23 Treatment of Periprosthetic Joint Infections with Resistant Organisms

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23.1 Introduction

The successful eradication of periprosthetic joint infection (PJI) depends on various host factors, treatment modalities, and infection characteristics. Infections caused by antibiotic-resistant organisms have been increasing in recent years [1, 2]. Studies have clearly demonstrated the difficulty of treating PJI caused by organisms including methicillin-resistant *Staphylococcus epidermidis* (MRSE), methicillin-resistant *Staphylococcus aureus* (MRSA), and *enterococcus* [1, 3–6]. It is vital to understand the treatment ramifications of the various resistant organisms when treating PJI.

23.1.1 *Staphylococcus epidermidis*

Staphylococcus epidermidis (*S. epidermidis*) was previously thought of as an innocuous bacterial colonizer on human skin. However, it is now recognized as an opportunistic pathogen that is responsible for the greatest proportion of infections on all indwelling medical devices [7]. *S. epidermidis* falls into the broader category of coagulase-negative staphylococci which causes 30–43% of all PJIs [8]. *S. epidermidis* first non-specifically binds to implanted prostheses, then subsequent biofilm formation occurs via a polysaccharide intercellular adhesin [9]. It is this ability to develop a strong glycocalyx that accounts for the difficulty of eradication of this low-virulent organism [1]. For these reasons, aggressive treatment of *S. epidermidis* is recommended (especially when methicillin resistance is encountered).

23.1.2 *Staphylococcus aureus*

Staphylococcus aureus (*S. aureus*) is a Gram-positive human commensal organism that has shown persistent nasal colonization in 20–25% of adults and intermittent colonization in up to 60% [10]. *S. aureus* infection causes 10–23% of all PJIs. *S. aureus* interacts with host fibronectin, fibrinogen, and collagen to cover a prosthesis immediately after implantation [8, 11]. A subcutaneous foreign body reduces the minimum infection causing inoculum with *S. aureus* more than 100,000×. The susceptibility to PJI caused by *S. aureus* combined with emerging and worsening resistance has increased recurrent infection rates [1]. Successful infection eradication of PJIs

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caused by methicillin-resistant *S. aureus* (MRSA) with debridement and implant retention (DAIR) is reported as low as 20% and is generally not recommended [12]. Even two-stage revision for MRSA infections has demonstrated low rates of infection eradication, thus highlighting the difficulty in managing this virulent and resistant organism [3].

23.1.3 *Enterococcus*

Enterococcus is a Gram-positive, facultative anaerobe which has been reported to cause 2–3% of all PJIs [4, 13]. El Helou et al. reported 94% success with two-stage exchange for enterococcal infections; however, 46% of their cohort were treated with definitive resection while only 34% underwent two-stage revision. Rasouli et al. achieved successful eradication of enterococcal PJIs in only 20% of cases treated with DAIR and only 44% treated with two-stage revision [4]. An additional challenge treating enterococcal PJIs occurs when the bacteria are resistant. Vancomycin-resistant *enterococcus* (VRE) infections remain exceptionally difficult to treat with reimplantation rather than salvage options such as definitive resection, fusion, or above-knee amputation [4, 14].

23.2 Debridement and Implant Retention

Debridement and implant retention (DAIR) is commonly utilized for the treatment of acute periprosthetic joint infections as discussed in previous sections. The success rates vary widely in the literature and largely depend on the infecting organism. Duque et al. report successful infection eradication with DAIR in only 20% of MRSA and 33.3% of *Pseudomonas aeruginosa* infections compared to 85.3% for all other bacteria [12]. Other authors have reported on similar difficulties and comparable failure rates when treating staphylococcal infections with DAIR [15–17]. Chung et al. have recently reported on improved success of a planned two-stage DAIR [18]. In their protocol, the first stage consists of a thorough debridement with placement of antibiotic cement beads, while the second stage (occurring 5 days later) involves an additional debridement with exchange of modular components. They report successful infection eradication in 89.6% of TKAs (93.5% in primary TKAs), including overall successful treatment of 70% of MRSA infections [18].

The addition of rifampin to targeted intravenous (IV) antibiotic therapy is recommended for all cases of DAIR, especially those caused by staphylococcal species [19–24]. The successful results of adding rifampin are thought to result from its ability to penetrate biofilm when used in DAIR [8].

