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Short Research Communication

Case Report – Infection of Total Knee Arthroplasty Treated with One-Stage Surgery and Linezolid

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Abstract

Staphylococcus spp meticillin resistant infection can be treated with Linezolid. This is a case report of an orthopaedic implant infection in a 60 year-old male treated orally with Linezolid and Rifampicin for three months after one-stage arthroplasty. This is possible provided that platelet count is closely monitored throughout the course of treatment.

Key words: Arthroplasty, Infection, Linezolid.

Introduction

The treatment of infection of TKA: total knee arthroplasty requires the use of antimicrobial for a prolonged period, normally between 3 to 6 months.[1,2,3] *Staphylococcus* spp is the principal agent isolated in prosthesis infection, *S. aureus* being the most common in early stage and *Staphylococcus* coagulase negative in the late stage.[1,4]

Linezolid is an oxazolidinone, the latest class of antimicrobial developed and is recommended for treatment of infection of *Staphylococcus* spp. Administration of this drug for a period longer than two weeks increases the risk of developing thrombocytopenia, however it is a reversible adverse reaction which is possible to control by monitoring the platelet count. [5,6] This antibiotic has also been indicated for the treatment of osteoarticular infection, however its use has been avoided due to the lack of evidence regarding safety and efficacy, and susceptibility to low platelet count when administered for more than 28 days. [7,8,9,10]

A case of chronic infection of orthopedic implant that had success with Linezolid associated with Rifampicin treatment after one-stage arthroplasty surgery and three months of antibiotic therapy is described below.

Case Report

Male, 61 year old soccer coach, from São Paulo, Brazil weighing 80 Kg, admitted with a history of TKA in the right knee carried out in 2009 developed infection and underwent subsequent removal of implant, use of spacer and treatment with various antibiotics such as ciprofloxacin and clindamicin for seven months followed by the reinsertion of the prosthesis in 2010. In 2012 the patient suffered a periprosthetic fracture of the right tibia and was admitted for surgical intervention with a non-conventional prosthesis for reconstruction of the inferior limb (*Zimmer NexGen* LCCK) carried out in one stage. Six bone fragments and periprosthetic tissue were collected together with the sonication of the implant with the introduction of antibiotic therapy.

Treatment was initiated with 10mg/kg (800mg) of Teicoplanin per day in conjunction with Cefepime (6g/day). On the fifth day after surgery during

antibiotic treatment the patient presented signs of infection and devitalization of tissue surrounding the surgical wound (Figure 1) and in all cultures, growth of SCoN: *Staphylococcus* coagulase negative, was seen.

In the peri prosthetic tissue and the fragment of bone, SCoN was susceptible only to Glycopeptides, Sulfametoxazol-Trimetoprim (SMT), Rifampicin and Linezolid. Patient had CRP: C-Reactive Protein = 29,31mg/dL (reference ≤ 1); il-6: Interleukin 6 =10,2 pg/mL (reference ≤ 5,90), ESR: Erythrocyte Sedimentation Rate =70mm/h (reference ≤ 15), Hb: Hemoglobin =10,5g/dL, Ht: Hematocrit = 33,3%, 9.230 leukocytes, platelets=261K, creatinine=1,16mg/dL and in x-ray, the implant was stable. (Figure 2)

The condition of the patient's wound deteriorated with the use of Teicoplanin and showed an adverse reaction to SMT. A dose of 1.2g/day of Linezolid was administered in conjunction with 600mg/day of Rifampicin for three months. Due to the proximity of the skin lesion to the bone and implant, and the risk of implant exposure with the surgical debridement of the soft tissue, a dressing of 20% papain was applied with clinical follow-up of the healing process.

Throughout the treatment the patient was kept under clinical observation with weekly blood work-up. During the administration of Linezolid patient presented no sign of bleeding and the platelet count dropped to a minimum value of 145K and rose to 387K after suspension of medication. At this time exams showed CRP = 1.7mg/dL; il-6 = 3.7pg/mL ESR= 27mm/h; Hb=12.0g/dL, Ht=36.9% and 8.000 leukocytes.

Patient showed satisfactory clinical response to treatment (Figures 3) without secretion and with complete healing of the wound. Until the present, four years after the last TKA, patient continues to practice sport and the implant remains stable.

