



## Case report

# Successful treatment of a prosthetic hip infection due to *Enterococcus faecalis* with sequential dosing of oritavancin and prosthesis preservation without prosthetic joint surgical manipulation



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## ABSTRACT

A patient with a prosthetic joint infection (PJI) complicated with deep surgical site infection due to vancomycin-susceptible *Enterococcus faecalis*. The initial treatment consisted of 10 days with daptomycin plus ampicillin. The hip prosthesis was retained and salvaged with six outpatient sequential doses of oritavancin 1200 mg every seven days without intra-articular irrigation or other surgical interventions. The patient was ambulating independently without symptoms after ten months of the last treatment of oritavancin.

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## Introduction

Enterococcal infections have presented a variety of treatment challenges for decades. *Enterococcus* sp., mostly *E. faecalis* and *E. faecium*, possess intrinsic characteristics that convey resistance to aminoglycosides, aminopenicillins, and cephalosporins. Enterococcus can develop resistance to glycopeptides through the acquisition of resistance genes located within plasmids and transposons. Enterococci may undergo spontaneous mutations by increasing the minimum inhibitory and bactericidal concentrations against some antimicrobials [1].

*Enterococcus* sp. has been considered a bacterium with low pathogenicity despite its known ability to cause endocarditis. An increased risk of enterococcal infection is associated with immunosuppression, previous surgery, indwelling urinary or vascular catheters, prolonged hospitalizations, and previous

antibiotic therapy. Sites of enterococcal infection include surgical procedural areas like intravascular catheters or intrabdominal spaces. Bacteremia may cause a native heart valve infection.

The complications and failures in treatment are significant after the infection of a prosthetic joint in a total hip arthroplasty (THA). Salvage therapies are frequently attempted due to the limited available therapeutic options. The bacterium's ability to develop multiple mechanisms of resistance often carries unfavorable clinical outcomes, even if there is in vitro laboratory susceptibility.

## Case report

A 62-year-old Hispanic female with essential hypertension, obesity (BMI 30.9 kg/m<sup>2</sup>) had severe osteoarthritis of both hips for six years. Progressive pain and debility in the right hip significantly impacted her quality of life and independence. There were no comorbidities, such as diabetes mellitus, autoimmune disorders, coagulopathy, peripheral vascular disease, cardiopulmonary disease, and renal disease. The patient had a left total hip arthroplasty performed in the past.

A right total hip replacement was performed without complications. The patient was discharged the next day with outpatient physical therapy and wound care. After seventeen days, most of the staples were removed with four staples remaining. There were no

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eleven days after revision (35 days after THR), with additional treatments delivered an outpatient (Fig. 2).

During the following three days, the patient experienced significant improvement in pain and swelling, allowing her to begin weight-bearing activities. The patient completed six weekly dosages of intravenous oritavancin 1200 mg. Inflammatory markers were measured to follow up as an outpatient. CRP and ESR markers were within normal limits after completion of treatment. After ten months of completing therapy, the patient has been able to ambulate independently without a walker or associated pain.

**Discussion**

The annual prosthetic joint infection (PJI) incidence rate in the United States, expressed as a percentage of the total number of hip arthroplasties performed, increased from 1.99% in 2001 to 2.18% in 2009 [2]. Risk factors for PJI include the presence of comorbidities such as rheumatoid arthritis, diabetes mellitus, malignancy, chronic kidney disease, obesity, lymphedema, chronic use of steroids, immunosuppression, and prior infection at the surgical site [3]. Most early-onset PJIs present with acute onset of one or more of the following findings: joint pain, warmth, erythema, induration or edema at the incision site, wound drainage, or dehiscence, joint effusion, and fever.

In a 2013 consensus report of experts (including orthopedic surgeons, infectious disease specialists, and clinical researchers), success after PJI treatment was defined by three factors: (1) eradication of infection, (2) no further surgical intervention for infection, and (3) no mortality associated with PJI [4].