23.3 Two-Stage Revision

Two-stage revision remains the gold standard for treatment of chronic periprosthetic joint infection. Overall success rates between 80% and 100% are commonly quoted for infection eradication utilizing a two-stage approach [25–29]. However, when stratifying these results based on type of organism, treatment outcomes worsen with resistant bacteria. Kilgus et al. report 89% success treating methicillin-sensitive *S. aureus* (MSSA) compared to only 18% infection eradication of MRSA and MRSE infections utilizing a two-stage approach [3]. Mittal et al. found 24% reinfection rate when treating MRSA and MRSE in a two-staged fashion [1]. However, 14% were reinfected with new organisms rather than recurrence, therefore they recommend two-stage revision as a viable treatment option in this setting [1]. Rasouli et al. successfully eradicated enterococcal PJIs with two-stage revision in only 7 of 16 patients. Six patients were treated with definitive resection and 3 had either knee fusion or above-knee amputation [4].

Case Example

This is a 61-year-old male with a complex history starting with right total knee arthroplasty, subsequent revision for polyethylene wear, and then complete revision TKA. This was complicated by subsequent hematogenous MRSA PJI which was treated with a single-stage revision. Four years subsequent to that he was found to have an MSSA PJI which was treated with two-stage exchange which was complicated by a traumatic wound dehiscence. At this time he presented to our practice with a draining sinus and chronic extensor mechanism disruption with revision components in place (Fig. 23.1). He underwent resection and placement of a static antibiotic cement spacer with multiple intraoperative cultures demonstrating enterococcus. This required 2 additional repeat debridements with 1 spacer exchange before the infection was cleared and the knee was reimplanted (Fig. 23.2). At most recent follow-up 2 years after reimplantation, he demonstrated no evidence of infection and was off all antibiotics.

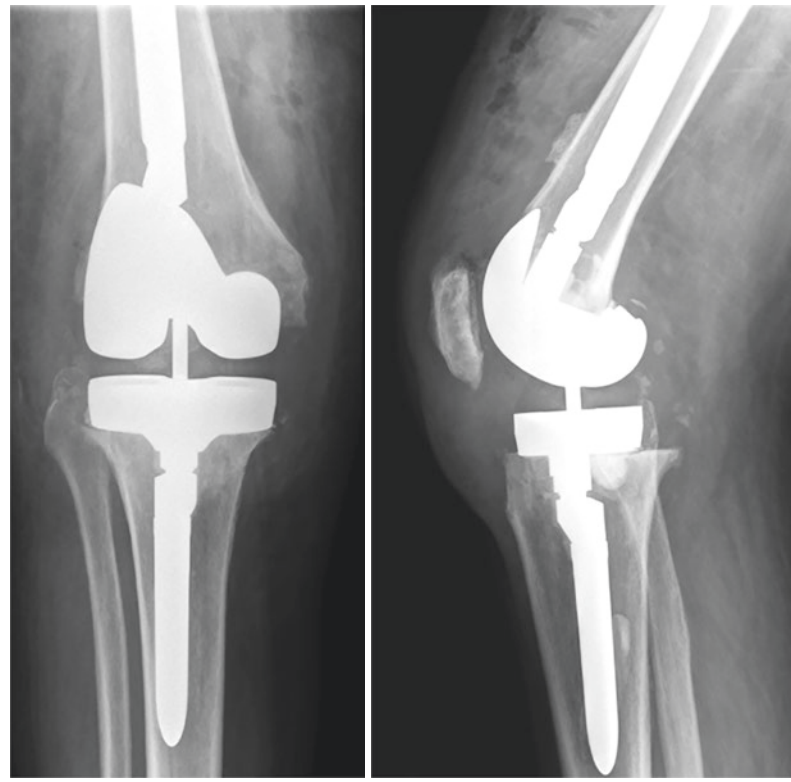

Fig. 23.1 Anteroposterior (AP) and lateral radiographs at presentation demonstrating revision components without evidence of implant loosening

