimore, Maryland. Linkage to the Johns Hopkins Hospital microbiology database system was used to identify cases from January 2000 through December 2013. Patients aged 18 years and older with a positive *P. acnes* culture from the shoulder joint with a prior shoulder prosthesis were identified for study inclusion. This study was approved by the Johns Hopkins Institutional Review Board.

Specimen Collection and Microbiologic Assessment

Joint fluid aspirates and operative tissue specimens were collected using standard protocols and transported to the Microbiology Laboratory for processing. Joint fluid aspirates were transported in BD BBL Port-A-Cul vials (Becton, Dickinson and Company, Sparks, MD), and tissue specimens were placed in a sterile container and transported to the Microbiology Laboratory within 1 hour of collection. Specimens were then processed and inoculated onto standard agars, including Brucella blood agar (Anaerobe Systems, Morgan Hill, CA), and BD BBL Chopped Meat Broth (Becton, Dickinson and Company). Aerobic plates and chopped meat broths were incubated in 5% CO₂ at 35°C. Anaerobic plates and broth subcultures were incubated in an AS-580 anaerobe chamber (Anaerobe Systems) at 35°C. Aerobic blood and chocolate agar plates, as well as anaerobic Brucella and Phenyl-Ethyl-Alcohol agar plates, were held for 14 days. Chopped meat broths were subcultured both aerobically and anaerobically when turbid or terminally subcultured at day 10 if clear. Organism identification was obtained using the Bruker Microflex LT MALDI-TOF mass spectrometry system (Bruker Daltonics, Billerica, MA), as well as Gram stain,

spot tests, and/or biochemical reagents. The extended culture incubation protocol for *P. acnes* was implemented in January 2009, with extension from 5 to 14 days of incubation for both aerobic and anaerobic culture media.

Definition

A PJI was defined based on previously detailed criteria [1, 3, 22, 29, 30]. A case was considered definite (1) if 2 or more culture specimens were positive for *P. acnes* with no other organisms on culture or (2) if 1 culture specimen was positive for *P. acnes* with no other organisms on culture and there was evidence of either joint purulence, histopathologic inflammation, or a sinus tract communicating with the prosthesis. A case was considered probable if 1 culture specimen was found to be positive for *P. acnes* and 1 of the following concomitant symptoms was present: fever, constitutional symptoms (chills, fatigue, night sweats, weight loss, and anorexia), joint pain, joint swelling, joint warmth, wound drainage, or loss of range of motion. Cases were excluded if there was an alternative explanation for these symptoms (such as gout or rheumatoid arthritis responsive to therapy). There were no coexisting pathogens isolated in any of the cases included in this study.

Data Collection

Medical chart abstraction was performed using a standardized case report form to retrieve demographic, clinical, and laboratory data. Demographic data included age, sex, and race. Laboratory data included erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cell (WBC) count, and percentage of neutrophils in the blood and synovial fluid. Imaging findings from plain films and computerized tomography scans were recorded. Laboratory and radiologic data recorded at diagnosis reflect findings before any surgical PJI treatment. The time from index surgery to diagnosis was recorded as the time from the last surgical procedure performed pre-diagnosis to the first positive *P. acnes* culture. Episodes were classified as early (<3 months after surgery), delayed (3–24 months), or late (>24 months) as previously described [6]. Time to culture positivity was recorded as the time from joint specimen attainment to positive culture growth.

Antimicrobial Susceptibility Patterns

The susceptibilities of *P. acnes* isolates were tested against a range of standard antimicrobial agents. Isolates were classified as susceptible as per the minimum inhibitory concentration (MIC) breakpoints set by the Clinical and Laboratory Standards Institute (CLSI): penicillin (≤ 0.5 $\mu\text{g/mL}$), piperacillin/tazobactam ($\leq 32/4$ $\mu\text{g/mL}$), ertapenem (≤ 4 $\mu\text{g/mL}$), clindamycin (≤ 2 $\mu\text{g/mL}$), moxifloxacin (≤ 2 $\mu\text{g/mL}$), and metronidazole (≤ 8 $\mu\text{g/mL}$) or by the European Committee on Antimicrobial Susceptibility Testing (EUCAST): vancomycin (< 2 $\mu\text{g/mL}$) and rifampin (≤ 0.5 $\mu\text{g/mL}$) [11]. No CLSI or EUCAST breakpoints were available for minocycline. The absolute MICs for isolates against minocycline are thus reported. Susceptibility

testing for penicillin was initiated in 2001; susceptibility testing for clindamycin, moxifloxacin, and vancomycin was initiated in 2009; susceptibility testing for piperacillin/tazobactam, ertapenem, and metronidazole was initiated in 2010; and susceptibility testing for rifampin was initiated in 2012.

