Foot and Ankle Surgery 25 (2019) 13–18

Contents lists available at ScienceDirect

Foot and Ankle Surgery

journal homepage: www.elsevier.com/locate/fas

Foot and ankle infections: Debridement, early fixation and rifampicin provide earlier recovery of function and quality of life☆

Daniel Pérez-Prieto[a,*], María E. Portillo[b], Gemma González-Lucena[a], Alberto Ginés-Cespedosa[a]

[a] Orthopedic Department, Hospital del Mar — Universitat Autònoma de Barcelona, Barcelona, Spain
[b] Microbiology Department, Complejo Hospitalario de Navarra, Pamplona, Spain

ARTICLE INFO

Article history:
Received 21 May 2017
Received in revised form 28 June 2017
Accepted 21 July 2017

Keywords:
Foot and ankle infection
Biofilm
Quality of life
Rifampicin

ABSTRACT

Background: Infection after foot and ankle fractures is a major concern for orthopedic surgeons. It is widely believed that final osteosynthesis should be delayed until the infection is cured. However, there is no literature that supports this practice. In addition, the delay impairs patient function and quality of life (QoL).
Methods: In the present study, four cases of ankle infection treated with aggressive debridement, early fixation and antibiofilm antibiotics are described. It is thought that, like other implant related infections, ankle infections can be rapidly treated with the definitive fixation and by curing the infection to make for a fast recovery of QoL and function.
Results: The infections were caused by MSSA and *Pseudomonas aeruginosa* in case 1, MSSA in case 2 and MRSA as well as *K. pneumonia* in case 3. Case 4 was a culture negative infection. They were susceptible to antibiofilm antibiotics (the gram-negative bacilli susceptible to ciprofloxacin and the gram-positive cocci susceptible to rifampicin). Cases 1, 3 and 4 were treated with a tibio-talo-calcaneal arthrodesis and case 2 was treated with a de-rotational fibular osteotomy and a medial closing wedge supramalleolar osteotomy. All cases improved at a median time of 4 weeks in terms of quality of life (SF-36) and function (AOFAS). At 2-years follow-up, no recurrence of infection was observed in any of the cases. All the cases achieved fusion or osteotomy healing at final follow-up.
Conclusions: Early fixation after debridement combined with antibiofilm antibiotics can be performed in foot and ankle inflections to provide early recovery of QoL and function in patients.

1. Introduction

Infections related to orthopedic devices are among the main complications for orthopedic surgeons [1]. When it comes to foot and ankle, it can be even worse as this area provides little soft tissue coverage and a sometimes scarce blood supply [1–3].

Infection is very frequent after ankle and pilon fractures and has an infection rate of 10%, even higher those cases of high energy and open fractures. Ankle and pilon fractures represent about 30%–50% of all foot and ankle infections [4,5]. They are followed by neuropathic arthropathies that represent some 15%–25% of foot and ankle infections [6].

Orthopedic surgeons concern with infections has led to delaying the definitive surgical treatment several months (or even years) until after the infection is cured [3,7]. However, there is no study that supports this practice. Moreover, this postponement of the definitive surgery impairs patient function and quality of life (QoL) [8,9].

On the other hand, there is growing evidence that prostheses can be implanted even though the infection is not yet cured in prosthetic joint infection (PJI) [10]. It can be performed whenever antibiofilm antibiotics are available [11]. It has also worked in other orthopedic infections [12]. In foot and ankle cases, good results have been achieved after early external fixation associated with extensive debridement and proper antibiotics [13]. However, very few cases of early internal fixation have been reported [14].

☆ Level of evidence: level IV, case series.

* Corresponding author at: Department of Orthopaedic Surgery and Traumatology, Hospital del Mar — Universitat Autònoma de Barcelona, Passeig Marítim, 25, Barcelona, Spain.
E-mail address: dperezprieto@parcdesalutmar.cat (D. Pérez-Prieto).

http://dx.doi.org/10.1016/j.fas.2017.07.644
1268-7731/

The aim of the present study is to describe four cases of ankle infection in which early fixation was performed along with the use of antibiofilm antibiotics.

2. Methods

A case series of 4 patients is here presented. All four surgeries were performed by the same two surgeons on an in-patient basis in the same hospital.

