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MAJOR ARTICLE

Defeating the Hidden Foe: Antibiotic Therapy and Clinical Outcomes of *Cutibacterium acnes* Spinal Implant Infections

Don Bambino Geno Tai,[1,2] Brian Lahr,[3] Gina A. Suh,[2] Elie F. Berbari,[2] Paul M. Huddleston,[4] and Aaron J. Tande[2]

[1]Division of Infectious Diseases and International Medicine, University of Minnesota, Minneapolis, Minnesota, USA, [2]Division of Public Health, Infectious Diseases, and Occupational Medicine, Mayo Clinic, Rochester, Minnesota, USA, [3]Division of Clinical Trials and Biostatistics, Department of Quantitative Health Sciences, Mayo Clinic, Rochester, Minnesota, USA, and [4]Department of Orthopaedic Surgery, Mayo Clinic, Rochester, Minnesota, USA

Background. *Cutibacterium acnes* can cause spinal implant infections. However, little is known about the optimal medical management and outcomes of *C. acnes* spinal implant infections (CSII). Our study aims to describe the management of patients with CSII and evaluate the clinical outcomes.

Methods. We performed a retrospective cohort study of patients aged 18 years or older who underwent spinal fusion surgery with instrumentation between January 1, 2011, and December 31, 2020, and whose intraoperative cultures were positive for *C. acnes*. The primary outcome was treatment failure based on subsequent recurrence, infection with another organism, or unplanned surgery secondary to infection.

Results. There were 55 patients with a median follow-up (interquartile range) of 2 (1.2–2.0) years. Overall, there were 6 treatment failures over 85.8 total person-years, for an annual rate of 7.0% (95% CI, 2.6%–15.2%). Systemic antibiotic treatment was given to 74.5% (n = 41) of patients for a median duration of 352 days. In the subgroup treated with systemic antibiotics, there were 4 treatment failures (annual rate, 6.3%; 95% CI, 1.7%–16.2%), all of which occurred while on antibiotic therapy. Two failures occurred in the subgroup without antibiotic treatment (annual rate, 8.8%; 95% CI, 1.1%–31.8%).

Conclusions. Our study found that the estimated annual treatment failure rate was slightly higher among patients who did not receive antibiotics. Of the 6 failures observed, 4 had recurrence of *C. acnes* either on initial or subsequent treatment failures. More studies are warranted to determine the optimal duration of therapy for CSII.

Keywords. antibiotic therapy; *Cutibacterium acnes*; spinal implant infection; spine surgery complications; surgical site infections.

Cutibacterium acnes (previously *Propionibacterium acnes*) is a Gram-positive bacterium found on normal skin flora of humans, particularly within the sebaceous glands and hair follicles. *C. acnes* is one of the most common pathogens in spinal implant infections [1, 2]. Musculoskeletal infections associated with spinal implants can lead to significant morbidity, extended hospital stays, and additional operations. Therefore, clinicians must understand the significance, management, and outcomes of isolation of *C. acnes* during the index spinal instrumentation and subsequent revisions. This includes medical management with systemic antibiotics and surgical interventions. By understanding the pathogenicity and management of *C. acnes* infections, clinicians may improve patient outcomes and reduce the burden of infection associated with instrumented spinal fusion.

The literature on the medical management and outcomes of treatment of CSII is sparse [3]. Our study aimed to advance the science by evaluating the outcomes of patients diagnosed with CSII. Specifically, our objectives were to investigate the clinical outcome of patients with CSII based on treatment failure rates. We also computed failure rates in the subgroups that did and did not receive systemic antibiotics.

METHODS

We performed a retrospective cohort study of patients aged 18 years or older who underwent spinal fusion surgery with instrumentation between January 1, 2011, and December 31, 2020. We identified patients with positive *C. acnes* isolates from spine tissue using the clinical microbiology database. We categorized the culture results as confirmed infection if 1 of the following criteria was met: (1) *C. acnes* was isolated

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Correspondence: Don Bambino Geno Tai, MD, University of Minnesota, 420 Delaware Street SE, Minneapolis, MN 55455 (geno@tai-md.com); or Aaron Tande, MD, Mayo Clinic, 200 First Street SW, Rochester, MN 55905 (tande.aaron@mayo.edu).