Follow-Up and Treatment Outcomes

Antimicrobial therapeutic regimens and treatment outcomes were assessed through the last recorded clinical visit. Decisions on therapeutic regimens were based on the clinical judgment of the infectious disease and surgical specialist providers. The type, delivery method, and duration of antimicrobial therapy were recorded. In all cases, susceptibility profiles informed drug choice. Concomitant use of rifampin was also per the clinical judgment of the infectious disease physician with consideration of patient tolerability. Chart abstraction did not allow for precise determination of duration of intravenous (IV) versus oral therapy. However, of those who received IV antimicrobial therapy, the majority of patients received at least a 4- to 6-week course of IV therapy prior to transition to an oral regimen. The final clinical outcome was determined as per the clinical status at the last recorded clinical visit. An outcome was defined as favorable if there was a recorded improvement in pain symptoms and functional performance relative to a patient's preintervention clinical status, without requirement for unplanned additional surgical debridement for putative persistent infection. Statistical analysis was performed using Fisher's exact test and the Wilcoxon rank-sum test. A *P* value of <.05 was considered to be statistically significant.

RESULTS

There were 24 cases of *P. acnes* prosthetic shoulder joint infections identified over the 14-year period of this study. Of these, 11 (46%) met criteria for definite infection and 13 (54%) met criteria for probable infection. Right and left shoulder sites were similarly affected (54% and 46%, respectively). The demographic and clinical characteristics of these cases are reflected in Tables 1 and 4.

Clinical and Laboratory Characteristics

The median time from index surgery to diagnosis was 15.9 months (range, 0.4–251). The majority of diagnoses were delayed (42%) or late (46%), with only 3 cases (12%) diagnosed <3 months after surgery. All 24 cases presented with joint pain (Table 1). The majority of cases (88%) demonstrated impaired range of motion. Joint swelling (21%), joint warmth (8%), joint erythema (12%), and constitutional symptoms (8%) were uncommon. No fever or wound drainage was noted. There was no significant difference in clinical presentation by time to diagnosis (early vs delayed vs late) or by PJI type (definite vs probable infection). The proportion with an elevated ESR (>20 mm/hour) was 47% and elevated CRP (>0.5 mg/dL) was 44%. Peripheral WBC data, when obtained, was primarily in the normal range. The median synovial leukocyte count of aspirated joints was 2648 cells/mm³ (n = 13), with median synovial neutrophil

Table 1. Demographic and Clinical Characteristics of 24 Patients With *Propionibacterium acnes* Shoulder Prosthetic Joint Infection

Variable	No. (%) ^a
Age, years ^b	62 (40, 81)
Male	19 (79)
White	21 (88)
Time from index surgery	
Early (<3 mo)	3 (12)
Delayed (3–24 mo)	10 (42)
Late (>24 mo)	11 (46)
Time from specimen collection to culture positivity, days ^b	4.5 (3–14)
Clinical signs and symptoms	
Joint pain	24 (100)
Loss of range of motion	21 (88)
Swelling	5 (21)
Erythema	3 (12)
Warmth	2 (8)
Constitutional symptoms	2 (8)
Wound drainage	0 (0)
Fever	0 (0)
Intraoperative findings	
Purulence	7 (47)
Histopathologic inflammation	10 (67)
Laboratory parameters ^b	
ESR, mm/hr	15 (3–>130)
CRP, mg/dL	0.4 (<0.1–10.3)
WBC count (synovial fluid), cells/mm ³	2648 (4–141 546)
%Neutrophils (synovial fluid)	86 (0–98)
Radiologic findings	
Radiolucency	4 (20)
Component Loosening	2 (10)
Subluxation	2 (10)
Fracture	1 (5)
Osteolysis	0 (0)

Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PJI, prosthetic joint infection; WBC, white blood cell.

^a Data are number (%) of cases, unless otherwise indicated.

^b Median (range of values for PJI cases).

percentage of 86% (n = 13). Of 15 cases undergoing operative intervention, intraoperative purulence was noted in 47% and tissue histopathologic inflammation in 67%.