2.1. Microbiological protocol

As part of a standardized protocol, 5 tissue samples were taken for microbiological cultures [15]. In addition, one sample was sent for a histopathological study. Should there be any foreign body, it was always sent for sonication and microbiological study.

Cultures were defined as positive when there was microorganism growth in preoperative aspirate, periprosthetic tissue cultures, or sonication fluid cultures. It was considered a positive sonication fluid culture when the same organism grew 50 or more colony-forming units (CFU)/mL. However, any growth in sonication fluid culture was considered positive when the patient had previously received antibiotics [16]. In that sense, preoperative prophylaxis was not considered as it has been shown to have no influence on cultures [17]. Low-virulence microorganisms such as Coagulase-negative staphylococci (CNS), *Corynebacterium* spp., *Bacillus* spp., or *Propionibacterium* spp. were considered pathogens if the same organism was isolated in at least two samples [15].

Sonication consists of the application of ultrasound to the implants removed and the submerged in saline to dislodge biofilm and therefore the bacteria. The ultrasound beam focuses on the surface of the implant and dislodges biofilm and dormant bacteria that can be further studied. It has proven to be a very reliable technique in implant related infections, especially low-grade and chronic infections [15,16,18,19].

2.2. Outcome measures

For all the cases, a minimum follow-up of 2 years without any local symptom and a pain-free joint was required to consider the infection cured.

To assess QoL, the Spanish version of the Short Form 36 (SF-36) was used. The values of the Mental Composite Score (MCS) and the Physical Composite Score (PCS) were analyzed and reported. To

Fig. 1. (a) Preoperative anteroposterior and lateral standing radiographs. (b) Postoperative standing radiographs at one year of follow-up.

evaluate function, the ankle version of the American Orthopedic Foot and Ankle Society (AOFAS) was used.

3. Case presentation

3.1. Case 1

A 74-year-old woman was diagnosed with idiopathic sensitive neuropathy presented with severe hindfoot deformity and a medial ulceration due to tibial malleolus pressure. Radiographs showed a Charcot arthropathy with a complete subsidence of the talus and tibia causing a rocker-bottom hindfoot (Fig. 1a). An external fixator was put in place to correct and maintain the deformity but ulceration of the medial malleolus worsened and an infection of the distal pins developed after 2 weeks. After refusing the amputation proposed in another hospital, she was transferred to our unit. Possible complications associated with the proposed surgery were discussed with the patient and she agreed with us to preserve the limb. Empiric intravenous antibiotic treatment (amoxicillin/clavulanic acid 2 g/8 h) was started and a thorough debridement was performed, the external fixator was removed and a total contact cast was put in place. Deep tissue samples were taken and cultures were positive for *S. aureus* (rifampicin and quinolones susceptible) and *Pseudomonas* aeruginosa (ciprofloxacin susceptible).

After 2 weeks, the definitive cultures did not show any additional growth and the medial ulceration and the rest of the soft tissues were doing well. At that point, another debridement along with a tibio-talo-calcaneal arthrodesis (TTC-A) were performed (T2 Ankle Athrodesis Nail®. Stryker, Schönkirchen. Germany). The deformity was corrected with bony resectioning and the talus void was filled with femoral head allograft previously soaked in the vancomycin solution (5 mg/ml), as previously reported (Fig. 1b) [20].

One week after surgery, the soft tissues had an excellent evolution and the wounds were dry. The soft tissues were completely healed by the 2nd week, including the medial ulceration. She was then discharged with oral antibiotics (rifampicin 600 mg/24 h plus ciprofloxacin 750 mg/12 h) that were continued for a 6-week period. Radiographic ankle fusion was achieved at 8 months follow-up.

The patient was allowed weight-bearing with a walker cast 2 weeks after TTC-A. At 6 weeks after the onset of infection, the AOFAS score improved from 49 points to 86 points. The MCS of the SF-36 improved from 45.61 points to 48.50 points and the PCS improved from 33.10 points to 41.51 points.