The management approach of prosthetic joint infections depends on the timing and microbiology of the infection, condition of the joint and implant, quality of the soft tissue envelope, and individual patient circumstances. Over the last three decades, there has been significant debate around the corrective surgical approach for PJI. The three most common surgical techniques include a one-stage procedure (OSE), a two-stage procedure (TSP), and most recently, a combined approach known as debridement, antibiotics and implant retention (DAIR). Each of these procedures has its advantages and disadvantages. A multicenter, retrospective cohort study performed by Kandel et al. reported a combined treatment failure rate of 24.8% at two years following OSE or TSP; at four years, the failure rate for OSE was reported as 36% and 32% for TSP [5].

The surgical therapeutic approach involves the culture of the affected tissue before antimicrobial therapy. Targeted therapy should include a treatment course of 4–8 weeks with intravenous or oral treatment. Prosthetic joint infections with streptococci and enterococci occur in approximately 10% of cases [2, Table 1 from 2]. Enterococcal prosthetic hip infections are rare, but their occurrence generally portends a poor prognosis. Failure of treatment

**Table 2**  
Synovial Fluid Analysis.

Synovial Fluid Analysis	Post-Operative Day 35
Source	Synovial
Color	Red
Appearance	Cloudy
Viscosity	Highly Viscous
WBC (Auto)	40,405 cells/mm <sup>3</sup>
RBC (Auto)	33,000 cells/mm <sup>3</sup>
Neutrophils	92 cells/ $\mu$ L (H)
Lymphocytes	8 cells/L
Fibrin Clot	Not Present

correlates to the unique microbiological features of various enterococcal species, which restricts the selection of therapeutic options within *in vivo* activity against deep-seated infections. Factors to be considered to achieve successful outcomes are drug interactions, joint space and bone concentrations, and patient's allergic profiles.

The treatment of enterococcal infections depends on the complexity of the case. Some examples include infections of the urinary tract, the surgical site involving skin and soft tissue, and uncomplicated septicemia from a retained intravascular device. However, even for uncomplicated infections, failure rates with monotherapy could be as high as 60%. The combination of daptomycin and ampicillin has been effective in small cohorts in patients with higher comorbidity index scores involving chronic kidney disease, renal replacement therapy, and renal transplant recipients [6]. However, published reports on the use of this antibiotic combination is rare on deep-seated infections associated with joint hip arthroplasty.

Oritavancin has been recently used successfully in bone and joint infections and in cases in which a hip prosthetic device was salvaged with sequential dosing. Two case reports of single-stage revision with antibiotic spacer and subsequent dosing of oritavancin have proven successful [7]. We used oritavancin as salvage therapy with excellent clinical outcomes.

Oritavancin is a long-acting lipoglycopeptide antibiotic initially approved for the treatment of acute bacterial skin and skin structure infection (ABSSSI) and supported by the phase 3 SOLO program [8–11]. Its terminal half-life is 245 h. Dosage adjustments are unnecessary for patients with mild to severe renal or mild to moderate hepatic impairments [8–12]. Given its protein binding of 85%, with a single dose of 1200 mg, the predicted free drug concentrations at seven days would exceed the breakpoints for labeled pathogens [12]. The pharmacokinetic profile has been unexplored in humans [13]. The pharmacokinetic profile of oritavancin in rabbits showed rapid distribution in bone tissues. Oritavancin exerts bactericidal activity against gram-positive bacteria, including *E. faecalis* and *E. faecium*, regardless of vancomycin susceptibility [14]. Phase 3 SOLO studies and real-

**Table 1**  
Inflammatory Markers.

Post-Operative Day (POD)	21	24	25	26	27	28	29	31	35	37	38	48
ESR					18.00	25.00	26.00	39.00	39.00		31.00	28.00
CRP					1.62	1.10	1.21	2.80				0.23
Procal							<0.05	<0.05				
WBC	7.52	14.70	7.60	11.30	9.80	8.30	8.30	10.40	8.05	6.66		
NEU%		57.80	66.20	46.20	29.00	33.00	28.00	37.00	55.00			
BAND%					0.00	0.00	0.00	0.00				
LYM%		27.90	26.40	42.30	58.00	42.00	50.00	37.00	33.80			
MON%		13.40	7.00	9.60	5.00	17.00	14.00	19.00	9.60			
EOS%		0.30	0.00	1.30	8.00	7.00	8.00	7.00	0.90			
BAS%		0.30	0.10	0.30	0.00	0.00	0.00	0.00	0.50			
IG%		0.30	0.30	0.30	0.30	0.40	0.40	0.40	0.20			