Radiologic Characteristics

Abnormal radiologic findings were noted in a minority of cases. Radiolucency was observed in 20% of cases. Loosening of the prosthesis or subluxation was observed in 10% of cases, and fracture was observed in 5% of cases. No osteolysis was observed.

Microbiologic Characteristics and Antimicrobial Susceptibility Patterns

The majority of cases (92%) were identified after implementation of the extended culture protocol in 2009. The median time to culture positivity was 4.5 days (range, 3–14 days), which was unchanged in the extended culture period. However, 7 (29%) cases identified in the 2009–2013 period required a culture

duration of >5 days for organism recovery. There was no significant difference in clinical presentation for cases with recovery at >5 days relative to those with earlier culture detection. All tested isolates were susceptible to β -lactams (penicillin, piperacillin/tazobactam, ertapenem), vancomycin, moxifloxacin, and rifampin (Table 2). As is typical of *P. acnes*, all were resistant to metronidazole. The rate of resistance to clindamycin was 6%. The MIC range for minocycline was 0.03–0.25 $\mu\text{g/mL}$.

Antimicrobial and Surgical Treatment

There were 21 patients (88%) who received antibiotic treatment and 15 (62%) who received surgical intervention. There were 7 patients (29%) who received antibiotic treatment only and 14 (58%) who received concomitant antibiotic and surgical treatment (Tables 3 and 4); 1 patient received surgical intervention without antibiotic therapy. Of the 15 surgical cases, 1 (7%) underwent debridement and retention, 4 (27%; 1 planned, 3 unplanned) underwent a 1-stage procedure, 7 (47%) underwent a 2-stage procedure, and 3 (20%) underwent prosthesis removal with spacer placement without reimplantation. All 3 prosthesis removals were per patient preference. The median duration of antibiotic administration was 6.3 months (range, 1.3–50.7); 7 months (range, 4.1–50.7) for those receiving antibiotic only and 5.5 months (range, 1.3–21.3) for those receiving both antibiotic and surgery. The majority of antibiotic regimens (67%) used a β -lactam (penicillin or amoxicillin). Other antimicrobial agents used included minocycline or doxycycline, vancomycin, and clindamycin. Rifampin was used in 15 (71%) cases. The median duration on rifampin therapy was 3.9 months (range, 0.3–17.8). Of the 7 cases receiving antibiotic therapy only, the rationale for the decision for no surgical intervention included the presence of metastatic rectal cancer (1), poor surgical risk secondary to multiple comorbidities (1), insurance limitations (1), stable prosthesis (1), limited pain (1), and patient preference (2).

Table 2. Microbial Susceptibility Patterns of *Propionibacterium acnes* Isolates

Antimicrobial Agent	No. (%) ^a
Penicillin	19 (100)
Piperacillin/tazobactam	7 (100)
Ertapenem	7 (100)
Moxifloxacin	10 (100)
Rifampin	6 (100)
Vancomycin	14 (100)
Clindamycin	17 (94)
Metronidazole	0 (0)
Minocycline MIC 0.03–0.25 $\mu\text{g/mL}$ ^b	

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; MIC, minimum inhibitory concentration.

^a Data are number (%) of cases, unless otherwise indicated; susceptibilities determined as per CLSI/EUCAST breakpoints.

^b Range of MIC values for 11 tested isolates; no CLSI interpretive breakpoints are available for minocycline; tetracycline susceptible MIC breakpoint is $\leq 4 \mu\text{g/mL}$.

Table 3. Treatment Outcomes for *Propionibacterium acnes* Shoulder Prosthetic Joint Infection

Treatment	Total Treated No. (%)	Favorable Outcome ^a No. (%)
Type of treatment*		
Antibiotic therapy only	7 (29) ^b	4 (67)
Antibiotic therapy + surgery	14 (58)	10 (71)
Surgical type*		
1-stage exchange	4 (27) ^c	3 (75)
2-stage exchange	7 (47)	6 (86)
Rifampin therapy*		
Yes	15 (71) ^d	11 (73)
No	5 (24)	3 (60)

^a Data are number (% of treated cases).

^b Data are number (% of all cases).

^c Data are number (% of surgical cases).

^d Data are number (% of cases receiving antibiotic therapy).

* $P > .05$.