3.2. Case 2

A 52-year-old woman suffered a distal extrarticular tibial fracture associated with a syndesmotic fibular fracture. The fractures were partially reduced and the tibia was plated (one intraarticular screw, Fig. 2a). Two weeks later, she was transferred to our institution. Purulent drainage was observed through an unusual tibial approach. Empiric intravenous antibiotic treatment (amoxicillin/clavulanic acid 2 g/8 h) and meticulous debridement and hardware removal were performed. Tissue samples and sonication were positive for *S. aureus* (rifampicin susceptible).

Fig. 2. (a) Anteroposterior and lateral radiographs and CT detail showing the inicial plating and the intrarticular srew. (b) Postoperative radiographs at one year of follow-up.

Whole-leg radiographs and a CT scan were performed to determine the appropriate surgical treatment. The CORA angle and fibular malrotation were measured. At 2 weeks of debridement, a medial closing wedge lower tibial osteotomy and a Valderrabano fibular osteotomy were performed (LCP Synthes. West Chester, PA. USA) [21]. The same previous approach was used upon the advice of a plastic surgeon (Fig. 2b).

As soon as the wounds were dry and the soft tissues showed no signs of complication, antibiotic treatment was switched to oral rifampicin (600 mg/24 h) plus levofloxacin (750 mg/24 h) and the patient was discharged. She completed a 12-week period of antibiotic treatment, in accordance with the protocol followed in previous studies on osteolmyelitis [22,23].

Weight-bearing was delayed until the 6th week and then the leg was protected with a walker cast for 6 additional weeks. Radiographic healing of the osteotomy was observed at 6 months follow-up.

In this one case, function and QoL did not recover until the 12th week after the onset of infection. The AOFAS score improved from 45 points to 86 points, the MCS of the SF-36 improved from 49.50 points to 62.50 points and the PCS of the SF-36 improved from 37.0 points to 67.61 points.

3.3. Case 3

A 70-year-old male suffered a car accident that resulted in a tibial pilon open fracture (Gustilo III-B, Fig. 3a). He was immediately treated with debridement and an external fixator. A Vacuum Assisted Closure (VAC) was used to cover the skin defect. The following day, a consultation with a plastic surgeon was requested to perform definitive coverage. Unfortunately, it was not advised because the patient suffered from idiopathic thrombocytopenic purpura. Two treatments were offered at that point. They were continuing with VAC therapy and avoiding weight bearing or amputation. At 3 months after the accident, that patient was transferred to our unit. No pin infection was observed but a medial skin defect of 4×2 cm and exposed necrotic bone was seen beneath the VAC sponge. A TTC-A was proposed along with a prior necrotic bone resection with the aim of wound closure after shortening (Fig. 3b). The patient was informed of the high risk of multi-resistant bacterial infection and subsequent failure but he accepted the risks it entailed. Aggressive debridement and a necrotic bone resection was performed. Limb shortening and a TTC-A was carried out (T2 Ankle Athrodesis Nail®. Stryker, Schönkirchen. Germany). Skin closure was possible except for a small 5 mm diameter defect that was covered with an artificial skin matrix (Integra® Dermal Regeneration, New Jersey. USA). Antibiotic prophylaxis was modified in this case because of the antecedent open fracture, prolonged in-hospitalization and VAC therapy (daptomicin 800 mg/24 h + meropenem 2 g/8 h). Intraoperative cultures revealed the growth of MRSA in 4 out of 5 samples and *K. pneumoniae* producing ESBL in 2 out of 5 samples. Fortunately, MRSA was rifampicin susceptible and *K. pneumonie* was ciprofloxacin susceptible. Two weeks later, the evolution was favorable and no additional bacteria were reported. The patient was then discharged with progressive weight-bearing using a walker orthosis. Additionally, oral antibiotics with rifampicin (600 mg/24 h) plus ciprofloxacin (750 mg/12 h) for a total of 12 weeks were prescribed. Radiographic TTC fusion was observed at 10 months follow-up.

Fig. 3. (a) Clinical look and radiographs at arrival into the emergency room. (b) Postoperative radiographs at one year of follow-up and whole standing view after nail removal.

AOFAS rapidly improved from 35 points to 86 points in 6 weeks. Relative to QoL, the MCS of the SF-36 increased from 42.0 points to 50.0 points and the PCS improved from 39.50 to 59.86 points. The only complaint that the patient referred to was plantar pain due to nail protrusion that was resolved with nail removal one year after TTC-A.