**Table 3**  
Antimicrobial Resistance. Organism: Enterococcus Faecalis.

Antimicrobial	MIC	Systemic
Ampicillin	<= 2	S
Gent. Synergy	<= 500	S
Levofloxacin	2	S
Ceftriaxone	> 32	R*
Ciprofloxacin	<= 1	S
Clindamycin	> 4	R*
Daptomycin	2	S
Penicillin	2	S
Tetracycline	<= 4	S
Trimeth/Sulfa	<= 0.5/0.95	R*
Vancomycin	2	S
Linezolid	2	S

world experience demonstrated the safety and tolerability of oritavancin [8–11,15].

Recent studies showed clinical success with multiple sequential doses of oritavancin when used as initial or salvage therapies in bone and joint infections caused by *S. aureus* [16–20]. However, data on the treatment of enterococcal infections using oritavancin are sparse. Our case provides additional information regarding the practical and well-tolerated administration of oritavancin as salvage therapy for a complicated enterococcal prosthetic device infection.

We conducted a literature review to identify similar cases involving prosthetic total hip infections with enterococci. Kheir et al. provide data of 87 patients with hip PJIs, of whom 33 of them had monomicrobial or mixed microbiology with *Enterococci species*. The cases tabulated by Kheir et al., include data on several patient indices, including age, gender, body-mass-index, age-adjusted Charlson Comorbidity Index (aCCI), medical comorbidities, presence or absence of a detectable sinus tract, surgical treatment procedure(s), antibiotic therapies, and subsequently clinical and microbiologic outcomes. With regards to surgical management, 24 % of patients underwent a 1-stage surgical procedure, 24 % experienced a 2-stage surgical procedure, and the remaining patients underwent incision and drainage of the joint without debridement. Approximately 47 % of patients undergoing a surgical procedure plus antibiotics with or without lavage were clinical failures.

Among the orthopedic literature, it is clear that infected prosthetic joints must undergo debridement and lavage in addition to one of the three recognized surgical approaches. Our case is different from those of Kheir et al. because the joint capsule was not lavaged surgically. The only intervention that involved the patient's joint capsule was the diagnostic CT-guided fluoroscopic arthrocentesis. We attribute this patient's success to multiple factors. First, daptomycin and ampicillin susceptibilities were identified early in the course with seven days of administration. Several studies suggest MICs  $\leq$  0.25 mg/L for vancomycin-susceptible *E. faecalis* is an accepted criterion for oritavancin use. The general well-being of the patient besides the PJI may have contributed to a favorable outcome.

## Conclusion

Prosthetic joint infections treatment includes debridement, surgical lavage, local and systemic antimicrobial therapy. A literature review on enterococcal monomicrobial and mixed infections of prosthetic hip devices reveals microbiological eradication in 28 of 33 (85 %) patients treated with multiple antibiotic regimens, mostly ampicillin and vancomycin. The infecting pathogen in our patient showed susceptibility to ampicillin, vancomycin, and daptomycin, although borderline

susceptibility to the latter. After an extensive review of the English literature, this case is unique. The hip prosthesis infected with *Enterococcus faecalis* was retained and salvaged with six sequential doses of oritavancin 1200 mg intravenously weekly without intra-articular irrigation or any other surgical intervention.

## Disclosures

The patient signed informed consent to publish this article.

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## Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

## CRediT authorship contribution statement

**Jullian P. Nguyen:** Investigation, Writing - original draft, Data curation. **Brian X. Contreras:** Investigation, Writing - original draft. **Miguel Sierra-Hoffman:** Conceptualization, Writing - review & editing. **Kim Saddler:** Investigation, Writing - original draft. **Mark L. Stevens:** Methodology, Supervision, Project administration. **Miriam T. Castro-Lainez:** Supervision, Writing - review & editing. **Brett Knox:** Investigation, Writing - original draft. **Rafael J. Deliz:** Writing - original draft, Writing - review & editing.

## Declaration of Competing Interest

The authors do not have any competition or financial conflicts of interest to disclose. The authors declare that the study was unfunded and was the result of volunteer work.

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