Treatment Outcomes

The median follow-up duration was 24 months (range, 4.6–65.9). Antibiotic-only approaches were first initiated in mid-2009. Consequently, the median follow-up duration for those receiving antibiotic therapy only was 12.2 months (range, 4.6–51) compared with 27.8 months (range, 7.3–65.9) for those receiving both antibiotic therapy and surgery ($P = .14$).

The proportion of cases with a favorable outcome was similar for those treated with antibiotic therapy and surgery (71%) compared with those treated with antibiotic therapy only (67%) (Table 3; $P = 1.0$). Outcomes were similar for those who underwent a 1-stage (75%) or 2-stage procedure (86%) ($P = 1.0$). A favorable outcome was noted for 73% of cases with rifampin therapy compared with 60% without rifampin therapy ($P = .61$). However, of the 15 cases in which rifampin was administered, this agent had to be discontinued in 6 (40%) due to adverse reactions ranging from gastrointestinal and influenza-like symptoms (resolved post cessation) to angioedema and severe rash including a case of acute generalized exanthematous pustulosis requiring hospitalization.

DISCUSSION

It has generally been considered that the optimal management of PJIs beyond the early period requires the combination of antimicrobial therapy with surgical intervention [1, 3, 6, 14, 23]. Antimicrobial therapy in the absence of surgical intervention has been considered to primarily result in unacceptably high rates of failed outcomes [1, 28]. However, few studies have examined the comparative management of *P. acnes* infections with nonsurgical approaches. In this 14-year series of 24 *P. acnes* prosthetic shoulder infections, we found treatment with a nonsurgical antibiotic-only approach to have an outcome comparable to that of a traditional combined medical-surgical approach. Our findings suggest that for *P. acnes* shoulder

Table 4. Individual Clinical Characteristics and Outcomes of 24 Patients With *Propionibacterium acnes* Shoulder Prosthetic Joint Infection

Case No.	Clinical Signs and Symptoms	Time to Culture Positivity– Days (No. of Positive Specimens ^a)	Time From Index Surgery–Months (Year of Diagnosis)	Laboratory Markers, Radiographic and Operative Findings	Treatment (Antibiotic Duration– Days)	Favorable Clinical Outcome
1	Joint pain, ↓ROM	3 (3)	1.9 (2001)	ESR > 130, CRP 10.3 Purulence, Tissue inflammation	Abx Surgery 2 stage Rifampin (45)	Yes
2	Joint pain, ↓ROM, Joint swelling	3 (1)	7.1 (2009)	ESR 7, CRP 0.3	Abx Surgery Debridement Rifampin (408)	No
3	Joint pain, ↓ROM, Joint swelling, Erythema	3 (1)	8.4 (2010)	Tissue inflammation	Abx Surgery 1 stage Rifampin (580)	Yes
4	Joint pain, ↓ROM	4 (1)	6.5 (2012)	ESR 5, CRP 0.1	Abx Rifampin (196)	No
5	Joint pain, ↓ROM	4 (1)	15 (2009)	Purulence, Tissue inflammation	Abx Surgery Removal Rifampin (118)	Yes
6	Joint pain, ↓ROM, Joint swelling, Erythema	4 (1)	16.7 (2011)	ESR 30, CRP 2.1 Radiolucency Purulence, Tissue inflammation	Abx Surgery 2 stage Rifampin (162)	Yes
7	Joint pain, ↓ROM	4 (1)	4.6 (2011)	Radiolucency, Component loosening Purulence, Tissue inflammation	Abx Surgery 2 Stage (83)	Yes
8	Joint pain, ↓ROM	4 (1)	7.4 (2009)	ESR 10, CRP 0.4	Abx Rifampin (1540)	Yes
9	Joint pain, ↓ROM	4 (1)	54.4 (2012)	ESR 11, CRP 1.2 Radiolucency	Abx	LTFU
10	Joint pain, ↓ROM	4 (1)	9 (2009)		Abx Surgery 1 Stage Rifampin (349)	Yes
11	Joint pain, ↓ROM	4 (1)	251 (2010)		Abx Surgery 1 Stage Rifampin (419)	Yes
12	Joint pain, ↓ROM	4 (1)	37 (2012)	ESR 8, CRP 0.1	Surgery 1 Stage	No
13	Joint pain	5 (1)	4.3 (2009)	ESR 40, CRP 2.3 Component loosening Tissue inflammation	Abx Surgery 2 Stage Rifampin (649)	No
14	Joint pain, ↓ROM, Joint swelling	5 (1)	55.4 (2010)	ESR 26, CRP 0.2	Abx Rifampin (232)	Yes
15	Joint pain, ↓ROM	5 (2)	12.4 (2008)	ESR 20, CRP 0.3 Purulence	Abx Surgery 2 Stage Rifampin (420)	Yes
16	Joint pain, ↓ROM	5 (1)	112 (2012)	ESR 25, CRP 0.3 Tissue inflammation	Abx Surgery 2 Stage (170)	Yes
17	Joint pain, ↓ROM, Warmth, Constitutional symptoms	5 (1)	2.8 (2011)	ESR 37, CRP 4	Abx Rifampin (770)	Yes

Table 4 continued.