3.4. Case 4

A 68-year-old woman suffered a bimalleolar fracture that was complicated by the loss of fixation and early osteoarthritis. In addition, the plate and screws protruded and purulent drainage was observed. Empiric intravenous antibiotic treatment (amoxicillin/clavulanic acid 2 g/8 h) was started and implant removal and debridement were performed. All 5 tissue cultures and implant sonication were negative (culture negative infection). After 2 weeks, a TTC-A was performed (T2 Ankle Athrodesis Nail®. Stryker, Schönkirchen. Germany) and the patient was discharged 5 days later with oral rifampicin (600 mg/24 h) and levofloxacin (750 mg/24 h) for a total of 6 weeks.

Weight-bearing was immediately allowed with a walker orthosis. Radiographic fusion was achieved at 6 months follow-up. QoL and function were better at 6 weeks. In this case, the AOFAS improved from 21 to 82 points. In the SF-36, the MCS improved from 30.31 to 48.50 points and the PCS increased from 28.86 points to 53.80 points.

4. Discussion

The main result of the present study is that early fixation and early discharge with oral antibiotics is possible in patients with foot and ankle infections. Two fundamentals were required to do so, the patient must have local soft tissues in an adequate state and the infection must be caused by microorganisms that are susceptible to antibiofilm antibiotics. The secondary result is that early fixation makes for an early recovery of function and QoL. However, due to the difficult management of these complications, it is essential for treatment to be carried out by a specialized multidisciplinary team. That team would include orthopedic surgeons, infectious diseases specialists, microbiologists and, in some cases, plastic surgeons.

Foot and ankle infections related to fixation devices, similar to other foreign body infections including PJI, characteristically facilitate bacteria attachment to the hardware and produce the biofilm that protects bacteria against antibiotics [22]. It is thought that once the foreign body is removed, the infection is cured. Moreover, the longer the wait for final internal fixation without local symptoms, the more possibilities exist to succeed in terms of infection cure [4,7]. This is partially true as bacteria can lie dormant beneath bone sequestrum [24]. Additionally, biofilm can also be present in these chronic infections without implants [22,24]. Therefore, waiting is not the answer. Delaying surgery is not only a waste of time but also can facilitate multi-resistant bacterial selection, especially when this delay is combined with VAC therapy as was seen in case 3 and as previously reported [25].

The most important point in dealing with bony infections is to perform a thorough and extensive debridement rather than waiting. That means removing necrotic or non-viable tissue (including bone), any foreign material and irrigating with a substantial amount of saline [10,26]. Antibiotic treatment must be added, always according to the deep tissue cultures. In those cases of infection produced by bacteria that are susceptible to antibiofilm antibiotics, the infection will be completely cured if combined with proper debridement [10]. Additionally, the fact of performing internal fixation after debridement should not worry the orthopedic surgeon as these bacteria will be killed off by the previously mentioned antibiotics (even if some biofilm remains after debridement) [23]. In the case of gram positive cocci (e.g. *S. aureus*), rifampicin has proven to be effective against the biofilm these bacteria produce [11]. It is important to combine rifampicin with another antibiotic in every instance to avoid resistance (e.g levofloxacin, trimethoprim/sufamethoxazole). Moreover, never start rifampicin until wounds are dry for the same reason [27]. The combination of rifampicin and levofloxacin was the treatment of choice in case 2 in the current series. For the treatment of gram negative bacilli infections (e.g. *P. aeruginosa*,*Escherichia coli*), the most effective antibiotic is ciprofloxacin [28]. It can be used alone but it is necessary to combine it with rifampicin in polymicrobial infections in the presence of gram positive cocci. This was done in cases 1 and 3 in the present study. Culture negative infections can be treated as staphylococcal infections as those are the most frequent bacteria isolated in foot and ankle infections (as in case 4) [3].

The most important factor is the multidisciplinary management. It is not possible to cure these infections with only antibiotic treatment or with surgery alone. A thorough debridement, maintaining a stable implant and using antibiofilm antibiotics are crucial to success.