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from 2 intraoperative specimens obtained during primary or revision instrumentation; (2) *C. acnes* was isolated from 1 intraoperative specimen PLUS (a) intraoperative purulence or secondary wound dehiscence with the implant visible, (b) radiographic evidence of inflammation, (c) systemic signs of inflammation such as fever (>38°C) without other recognized cause, (d) histopathology showing acute inflammation, (e) pseudarthrosis or unexpected hardware failure suspected to be caused by infection. We excluded cases in which other organisms were isolated and cases that were not hardware associated. Patients who did not provide research authorization were also excluded from the study.

We defined antibiotic treatment as receiving >2 weeks of systemic antibiotics. The primary outcome in our study was treatment failure, as defined by any of the following events during follow-up: diagnosis of spinal implant infection either with *C. acnes* (ie, recurrence) or other microorganisms or unexpected surgery secondary to infection. The first event meeting the definition of failure was recorded as the classified outcome, but subsequent cultures positive for *C. acnes* were recorded and described in the text. Using the institution's electronic medical record system, patients were followed from the date of isolation of *C. acnes* to the last medical visit or to the time of the first event indicating a treatment failure. This study was reviewed by the Mayo Clinic Institutional Review Board and deemed exempt (IRB #21-010951).

Statistical Analysis

Descriptive statistics for patient and clinical characteristics were presented by the median and interquartile range (IQR) for continuous variables and frequency for categorical variables. Rates of first-time treatment failure were calculated by dividing the failures by person-years of follow-up, expressed as a yearly percentage. The 95% confidence intervals for rates were calculated assuming that the number of events was Poisson distributed. All analyses were performed using R (version 4.0.3; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

During the study period, 91 patients had at least 1 intraoperative culture positive for *C. acnes* during spinal instrumentation, of whom 36 (39.6%) were excluded because of not meeting the case definition of CSII (n = 13) or presenting with polymicrobial infection (n = 23). Among the remaining 55 patients included in these analyses, the median age (IQR) was 59 (45–68) years, and 76.4% were males (n = 42). Median follow-up (IQR) was 2.0 (1.4–2.0) years. The median number of positive cultures (IQR) was 2 (1–3) out of a median (IQR) of 4 (3–4) samples taken. Most patients (65.5%, n = 36) had 2 or more positive intraoperative specimens with or without overt signs of infection. The rest of the patients had 1 positive culture but presented with pseudarthrosis/hardware failure (23.6%, n = 13) or wound dehiscence (10.9%, n = 6). At the time of the isolation of *C. acnes*, most patients (87.3%, n = 48) were undergoing revision of implant (eg, exchange, addition, implant removal). The remaining patients (n = 7) underwent primary instrumentation with unexpected positive intraoperative cultures. Table 1 lists the clinical characteristics of the cohort.

Table 1. Baseline Characteristics of Patients

Characteristic	No.	Overall (n = 55)
Sex: male	55	42 (76.4%)
Age, y	55	58.9 (45.1–68.3)
Race: White	55	54 (98.2%)
Body mass index, kg/m²	55	27.7 (24.4–32.8)
Diabetes mellitus	55	4 (7.3%)
Heart disease	55	5 (9.1%)
Active nicotine use	55	2 (3.6%)
Serum leukocyte count, 10^9/L	49	6.8 (5.9–8.5)
Indication for surgery upon isolation of *C. acnes*[a]	55	
Wound dehiscence and infection		19 (34.5%)
Myelopathy/radiculopathy/stenosis		18 (32.7%)
Pseudoarthrosis		16 (29.1%)
Hardware failure		12 (21.8%)
Adjacent segment disease		4 (7.3%)
Recurrence of index disease		3 (5.5%)
Fracture		2 (3.6%)
Cancer		2 (3.6%)
Others		3 (5.5%)
Region[a]	55	
Cervical		24 (43.6%)
Thoracic		25 (45.5%)
Lumbar		27 (49.1%)
Sacral		12 (21.8%)
No. of vertebral levels involved	54	3 (2–7)
Revision of instrumentation	55	48 (87.3%)
No. of past instrumentations	55	1 (0–2)
History of steroid injections	47	26 (55.3%)

Values represent frequency (%) for categorical variables and median (quartile 1, quartile 3) for continuous variables. No. is the number of nonmissing values.