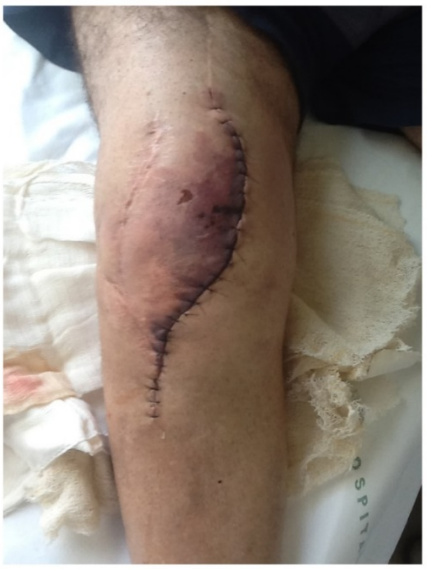

Figure 1. Wound on 5th day post-op of TKA

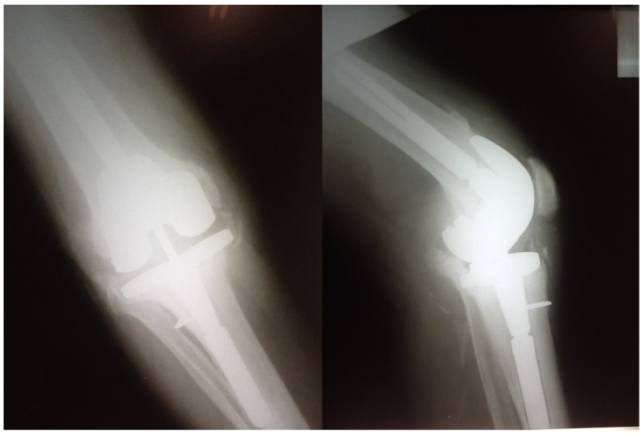

Figure 2. X-Ray of one-stage TKA

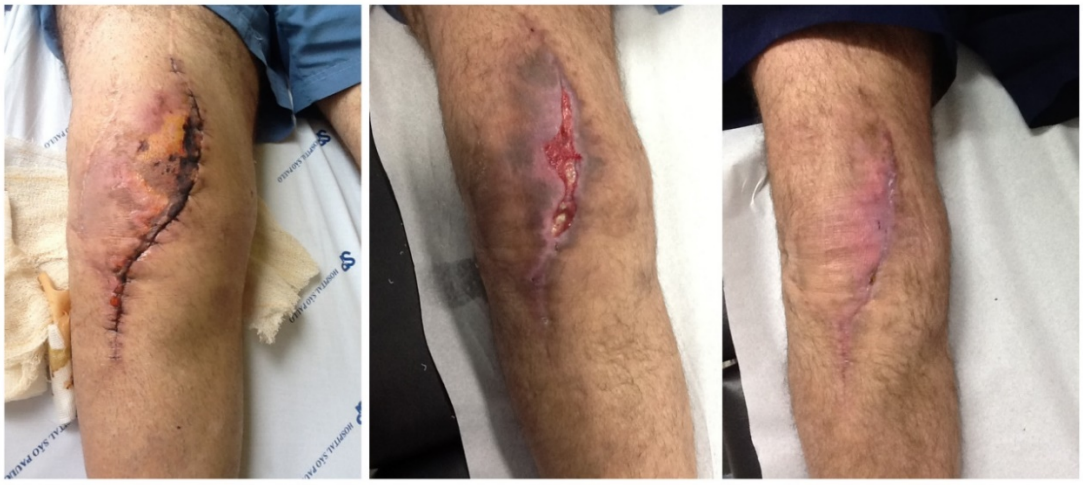

Figure 3. Surgical wound on the 13th, 44th and 79th days post-op respectively during treatment with topical papaina together with oral administration of Linezoilid and Rifampicin.