As previously stated, waiting until final fixation is not the key to succeeding. In addition, waiting only produces disability in the patient that requires the use of an orthosis or wearing external fixators for a longer period. This delay brings about an significant degradation in the patient's QoL and function [8,9]. This fact has been observed in the present study as all 4 cases had scores under 50% of the general population's mean values. Moreover, the fast recovery of those parameters after fixation in a median period of 4 weeks is the aim.

Several limitations can be found in the present study. The first is in the design of the study as only four cases are reported. Second, there is the lack of a control group with different approaches. Finally, different types of infections (acute and chronic) are included.

From the results presented here, our conclusion is that early fixation after debridement combined with antibiofilm antibiotics should be performed in foot and ankle inflections to provide early recovery of QoL and function in patients.

Disclosure statement

There is no conflict of interest in the present work.

Acknowledgment

We are grateful to Mr. Eric L. Goode for his help with English correction and style.

References

[1] Kessler B, Sendi P, Graber P, Knupp M, Zwicky L, Hintermann B, et al. Risk factors for periprosthetic ankle joint infection: a case-control study. J Bone Joint Surg Am 2012;94:1871–6, doi:http://dx.doi.org/10.2106/JBJS.K.00593.
[2] Ferrao P, Myerson MS, Schuberth JM, McCourt MJ. Cement spacer as definitive management for postoperative ankle infection. Foot Ankle Int 2012;33:173–8.
[3] Donley BG, Philbin T, Tomford JW, Sferra JJ. Foot and ankle infections after surgery. Clin Orthop Relat Res 2001;391:162–70.
[4] Malizos KN, Gougoulias NE, Dailiana ZH, Varitimidis S, Bargiotas KA, Paridis D. Ankle and foot osteomyelitis: treatment protocol and clinical results. Injury 2010;41:285–93, doi:http://dx.doi.org/10.1016/j.injury.2009.09.010.
[5] Ovaska MT, Madanat R, Honkamaa M, Makinen TJ. Contemporary demographics and complications of patients treated for open ankle fractures. Injury 2015;46:1650–5, doi:http://dx.doi.org/10.1016/j.injury.2015.04.015.
[6] Pinzur MS, Sammarco VJ, Wukich DK. Charcot foot: a surgical algorithm. Instr Course Lect 2012;61:423–38.
[7] Anakwenze OA, Milby AH, Gans I, Stern JJ, Levin LS, Wapner KL. Foot and ankle infections: diagnosis and management. J Am Acad Orthop Surg 2012;20:684–93, doi:http://dx.doi.org/10.5435/JAAOS-20-11-684.