Case No.	Clinical Signs and Symptoms	Time to Culture Positivity— Days (No. of Positive Specimens ^a)	Time From Index Surgery—Months (Year of Diagnosis)	Laboratory Markers, Radiographic and Operative Findings	Treatment (Antibiotic Duration— Days)	Favorable Clinical Outcome
18	Joint pain, ↓ROM	7 (1)	232.8 (2013)	Radiolucency, Subluxation Purulence, Tissue inflammation	Abx Surgery Removal (89)	No
19	Joint pain, ↓ROM	8 (1)	114.8 (2012)	ESR 5, CRP < 0.1	Abx Rifampin (126)	Yes
20	Joint pain, ↓ROM, Joint swelling, Erythema, Warmth, Constitutional symptoms	8 (1)	89.3 (2009)	ESR 80, CRP 4.1 Fracture Purulence, Tissue inflammation	Abx Surgery Removal Rifampin (46)	No
21	Joint pain	8 (1)	27.4 (2013)		Abx (189)	No
22	Joint pain, ↓ROM	9 (1)	0.4 (2011)	ESR 3, CRP 0.1 Tissue inflammation	Abx Surgery 2 Stage (41)	Yes
23	Joint pain, ↓ROM	9 (2)	163.7 (2011)	Subluxation	LTFU	LTFU
24	Joint pain, ↓ROM	14 (1)	41.9 (2011)	CRP 0.8	LTFU	LTFU

Abbreviations: Abx, antibiotic therapy; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LTFU, lost to follow up; ROM, range of motion.

^a Number of positive specimens = total number of specimens attained.

PJIs, an initial nonsurgical antibiotic-only approach may find relevance for select patients with stable prostheses, particularly for those in whom surgical intervention may be contraindicated or declined.

Prior series have suggested the incorporation of rifampin into the antimicrobial management of *P. acnes* shoulder infections [18, 19]. Rifampin has been considered active against biofilms, the formation of which has been considered integral to the pathogenesis of *P. acnes* in prosthetic and other device-related infections [11, 31]. *Propionibacterium acnes* isolates associated with invasive prosthetic infections have been shown to have stronger biofilm formation capability than isolates from healthy skin [32]. Such biofilm-associated isolates have demonstrated increased antimicrobial resistance in vitro [33, 34]. Moreover, there has been in vivo animal data suggesting the efficacy of rifampin against *P. acnes* foreign-body-associated infections [35]. Recent Infectious Diseases Society of America guidelines recommend penicillin or ceftriaxone as first-line treatment for *P. acnes* PJIs with clindamycin or vancomycin as alternatives, and minocycline or doxycycline for suppressive therapy [3]. Adjunctive rifampin therapy is not included in these recommendations for *P. acnes* PJI management. In this series, treatment outcomes were comparable with and without rifampin therapy. However, this drug was poorly tolerated and prematurely discontinued in 40% of cases. These findings suggest the role for rifampin in the management of *P. acnes* PJIs requires further study.

Recent studies have demonstrated the need for extended cultures to maximize recovery of pathogenic *P. acnes* isolates [27, 29]. In concordance with these findings, we observed a significant increase in the number of *P. acnes* shoulder PJIs subsequent to

institution of an extended *P. acnes* culture protocol. Twenty-nine percent of *P. acnes* PJIs would have been missed otherwise, affirming the importance of these techniques [29].

In clinical settings, the majority of cases in our series occurred among males. These cases were primarily delayed or late presentations as observed in prior reports [17, 19, 22]. The male predominance for *P. acnes* shoulder PJIs correlates with the previously reported higher *P. acnes* bacterial burden for men compared with women at shoulder sites [10]. The indolent nature of this organism likely accounts for its predominantly late presentation. The majority of PJIs in this series presented with pain and functional limitation without fever or constitutional symptoms. Whereas the presence of joint pain in all cases may seem evident, such universal occurrence has not been reported in other series [17]. Previous reports have also suggested the occurrence of more apparent clinical symptoms with early PJIs [1]. However, we noted no difference in clinical presentation by time to presentation.