Discussion

Prosthesis infection is a serious complication and a great concern in total arthroplasty and can have grave lasting effects which impede mobility and the practice of sports. Treatment requires the administration of an effective antibiotic for a long period. [1,2,3]

It is difficult to confirm if prosthesis infection is an incisional or deep surgical infection associated with osteomyelitis. Regarding incisional infection, a skin and soft tissue infection treatment could be efficacious with the use of Linezolid. In this case there were various indicators for the confirmation of bone infection. First the patient had been treated for a previous arthroplasty infection, suffered a peri-prosthetic fracture, had an increase in CRP and iL-6 and the isolation of bacteria in the bone and sonication of implant. [11,12, 13]

Despite the use of topical papaína, with the aim of thwarting the formation of biofilm on the wound, it is necessary to use an effective systemic antibiotic for the treatment of the wound infection.[14,15]

The treatment of prosthesis infection with removal of implant can be carried out in one or two-stage surgery.[1,3,11] Due to the presence of fracture, surgery was required to stabilize the limb. [16] The diagnosis of prosthesis infection was confirmed by cultures and increase in iL-6.

The aspect of the wound on the 5th day after surgery was initially suggestive of poor tissue perfusion (Figure 1) and could have been considered as a non-infectious complication of surgery. However, before undergoing surgery the patient presented two scars on the knee, one medial and the other lateral, which were the result of previous surgeries. An increase in bacteria and increase in devitilized tissue indicated a failure of initial antibiotic treatment of Teicoplanin and Cefepime. Subsequent to the alteration of antibiotics from Teicoplanin and Cefepime to Linezolid and Rifampicin, the aspect of the wound that initially presented signs of ecchymosis and necrosis with the possibility of loss of the prosthesis, due to the distance between the skin and the bone being minimal, began to show visible improvement and regression of the skin lesion. After three months of treatment, even with CRP above the normal threshold, the patient did not require further antibiotic treatment.

Coagulase-Negative Staphylococci are part of the normal flora of human skin and do not normally produce aggressive virulence factors. However this group of bacteria is capable of producing a set of factors which aid the colonization and infection process. The formation of biofilm is the principal factor associated with the pathogeny of this group and can be found in orthopedic implant infections.[1,4]

In the development of biofilm, CoNS are capable of activating or inhibiting certain genes responsible for "quórum sensing", in other words they can control the expression of virulence and adaptive mechanism which protect bacteria from antibiotics and immune system,[17] which could be the reason for the failure of Teicoplanin and Cefepime treatment.

In the case reported, Linezolid was chosen for its facility of oral administration allowing the patient to maintain his normal activities, without risk of complications related to CVC: central venous catheter. Linezolid has an affirmative effect in the treatment of infection caused by Staphylococcus spp, which are sensitive and resistant to methicillin, as it can act directly on biofilm and cells infected by bacteria.[5,6,18] Linezolid has a 100% oral bioavailability and reaches high concentrations in musculoskeletal tissues (skin, synovial fluid and bone) and has better results with the removal of the implant [20-21]

Despite the limited use of Rifampicin due to the facility of bacteria to develop resistance during its individual use, it has been recommended in the treatment of prosthetic infections caused by Staphylococcus spp, in conjunction with other antibiotics. The addition of Rifampicin to Linezolid would be reasonable, particularly when the implant is not removed, due to the potent activity of rifampicin against biofilm bacteria. [2,19,20]

Patients with osteoarticular implant infection treated with Linezolid and Rifampicin in general have fewer adverse reactions and a higher rate of relapse, although the difference is not statistically significant.[20]

The use of this combination must be carried out carefully since the serum concentration of linezolid may be reduced when associated to rifampicin. The serum concentration of Linezolid can be monitored or close attention paid to the possible failure to respond to treatment with the need for suspension of rifampicin.[22]

In this case report the patient was successfully treated for three months with combination of Linezolid and Rifampicin with significant regression of the infection. Despite the fall in the platelet count, it was not significant in thrombocytopenia and with the suspension of Linezolid, the platelet count increased.

Conclusion

In spite of the risk of developing thrombocytopenia with the prolonged use of Linezolid, this drug can be used for three months in the treatment of prosthesis infection providing that it is closely monitored with periodic examinations and blood work-up, in order to avoid complications which may arise from an adverse reaction to the drug.

From the favorable outcome of the case presented it is possible to affirm that Linezolid can be used safely in the treatment of *Staphylococcus* spp infection in total knee arthroplasty.

Competing Interests

The authors have declared that no competing interest exists.