[a]The cumulative sum exceeds the total number of cases, as cases may have affected 2 or more indications and regions.

Treatment of Spine Implant Infections

Systemic antibiotics were given to 41 patients (74.5%) for a median duration (IQR) of 352 (187–459) days. Treatment with initial intravenous (IV) antibiotics was used in 24 of these 41 patients (58.5%) for a median duration (IQR) of 42 (38–44) days, followed by a prolonged course of oral antibiotic therapy. The most common IV antibiotic used was ceftriaxone (n = 17), followed by daptomycin (n = 3). All 41 treated patients received oral antibiotics for a median (IQR) of 315 (143–415) days, including 17 patients (41.5%) who were given oral antibiotics alone. Seventeen patients were prescribed oral antibiotic suppression indefinitely (up to the last follow-up). The most common oral antibiotics used were first-generation cephalosporins (n = 16), tetracyclines (n = 14), and penicillin

(n = 10). Fourteen patients who met the criteria for CSII by having 2 or more positive cultures did not receive antibiotic treatment. The implant was retained in the majority of the patients (72.7%, n = 40).

Clinical Outcomes

Six treatment failures occurred over 85.8 cumulative person-years of follow-up, corresponding to an annual failure rate of 7.0% (95% CI, 2.6%–15.2%). The median time to failure for these 6 individuals (IQR) was 7 (2.1–12.4) months. All patients required reoperation. In the subgroup that received systemic antibiotics (n = 41), there were 4 failures during 63.2 total person-years (annual rate, 6.3%; 95% CI, 1.7%–16.2%). One had recurrence of *C. acnes*, while 3 were initially culture-negative. Of the latter 3 patients, 2 suffered recurrent treatment failures and eventually were positive for *C. acnes*. In the subgroup that did not receive antibiotic therapy (n = 14), 2 failures occurred over 22.7 cumulative person-years (annual rate, 8.8%; 95% CI, 1.1%–31.8%). One patient had recurrence of CSII, and the other had reinfection with *Klebsiella pneumoniae*. Table 2 summarizes the failure rates, and Table 3 describes the 6 patients in whom treatment failed.

Eighteen patients (32.7%) had spinal imaging at a median follow-up (IQR) of 1.2 (0.9–3.5) years. The imaging modalities used were x-ray (n = 13), computed tomography scan (n = 3), and magnetic resonance imaging (n = 2). Of those assessed, all but 1 were reported as normal (94.4%, n = 17); the 1 with an abnormal finding was due to a screw fracture.

Table 2. Outcomes of Different Management

	No.	Failures	Person-years of Follow-up	Annual Failure Rate (95% CI), %
All spinal implant infections	55	6	85.8	7.0 (2.6–15.2)
Antibiotic treatment[a]	41	4	63.2	6.3 (1.7–16.2)
IV (with or without oral)	24	3	34.2	8.8 (1.8–25.6)
Oral only	17	1	28.9	3.5 (0.1–19.3)
No antibiotic treatment[a]	14	2	22.7	8.8 (1.1–31.8)

Abbreviation: IV, intravenous.

[a]Antibiotic treatment was defined as the receipt of systemic antibiotics for more than 14 days.

DISCUSSION

Infection with *C. acnes* is a serious complication of spinal instrumentation surgeries, and it can lead to significant morbidity, rehospitalization, and additional procedures. *C. acnes* spinal implant infections usually present late (>12 months from the last instrumentation). While some cases can present as overt infection with abscess overlying the implants, many manifest from insidious symptoms of pain and dysfunction and diagnoses of pseudoarthrosis to implant failure or are identified only as unexpected intraoperative positive cultures [4, 5]. Risk factors include younger age, low body mass index (BMI), and thoracic instrumentation [6]. Previously published studies have not focused on medical management and treatment outcomes of CSII [7]. This study sought to describe the management of CSII in our center and evaluate the outcomes of patients with CSII.