Propionibacterium acnes infections have often been characterized by the absence of elevated inflammatory markers [1]. However, inflammatory marker elevation has been noted in a significant proportion of cases in some series, occurring in over 70% of cases in 1 recent study [22, 36]. In our series, a notable proportion of PJIs occurred without elevated inflammatory markers, yet there was still evidence of inflammatory marker elevation in just under 50% of cases. Intraoperative purulence was similarly noted in just <50% of cases. The proportion of cases with histopathologic inflammation in our series (67%) was similar to previously reported observations [29, 37].

There have been reports of a shift in antimicrobial susceptibility patterns of *P. acnes* in the setting of the increasing use of

antimicrobial agents for acne vulgaris [25, 26, 38]. Yet, there have been reports of phylogenetic differences between acne-related *P. acnes* isolates and deep device-related *P. acnes* isolates, suggesting shifting acne-related resistance patterns may not reflect trends in susceptibility patterns for deep-seated, prosthetic-related infections [11]. However, there have also been reports of increased antimicrobial resistance for biofilm-associated *P. acnes* isolates in vitro [33–35]. Furthermore, there have been recent reports of penicillin resistance even for *P. acnes* isolates recovered from the shoulder joint [39]. In this series, all isolates tested were susceptible to vancomycin, rifampin, and β -lactams including penicillin. There was limited resistance noted to clindamycin. Despite widespread use of the tetracycline class for acne, minocycline MICs for this study population were all within the expected susceptibility range. The observed susceptibility patterns were similar to those of other recent series of *P. acnes* shoulder isolates and suggest that in general, the broad antimicrobial susceptibility of *P. acnes* isolates in deep shoulder PJIs appears to be maintained [29, 39].

This study does carry the limitations of a primarily descriptive retrospective case series, without predefined diagnostic and therapeutic procedures, which could bias result interpretation. Assessment of clinical outcomes was also primarily qualitative. However, it is accepted that the primary goal of prosthetic joint replacement and PJI treatment is to improve quality of life by striving for a painless and functional joint, which were the criteria used to define a favorable study outcome [1, 6]. No gold standard exists for PJI diagnosis. However, we adapted previously applied criteria in our case definition [1, 3, 22, 29, 30]. On retrospective review, limited specimens were obtained for clinical evaluation. Furthermore, additional recent studies recovering *P. acnes* from native joints or at the time of initial prosthesis placement, without clinical symptoms, raise concerns for the positive predictive value of shoulder-derived *P. acnes* isolates [40, 41]. Although additional studies are needed comparing the prognostic value of isolates from patients with and without clinical symptoms, we note our cases reflect patients postimplant, with active clinical manifestations previously identified as being associated with PJI regardless of organism. There have been recent reports considering shorter culture duration for optimal *P. acnes* recovery [42]. However, clinical presentations were similar for patients with early or late *P. acnes* culture detection. The shorter median follow-up time for the antibiotic-only group provided less time for observation of clinical outcomes. In addition, antibiotic-only cases were all diagnosed via joint arthrocentesis without operative intervention and were thus all classified as probable infections. However, we found no significant difference in the characteristics of these cases compared with those with more definitive operative and tissue findings for infection. Determination of which cases received an antibiotic-only approach could have been subject to selection bias. However, the rationale behind such case selection

varied from patient preference and limited symptoms (ie, solid prosthesis with mild clinical symptoms) to severe comorbid disease (ie, nonoperative candidate), suggesting a wide clinical spectrum of host conditions selected for this approach, reducing the likelihood of this effect. All cases were treated with susceptible drugs.

CONCLUSIONS

Overall, this study contributes to better defining clinical characteristics of *P. acnes* prosthetic shoulder infections. Furthermore, it is one of the few descriptions of the potential utility of non-surgical management approaches for *P. acnes* infections, which could include a trial of antibiotic therapy prior to surgical considerations. Future, larger studies prospectively evaluating alternative surgical and nonsurgical management approaches, oral versus parenteral therapy, optimal antibiotic duration, and appropriate patient selection will be needed for the further optimization of the clinical management of *P. acnes* infections.

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