[8] C.-W.C Lin, Donkers NAJ, Refshauge KM, Beckenkamp PR, Khera K, Moseley AM. Rehabilitation for ankle fractures in adults. Cochrane Database Syst Rev 201211:CD005595, doi:http://dx.doi.org/10.1002/14651858.CD005595.pub3.
[9] Cutillas-Ybarra MB, Lizaur-Utrilla A, Lopez-Prats FA. Prognostic factors of health-related quality of life in patients after tibial plafond fracture. A pilot study. Injury 2015;46:2253–7, doi:http://dx.doi.org/10.1016/j.injury.2015.06.025.
[10] Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-joint infections. N Engl J Med 2004;351:1645–54, doi:http://dx.doi.org/10.1056/NEJMra040181.
[11] 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;279:1537–41.
[12] Perez-Prieto D, Trampuz A, Torres-Claramunt R, Eugenia Portillo M, Puig-Verdie L, Monllau JC. Infections after anterior cruciate ligament reconstruction: which antibiotic after arthroscopic debridement? J Knee Surg 2016;30(4):309–13, doi:http://dx.doi.org/10.1055/s-0036-1584559.
[13] Pinzur MS, Gil J, Belmares J. Treatment of osteomyelitis in charcot foot with single-stage resection of infection, correction of deformity, and maintenance with ring fixation. Foot Ankle Int 2012;33:1069–74, doi:http://dx.doi.org/10.3113/FAI.2012.1069.
[14] Gopal S, Giannoudis PV, Murray A, Matthews SJ, Smith RM. The functional outcome of severe, open tibial fractures managed with early fixation and flap coverage. J Bone Joint Surg Br Vol 2004;86(6):861–7.
[15] Portillo ME, Salvado M, Trampuz A, Siverio A, Alier A, Sorli L, et al. Improved diagnosis of orthopedic implant-associated infection by inoculation of sonication fluid into blood culture bottles. J Clin Microbiol 2015;53:1622–7, doi:http://dx.doi.org/10.1128/JCM.03683-14.
[16] Portillo ME, Salvado M, Alier A, Martinez S, Sorli L, Horcajada JP, et al. Advantages of sonication fluid culture for the diagnosis of prosthetic joint infection. J Infect 2014;69:35–41, doi:http://dx.doi.org/10.1016/j.jinf.2014.03.002.
[17] Perez-Prieto D, Portillo ME, Puig-Verdie L, Alier A, Gamba C, Guirro P, et al. Preoperative antibiotic prophylaxis in prosthetic joint infections: not a concern for intraoperative cultures. Diagn Microbiol Infect Dis 2016;86:442–5, doi:http://dx.doi.org/10.1016/j.diagmicrobio.2016.09.014.
[18] Renz N, Cabric S, Janz V, Trampuz A. Sonication in the diagnosis of periprosthetic infections: significance and practical implementation. Orthopade 2015;44:942–5, doi:http://dx.doi.org/10.1007/s00132-015-3192-y.
[19] Trampuz A, Piper KE, Jacobson MJ, Hanssen AD, Unni KK, Osmon DR, et al. Sonication of removed hip and knee prostheses for diagnosis of infection. N Engl J Med 2007;357:654–63, doi:http://dx.doi.org/10.1056/NEJMoa061588.
[20] Perez-Prieto D, Torres-Claramunt R, Gelber PE, Shehata TMA, Pelfort X, Monllau JC. Autograft soaking in vancomycin reduces the risk of infection after anterior cruciate ligament reconstruction. Knee Surg Sports Traumatol Arthrosc 2014;24(9):2724–8, doi:http://dx.doi.org/10.1007/s00167-014-3438-y.
[21] Barg A, Pagenstert GI, Horisberger M, Paul J, Gloyer M, Henninger HB, et al. Supramalleolar osteotomies for degenerative joint disease of the ankle joint: indication, technique and results. Int Orthop 2013;37:1683–95, doi:http://dx.doi.org/10.1007/s00264-013-2030-2.
[22] Renz N, Muller M, Perka C, Trampuz A. Implant-associated infections — diagnostics. Chirurg 2016;87(10):813–21, doi:http://dx.doi.org/10.1007/s00104-016-0234-x.
[23] Zimmerli W. Clinical presentation and treatment of orthopaedic implant-associated infection. J Intern Med 2014;276:111–9, doi:http://dx.doi.org/10.1111/joim.12233.
[24] Beck-Broichsitter BE, Smeets R, Heiland M. Current concepts in pathogenesis of acute and chronic osteomyelitis. Curr Opin Infect Dis 2015;28:240–5, doi:http://dx.doi.org/10.1097/QCO.0000000000000155.
[25] Clauss M, Baalbaki R, Nussbaumer F, Trampuz A, Borens O. Determination of bacterial quantity by sonication in vacuum-assisted closure (VAC) foams used for treatment of chronic wounds. J Bone Joint Surg Br Vol 2011;93–B:322.
[26] Haasper C, Buttaro M, Hozack W, Aboltins CA, Borens O, Callaghan JJ, et al. Irrigation and debridement. J Arthroplast 2014;29:100–3, doi:http://dx.doi.org/10.1016/j.arth.2013.09.043.
[27] Achermann Y, Eigenmann K, Ledergerber B, Derksen L, Rafeiner P, Clauss M, et al. Factors associated with rifampin resistance in staphylococcal periprosthetic joint infections (PJI): a matched case-control study. Infection 2013;41:431–7, doi:http://dx.doi.org/10.1007/s15010-012-0325-7.
[28] Widmer AF, Wiestner A, Frei R, Zimmerli W. Killing of nongrowing and adherent *Escherichia coli* determines drug efficacy in device-related infections. Antimicrob Agents Chemother 1991;35:741–6.