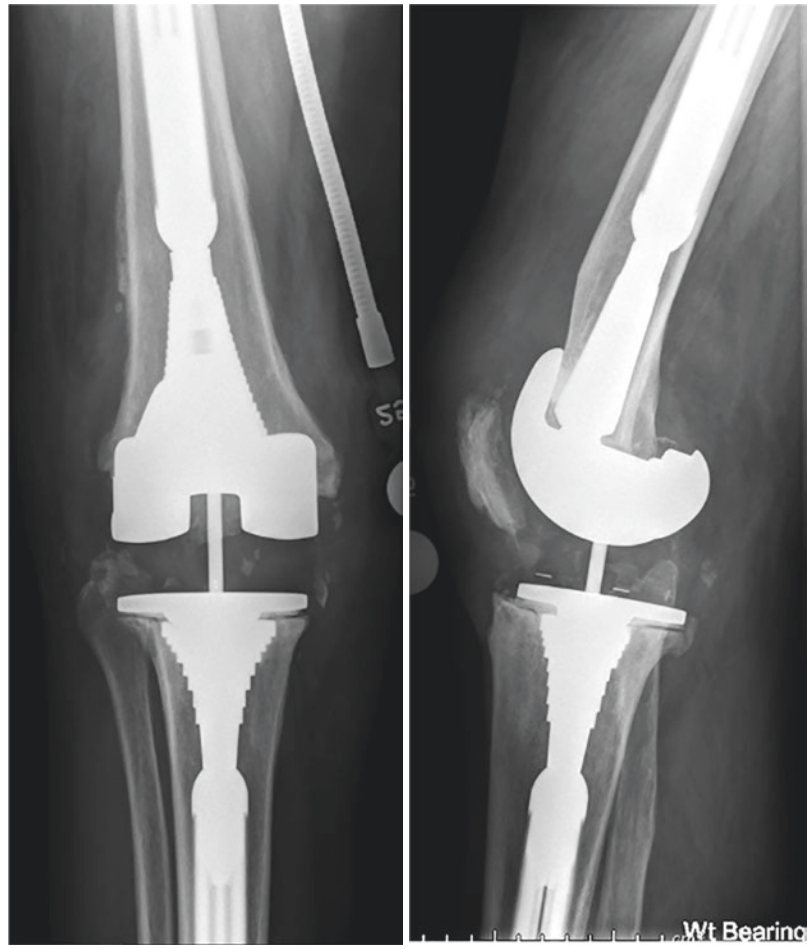

Fig. 23.2 Anteroposterior (AP) and lateral radiographs after reimplantation demonstrating sleeved revision components

23.4 Conclusion

Treatment of knee PJI with resistant organisms remains a challenge with high complication and reinfection rates. Two-stage revision is often the best approach to maximize chances of successful infection eradication. If DAIR is chosen, consideration should be given to performing a planned two-staged DAIR as described by Chung et al. [18]. Further, the addition of 6 months of oral rifampin to targeted IV antibiotic therapy when treating staphylococcal knee PJI with DAIR has demonstrated improved results. Regardless of treatment approach, infection recurrence remains high and salvage procedures such as fusion, definitive resection, and above-knee amputation are realistic outcomes despite best attempts to retain or reimplant prostheses.

References

1. Mittal Y, Fehring TK, Hanssen A, Marculescu C, Odum SM, Osmon D. Two-stage reimplantation for periprosthetic knee infection involving resistant organisms. J Bone Joint Surg Am. 2007;89(6):1227–31. https://doi.org/10.2106/JBJS.E.01192.
2. Garvin KL, Hinrichs SH, Urban JA. Emerging antibiotic-resistant bacteria. Their treatment in total joint arthroplasty. Clin Orthop Relat Res. 1999;369:110–23.
3. Kilgus DJ, Howe DJ, Strang A. Results of periprosthetic hip and knee infections caused by resistant bacteria. Clin Orthop Relat Res. 2002;404(404):116–24. https://doi.org/10.1097/00003086-200211000-00021.
4. Rasouli MR, Tripathi MS, Kenyon R, Wetters N, Valle Della CJ, Parvizi J. Low rate of infection control in enterococcal periprosthetic joint infections. Clin Orthop Relat Res. 2012;470(10):2708–16. https://doi.org/10.1007/s11999-012-2374-8.