Table 3. Description of Patients who Had an Adverse Outcome

Pt	Age/ Sex	BMI	Region	No. of Levels	Indication for Instrumentation	Indication for Revision	Abx Route	Abx	Time to Failure, mo	Type of Failure
1	66/M	38.9	Lumbar	4	Myelopathy/ radiculopathy	Pseudarthrosis	NT	NT	0.5	Infection with *Klebsiella pneumoniae*
2	44/M	27.1	Lumbar, thoracic	6	Fracture	Wound dehiscence	NT	NT	2.5	Recurrence of *C. acnes* infection
3	37/M	24.2	Thoracic, cervical	15	Cancer	Hardware failure	IV then oral	Daptomycin, doxycycline	1.9	Recurrence of *C. acnes* infection[a]
4	43/M	31.9	Lumbar, sacral	4	Myelopathy/ radiculopathy	Overt infection	IV then oral	Ceftriaxone, doxycycline	11.5	Unplanned reoperation, culture-negative[a]
5	67/M	25.9	Lumbar	3	Myelopathy/ radiculopathy	Hardware failure	Oral only	Cefadroxil	12.7	Unplanned reoperation[a]
										C. acnes isolated in subsequent treatment failure
6	51/M	25	Thoracic	5	Cancer, fracture	Wound dehiscence	IV then oral	Penicillin, cefadroxil	14.6	Unplanned reoperation[a]
										C. acnes isolated in subsequent treatment failure

Abbreviations: Abx, antibiotics; BMI, body mass index; IV, intravenous; NT, not treated; Pt, patient.

[a]Occurred while on antibiotic therapy.

We found that clinicians treated about 75% of the patients who met our definition for CSII using prolonged antibiotics for a median (IQR) of 352 (187–459) days. This approach reflects our management practice with patients with spine implant infections with other organisms [8]. Treatment failure occurred in 4 patients treated with systemic antibiotics; all 4 failed while on therapy or suppressive antibiotic therapy. Two patients who were not treated with antibiotics had a subsequent adverse outcome. While the rates between different treatment strategies and no antibiotic treatment were numerically comparable, we could not make a conclusion on which approach is superior. The approaches were likely to be affected by confounding by indication as clinicians are more likely to prescribe systemic antibiotics to more severe cases. It is reassuring to note that oral antibiotic therapy alone seems to be effective. Regarding surgical management, it was interesting to note that all patients who underwent complete implant removal had treatment success with or without antibiotic therapy. Implant removal alone might be sufficient to clear the infection if there is no associated discitis or osteomyelitis. Note that some patients in our cohort had a short course of antibiotics after the operation. This would be sufficient for skin and soft tissue infection [9].

There are no universally accepted criteria for diagnosis of SII, particularly those caused by *C. acnes* [8, 10]. In this study, we used the criteria by Kowalski et al., particularly 2 or more positive cultures. It remains to be seen if 2 or more positive intraoperative cultures are specific enough to diagnose infection for this nonvirulent and ubiquitous organism. We found that some clinicians opted not to treat some of the patients, even those with 2 or more positive cultures. The majority of these patients did not have recurrence of *C. acnes* infection. Some research suggests that clonality is not similar among isolates of *C. acnes*; therefore, for this nonvirulent organism, simply relying on the number of cultures might overdiagnose infection [11]. Furthermore, *C. acnes* is a notorious laboratory contaminant among specimens [2].

Our study has several limitations. First, as a retrospective cohort analysis, our study is subject to the inherent limitations of such designs. Second, our small sample size and low number of treatment failures precluded comparative analysis of event rates according to treatment strategy. Larger studies would be needed to detect therapeutic differences and elucidate risk factors.

In conclusion, treatment failure for *C. acnes* spine hardware infections appears to be uncommon even among those who did not receive prolonged antibiotic therapy. Prospective studies are needed to explore the optimal route and duration of antibiotic therapy.

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Patient consent. This study was reviewed by the Mayo Clinic Institutional Review Board and deemed exempt (IRB #21-010951).

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