

# Successful Treatment of *Cutibacterium acnes* Prosthetic Joint Infection With Single-Stage Exchange and Oral Antibiotics

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Interest has grown in less invasive surgical treatment and early use of oral antibiotics in the treatment of *Cutibacterium acnes* prosthetic joint infection. We report a series of patients who were successfully treated with single-stage exchange and an all-oral course of rifampin and linezolid.

**Keywords.** *Cutibacterium acnes*; prosthetic device infection; linezolid; rifampin.

*Cutibacterium acnes* (previously *Propionibacterium acnes*) is an anaerobic gram-positive bacillus that is part of the normal skin flora that has gained increased recognition as a cause of prosthetic joint infection (PJI) [1–3].

Postoperative infection with *C. acnes* can be difficult to diagnose and treat. Infections with this organism are associated with shoulder arthroplasty but have been described with other devices as well [4]. The most common approach to a PJI in the United States has been a 2-stage revision with removal of the device, treatment with intravenous antibiotics (IVABs), and device re-implantation when the infection is cleared [2, 5].

Debridement and antibiotics with implant retention (DAIR) and single-stage implant exchange (SSE) with immediate re-implantation are gaining interest as options to limit morbidity. Likewise, the use of oral rather than IVABs for bone and joint infections is increasingly used to limit risk without impacting outcome. However, the successful use of less disruptive surgical approaches and an oral-only antibiotic regimen (OAR) for *C. acnes* PJI has not been widely reported [3]. Indeed, patients

in the 2 largest reports on *C. acnes* PJI treatment received a course of IVAB [3, 6].

Linezolid and rifampin are oral agents that have favorable bioavailability, achieve good infiltration of bone and joints, and have reported ability to penetrate biofilms. Linezolid has demonstrated activity against *C. acnes* and has shown the ability to penetrate *C. acnes* biofilms in vivo and when used in conjunction with rifampin [7–12].

We report our successful experience using SSE and all oral for 9 patients with *C. acnes* PJI.

## METHODS

We performed a retrospective review of patients aged 18 and older with *C. acnes* PJI treated with SSE and OAR who were seen in consultation by 1 of the authors after referral from an orthopedic surgeon over an 8-year period from 2011 to 2018 at an academic-affiliated inpatient facility. Relevant clinical information including age, sex, medical history, location of the infected prosthesis, symptoms, timing from index surgery, antibiotic regimen, and length of follow-up was obtained.

The definition of PJI was adapted from previously described criteria [3, 6, 13]. All patients had 1 intraoperative culture collected. A case was defined as a positive intraoperative culture for *C. acnes* as well as the presence of  $\geq 1$  of the following symptoms: joint pain, swelling, fever, drainage, or presence of fistulous tract. The primary outcome was treatment success, defined as an absence of signs or symptoms following the conclusion of treatment, no evidence of relapse of infectious signs or symptoms, and no need for repeat operative intervention after a follow-up period of  $\geq 6$  months determined by 1 of the authors in coordination with the operating surgeon. Long-term follow-up for  $\geq 3$  years was obtained on all patients by telephone by 1 of the authors using a standardized questionnaire (Supplement 1).

## RESULTS

Nine patients were included in the study, with a median age (range) of 69 (25–77) years. One of the 9 patients was female. The median time from index surgery (range) was 60 (1–240) months. Seven of the 9 cases were diagnosed  $>24$  months after index surgery, 1 was diagnosed between 3 and 24 months, and 1 was diagnosed  $<3$  months after index surgery. All 9 intraoperative cultures were positive for only *C. acnes*. The median time to positive culture from specimen collection (range) was 10 (4–24) days.

Table 1 shows patient characteristics, the location of the infected prosthetic device, symptoms, treatment regimen, and symptoms at follow-up. The majority (6/9) of the infected devices were prosthetic shoulders, followed by hip (2/9) and knee

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**Table 1. Summary of Patient Characteristics, Infected Prosthesis Site, Treatment Regimen, and Symptoms at Follow-up**

	Age, Sex	Medical History	Prosthesis Site	Symptoms	Regimen, mg	Treatment Length, wk	Self-reported 3-Year Follow-up <sup>a</sup>
1	69, M	HTN, T2DM	Shoulder	Pain, swelling	Linezolid 600 mg BID/rifampin 300 mg BID Cefadroxil 1000 mg BID	20 (8 wk, 12 wk)	Not available
2	58, F		Hip	Pain, swelling	Linezolid 600 mg BID/rifampin 300 mg BID	24	Pain improved
3	70, M	HTN, HLD	Shoulder	Pain, swelling	Linezolid 600 mg BID/rifampin 300 mg BID	12	Pain improved
4	72, M	Seizure disorder	Shoulder	Pain, swelling	Linezolid 600 mg BID/rifampin 300 mg BID	12	Pain improved
5	51, M	HTN	Hip	Pain, swelling	Linezolid 600 mg BID/rifampin 300 mg BID	8	Asymptomatic
6	25, M	Asthma, HLD	Shoulder	Pain, swelling	Linezolid 600 mg BID/rifampin 300 mg BID	8	Asymptomatic
7	74, M	HTN	Knee	Pain, swelling, fever	Linezolid 600 mg BID/rifampin 300 mg BID	12	Pain improved
8	77, M	T2DM, HLD, A-fib	Shoulder	Pain, swelling	Cefadroxil 500 mg BID/rifampin 300 mg BID, linezolid 600 mg BID/rifampin 300 mg BID	14 (2 wk, 12 wk)	Asymptomatic
9	67, M	HTN	Shoulder	Pain, swelling	Linezolid 600 mg BID/rifampin 300 mg BID	12	Pain worse

Abbreviations: A-fib, atrial fibrillation; BID, twice daily; HLD, hyperlipidemia; HTN, hypertension; T2DM, type 2 diabetes mellitus.