5. Parvizi J, Azzam K, Ghanem E, Austin MS, Rothman RH. Periprosthetic infection due to resistant staphylococci: serious problems on the horizon. Clin Orthop Relat Res. 2009;467(7):1732–9. https://doi.org/10.1007/s11999-009-0857-z.
6. Hirakawa K, Stulberg BN, Wilde AH, Bauer TW, Secic M. Results of 2-stage reimplantation for infected total knee arthroplasty. J Arthroplasty. 1998;13(1):22–8. https://doi.org/10.1016/s0883-5403(98)90071-7.
7. Otto M. *Staphylococcus epidermidis*—the "accidental" pathogen. Nat Rev Microbiol. 2009;7(8):555–67. https://doi.org/10.1038/nrmicro2182.
8. Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-joint infections. N Engl J Med. 2004;351(16):1645–54. https://doi.org/10.1056/NEJMra040181.
9. Darouiche RO. Device-associated infections: a macroproblem that starts with microadherence. Clin Infect Dis. 2001;33(9):1567–72. https://doi.org/10.1086/323130.
10. Lister JL, Horswill AR. *Staphylococcus aureus* biofilms: recent developments in biofilm dispersal. Front Cell Infect Microbiol. 2014;4(37):178. https://doi.org/10.3389/fcimb.2014.00178.
11. Foster TJ, Höök M. Molecular basis of adherence of *Staphylococcus aureus* to biomaterials. Hoboken, NJ: Wiley; 2000. p. 27–39. https://doi.org/10.1128/9781555818067.ch2.
12. Duque AF, Post ZD, Lutz RW, Orozco FR, Pulido SH, Ong AC. Is there still a role for irrigation and debridement with liner exchange in acute periprosthetic total knee infection? J Arthroplasty. 2017;32(4):1280–4. https://doi.org/10.1016/j.arth.2016.10.029.
13. Helou El OC, Berbari EF, Marculescu CE, et al. Outcome of enterococcal prosthetic joint infection: is combination systemic therapy superior to monotherapy? Clin Infect Dis. 2008;47(7):903–9. https://doi.org/10.1086/591536.
14. Ries MD. Vancomycin-resistant Enterococcus infected total knee arthroplasty. J Arthroplasty. 2001;16(6):802–5. https://doi.org/10.1054/arth.2001.24951.
15. Brandt CM, Sistrunk WW, Duffy MC, et al. *Staphylococcus aureus* prosthetic joint infection treated with debridement and prosthesis retention. Clin Infect Dis. 1997;24(5):914–9. https://doi.org/10.1093/clinids/24.5.914.
16. Marculescu CE, Berbari EF, Hanssen AD, et al. Outcome of prosthetic joint infections treated with debridement and retention of components. Clin Infect Dis. 2006;42(4):471–8. https://doi.org/10.1086/499234.
17. Kuiper JW, Willink RT, Moojen DJF, van den Bekerom MP, Colen S. Treatment of acute periprosthetic infections with prosthesis retention: review of current concepts. World J Orthop. 2014;5(5):667–76. https://doi.org/10.5312/wjo.v5.i5.667.
18. Chung AS, Niesen MC, Graber TJ, et al. Two-stage debridement with prosthesis retention for acute periprosthetic joint infections. J Arthroplasty. 2019;34(6):1207–13. https://doi.org/10.1016/j.arth.2019.02.013.
19. Osmon DR, Berbari EF, Berendt AR, et al. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis. 2013;56(1):e1–e25. https://doi.org/10.1093/cid/cis803.
20. Drancourt M, Stein A, Argenson JN, Roiron R, Groulier P, Raoult D. Oral treatment of Staphylococcus spp. infected orthopaedic implants with fusidic acid or ofloxacin in combination with rifampicin. J Antimicrob Chemother. 1997;39(2):235–40. https://doi.org/10.1093/jac/39.2.235.
21. Aboltins CA, Page MA, Buising KL, et al. Treatment of staphylococcal prosthetic joint infections with debridement, prosthesis retention and oral rifampicin and fusidic acid. Clin Microbiol Infect. 2007;13(6):586–91. https://doi.org/10.1111/j.1469-0691.2007.01691.x.
22. Berdal J-E, Skråmm I, Mowinckel P, Gulbrandsen P, Bjørnholt JV. Use of rifampicin and ciprofloxacin combination therapy after surgical debridement in the treatment of early manifestation prosthetic joint infections. Clin Microbiol Infect. 2005;11(10):843–5. https://doi.org/10.1111/j.1469-0691.2005.01230.x.
23. Zimmerli W, Widmer AF, Blatter M, Frei R, Ochsner PE. Role of rifampin for treatment of orthopedic implant-related staphylococcal infections: a randomized controlled trial. Foreign-body infection (FBI) study group. JAMA. 1998;279(19):1537–41. https://doi.org/10.1001/jama.279.19.1537.
24. Helou El OC, Berbari EF, Lahr BD, et al. Efficacy and safety of rifampin containing regimen for staphylococcal prosthetic joint infections treated with debridement and retention. Eur J Clin Microbiol Infect Dis. 2010;29(8):961–7. https://doi.org/10.1007/s10096-010-0952-9.
25. Insall JN, Thompson FM, Brause BD. Two-stage reimplantation for the salvage of infected total knee arthroplasty. J Bone Joint Surg Am. 1983;65(8):1087–98.
26. Borden LS, Gearen PF. Infected total knee arthroplasty. A protocol for management. J Arthroplasty. 1987;2(1):27–36. https://doi.org/10.1016/s0883-5403(87)80028-1.
27. Rosenberg AG, Haas B, Barden R, Marquez D, Landon GC, Galante JO. Salvage of infected total knee arthroplasty. Clin Orthop Relat Res. 1988;226:29–33.
28. Wilde AH, Ruth JT. Two-stage reimplantation in infected total knee arthroplasty. Clin Orthop Relat Res. 1988;236:23–35.
29. Windsor RE, Insall JN, Urs WK, Miller DV, Brause BD. Two-stage reimplantation for the salvage of total knee arthroplasty complicated by infection. Further follow-up and refinement of indications. J Bone Joint Surg Am. 1990;72(2):272–8.