References

1. Zimmerli W, Trampuz A, Ochsner PE. Prosthetic Joint Infections. N Engl J Med. 2004; 351:1645-54.
2. Zimmerli W. Prosthetic-joint-associated infections. Best Pract Res Clin Rheumatol. 2006; 20(6):1045-1063.
3. Osmon DR, Berbari EF, Berendt AR, et al. Diagnosis and Management of Prosthetic Joint Infection: Clinical Practice Guidelines by the Infections Diseases Society of America. Clin Infect Dis. 2013;56(1):1-25.
4. Puig-Verdié L, Alentorn-Geli E, González-Cuevas A, et al. Implant sonication increases the diagnostic accuracy of infection in patients with delayed, but not early, orthopaedic implant failure. Bone Joint J. 2013;95B:244-9.
5. Clemett D, Markham A. Linezolid. Drugs. 2000;59(4):815-827.
6. Batts DH. Linezolid- A new option for treating gram-positive infections. Oncology. 2000;14(supp. 6):23-29.
7. Sia IG. Osteomyelitis. Best Pract Res Clin Rheumatol. 2006; 20(6):1065-1081.
8. Landersdorfer CB, Bulitta JB, Kinzig M, et al. Penetration of Antibacterials into Bone. Clin Pharmacokinet. 2009;48(2):89-124.
9. Bassetti M, Biagio A D, Cenderello G, et al. Linezolid Treatment of Prosthetic Hip Infections due to Methicillin-resistant Staphylococcus aureus (MRSA). Journal of Infection. 2001;43(2):148–149.
10. Jover-Sáenz A, Gaite FB, Ribelles AG, et al. Linezolid treatment of total prosthetic knee infection due to methicillin-resistant Staphylococcus epidermidis. Journal of Infection. 2003; 47(1):87–88.
11. Trampuz A, Widmer AF. Infections associated with orthopedic implants. Curr Opin Infect Dis. 2006, 19:349–356.
12. Trampuz A, Piper KE, Jacobson MJ, et al. Sonication of Removed Hip and Knee Prostheses for Diagnosis of Infection. N Engl J Med. 2007; 357:654-63.
13. Wasko M, Kowalczewski. Superficial site infections influence C-Reactive protein dynamics and not interleukin-6 dynamics in early postoperative period after total hip and knee replacement. The 31st Annual Meeting of the European Bone and Joint Infection Society – EBJIS 2012, oral presentation 64, pg. 54.
14. Stevens Dl, Bisno AL, Chambers HF, et al. Practice Guidelines for the Diagnosis and Management of Skin and Soft-Tissue Infections. Clin Infect Dis. 2005; 41:1373–406.
15. Rajan S. Skin and Soft-tissue infections: Classifying and Treating a Spectrum. Clev Clin J Med. 2012; 79(1):57-66.
16. Kim YH, Kim JS. Revision total knee arthroplasty with use of a constrained condylar knee prosthesis. J Bone Joint Surg Am. 2009; 91(6):1440-1447.
17. Vuong C, Kocianova S, Yao Y, et al. Increased colonization of indwelling medical devices by quorum-sensing mutants of Staphylococcus epidermidis in vivo. J Infect Dis. 2004;190(8):1498-505.
18. Liu CC, Bayer A, Cosgrove SE, et al. Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant Staphylococcus Aureus Infections in Adults and Children. Clin Infect Dis. 2011; 52(3):e18–e55.
19. Coiffier G, Albert JD, Arvieux C, et al. Optimizing combination rifampicin therapy for staphylococcal osteoarticular infections. Joint Bone Spine. 2013; 80:11-17.
20. Morata L, Senneville E, Bernard L et al. A retrospective review of the clinical experience of linezolid with or without rifampicin in prosthetic joint infections treated with debridement and implant retention. Infect Dis Ther. 2014; 3(2):235-43.
21. Morata L, Tornero E, Martinez-Pastor JC et al. Clinical.experience with linezolid for the treatment of orthopaedic implant infections. J Antimicrob Chemother. 2014; 69(1):i47-i52.
22. Hoyo I, Martinez-Pastor J, Garcia-Ramiro S et al. Decreased sérum linezolid concentrations in two patients receiving linezolid and rirampicin due to boné infections. Scand J Infect Dis. 2012;44(7):548-50.