<sup>a</sup>None of the patients required repeat surgery after self-reported 3-year follow-up.

(1/9). The most common symptoms experienced were pain (9/9), swelling (9/9), and fever (1/9). One patient had a fistulous tract. Five of the 9 patients had hypertension. Three had hyperlipidemia, and 2 had type 2 diabetes mellitus. One each had atrial fibrillation or a seizure disorder or asthma. All regimens contained linezolid 600 mg twice daily and rifampin 300 mg twice daily. The median treatment duration (range) was 12 (8–24) weeks. Two regimens used to treat shoulder PJI included cefadroxil. One patient received 12 weeks of cefadroxil 1000 mg twice-daily monotherapy following 2 weeks of rifampin and linezolid because of gastrointestinal intolerance; the other received 2 weeks of cefadroxil 500 mg twice daily in addition to rifampin before starting 12 weeks of rifampin and linezolid while he waited for insurance approval. There was no observed myelosuppression, neuropathy, or liver enzyme abnormalities during the median 12-week follow-up period.

Long-term follow-up for 3 years was obtained on 8 of the 9 patients using a standardized questionnaire (Supplementary Data). Seven of the 8 patients demonstrated treatment success without clinical evidence of ongoing infection. One patient reported worse pain.

## DISCUSSION

This case series describes the successful outcome of patients with *C. acnes* PJI who were treated with OAR after SSE.

Traditionally, infected prosthetic devices have been treated with a combination of operative intervention and intravenous antibiotics, with or without adjunctive oral antibiotics [2, 13]. The demonstration that bone and joint infections can be successfully treated with both 1-stage intervention and OAR has the potential to positively affect the treatment of infected prostheses [14]. The potential benefits of a treatment approach with limited surgical intervention and OAR include reduced morbidity from further operative intervention, avoidance of associated

complications of long-term intravenous catheters, improved patient experience, and lower potential cost to patients and the health care system [14]. The most effective treatment length and antibiotic regimen in the treatment of *C. acnes*-infected prosthesis are unknown, and the use of an all-oral regimen with SSE has thus far been based on limited data [3, 6, 13, 15–18].

Treatment of *C. acnes*-infected prosthetic devices can be challenging. *C. acnes* may manifest with subtle symptoms, is difficult to isolate in culture, and has the propensity to form biofilms [2, 19, 20]. A number of antibiotic regimens, including either all-intravenous or a combination of intravenous and oral, have been successfully used to treat *C. acnes* prosthesis infection. These include vancomycin, beta-lactams, tetracyclines, and clindamycin, typically over a course of several months [3, 5, 21, 22]. Concomitant use of agents with targeted activity against biofilms has shown mixed efficacy [3, 10, 15, 20, 23, 24].

Recently Li et al. demonstrated that oral therapy for successful treatment of PJI is possible, but few cases of *C. acnes* infection were included in this cohort [14]. Kusejko et al. reported treatment of *C. acnes* PJI with and without rifampin; however, the initial antibiotic course included intravenous treatment, and the antibiotic regimens were not described by specific drug [6]. They additionally reported a 32% failure rate of DAIR, regardless of antibiotic regimen [6].

Seven of 8 patients within our cohort had resolution of symptoms after 3 years, and 1 patient was not able to be reached (Table 1). One patient noted significant persistent pain at 3 years. This could represent ongoing occult infection with *C. acnes*, but the absence of inflammatory signs or symptoms and a reluctance to perform further surgery have precluded a definitive answer regarding the presence of an active infection. This compares favorably with patients whose devices were treated with a combination of surgery with or without oral regimens [3, 15]. The regimens were well tolerated, as no patients developed signs or symptoms of adverse drug reactions during their follow-up

period. Although we were concerned that the interaction between rifampin and linezolid could lower the concentration of linezolid, this did not appear to impact our results [25]. A potential reduction in the concentration of linezolid induced by rifampin may be the reason for the absence of major adverse effects including myelosuppression and neuropathy within our cohort. If linezolid is used for extended courses such as it was in our study, perhaps therapeutic drug monitoring should be considered to aid in the avoidance of adverse events.

Our study has several limitations. It is a retrospective study including a small cohort of patients identified from a single center. Patients were referred by an orthopedic surgeon after concern for infection was identified, a process susceptible to selection bias. Although patients were followed for  $\geq 3$  years to monitor for relapse, the subtle nature of *C. acnes* infection could mean that some patients may harbor an indolent infection. Success of the treatment course was dependent on self-reported outcomes from patients using a standardized questionnaire. Only 1 intraoperative culture was taken during each procedure, though all were positive for *C. acnes*. Additionally, while all patients were treated with linezolid and rifampin, the treatment regimens were not standardized. All of these limitations affect the external validity of our findings. Limitations to a treatment that uses extended courses of linezolid and rifampin include adverse drug reactions and interaction with other medications [26, 27]. Nonetheless, the majority remain clinically improved, with no progression of symptoms or evidence of active infection. This series suggests that a good clinical outcome can be achieved with a single-stage and oral approach for *C. acnes* PJI.

## CONCLUSIONS

Treatment of prosthetic devices infected with *C. acnes* after SSE with an all-oral antibiotic regimen can result in successful outcomes. Using linezolid and rifampin after appropriate surgical debridement appears to be a promising approach. Use of this approach requires further prospective studies to be considered in clinical practice.

## Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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