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Case report

Unusual *Listeria monocytogenes* hematogenous infection in total knee replacement treated with one-stage revision surgery

Fernando Diaz-Dilernia, MD *, Julian Costantini, MD, Tomas I. Nicolino, MD, Marisa del Lujan Sanchez, MD, Lisandro Carbo, MD

Institute of Orthopaedics "Carlos E. Ottolenghi", Italian Hospital of Buenos Aires, Buenos Aires, Argentina

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ABSTRACT

Septic arthritis due to *Listeria monocytogenes* (LM) is extremely rare and most infections due to this organism are seen in immunocompromised patients. We describe a patient without immunological compromise, with a late total knee arthroplasty infection caused by LM treated with one-stage revision surgery. She had an elevated erythrocyte sedimentation rate (79 mm/h) and C-reactive protein (13 mg/dL). Aspiration of the knee joint yielded purulent fluid; cultures showed LM. The patient was given 6 weeks of intravenous ampicillin, followed by trimethoprim/sulfamethoxazole, and finally amoxicillin orally for 7 months. Two years after revision surgery, radiographs showed no evidence of implant loosening. This is a single case and although one-stage approach seemed to have worked, it should not be recommended on the basis of a single report.

Introduction

Listeria monocytogenes (LM) is a small gram positive and aerobic facultative bacillus [1,2]. It can grow in multiple human cells, including epithelial cells and macrophages. Infections due to LM are uncommon and are a consequence of direct inoculation or hematogenous dissemination [1,2]. This pathogen was initially identified as a cause of perinatal infections in humans [3]. It is a rare cause of disease in the general population, although it has been widely identified as an important cause of bacteremia and meningoencephalitis in some high-risk populations, such as newborns, pregnant females, elderly and immunosuppressed patients. Other specific risk factors that must be taken into account are malignant disease, diabetes mellitus, chronic kidney disease, and liver disease [4-7]. It has also been isolated in several cases of endocarditis, osteomyelitis, endophthalmitis, conjunctivitis, pneumonitis, urethritis, cholecystitis, pericarditis, peritonitis, abscesses, and mononucleosis-like syndrome [8-10]. Most LM infections are asymptomatic in immunocompetent people or rarely cause a flu-like syndrome or a gastrointestinal disease [11,12]. Septic arthritis due to LM is extremely rare and most reported cases have occurred in immunocompromised patients [13,14]. Some cases have been described in patients with prosthetic valves, stent grafts, and prosthetic joints [15,16].

LM infections have been more frequent recently because of the increase in prosthetic joint replacement in patients receiving immunosuppressive therapy, such as for rheumatoid arthritis [7,15,17,18]. In this paper, we describe a previously healthy patient, without immunological compromise, with a late total knee arthroplasty (TKA) hematogenous infection caused by LM treated with one-stage revision surgery.

Case history

The patient's informed consent was taken for the purpose of publication of the case along with institutional review board clearance.

A 77-year-old female patient was admitted to our emergency department after 11 months of left knee pain. The patient had a left TKA performed at another institution 5 year prior to her visit with good results until symptoms started. The patient presented afebrile but had left knee pain, effusion, and restricted motion; the knee incision site was tender and erythematous (Fig. 1a). Standard radiographs of the left knee showed no femoral or tibial component loosening (Fig. 1b and c). Laboratory examination showed an

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* Corresponding author. 4247 Potosí Street, C1199ACK Buenos Aires, Argentina. Tel.: +54 9 11 6609 3453.

E-mail addresses: ferdiaz18@hotmail.com, fernando.diaz@hospitalitaliano.org.ar

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elevated erythrocyte sedimentation rate (ESR 79 mm/h) (normal value [NV]: 0-30 mm/h) and C-reactive protein (CRP 13 mg/dL) (NV: 0-1 mg/dL); the white blood cell count (WBC) was 10,158 cells/mm^3 with 71.1% polymorphonuclear neutrophils (PMNs) (NV WBC: 4500-10,000 cells/mm^3, NV PMN: 55%-70%). Blood cultures were positive for gram positive bacillus. Aspiration of the left knee joint showed a red cell count of 600 cells/mm^3, white cell count of 13,000 cells/mm^3, with 98% PMNs and 2% mononuclear cells; cultures showed LM.

A one-stage revision of the arthroplasty was performed. Femoral and tibial components were removed and a thorough debridement of all infected and devitalized tissue was performed (Fig. 2). After repeat prep and drape, after changing instruments table, a gentamicin-loaded rotating hinge prosthesis was implanted (Fig. 3). Finally, the incision was closed carefully with one deep suction drain. As expected, cultures from the debrided periprosthetic tissue and fluid from the left knee joint confirmed an LM infection. Accordingly with the antibiogram, the patient was given intravenous antibiotics (ATBs) for 6 weeks with clinical improvement. She received ampicillin (2 g/4 hours) for 1 week during in-hospital stay and completed the 6-week protocol with trimethoprim-sulfamethoxazole (160-800 mg/12 hours), and finally amoxicillin orally for 7 months. At 5 months, the patient was afebrile; the ESR was 45 mm/h, and the CRP was <1 mg/dL. The patient was kept by the Infectious Disease service on oral amoxicillin for another 2 months. Postoperative recovery evolved with an innocent patellar tendinitis treated with conservative measures. Two years after one-stage revision arthroplasty, the patient was symptom free; the ESR, CRP, and the WBC count were normal. Anterior-posterior and lateral view radiographs showed no evidence of implant loosening; nevertheless, a large periosteal reaction can be easily seen in both views (Fig. 4).

Discussion

Gram-positive cocci are causative in the majority of hip and knee periprosthetic joint infections (PJIs). *Staphylococcus aureus* (SA) and coagulase-negative staphylococci contribute to between 50% and 60% of PJIs, while streptococci and enterococci together account for almost 10% of cases [19-22]. Gram-negative bacteria and other unusual pathogens are becoming increasingly recognized in immunocompromised hosts. Several species of Listeria exist in nature [23]. The most common is LM, a gram-positive bacillus found commonly in soil, water, vegetation, and sewage, and is part of the normal fecal flora of many animals. In the majority of cases, infections occur by food origin inoculation. The literature suggests the small bowel as a reservoir and the main dissemination way of the infection [24]. Infectious arthritis caused by LM is rare. Most LM infections are asymptomatic in immunocompetent people or rarely cause a flu-like syndrome or a gastrointestinal disease [11,12]. There have been a few reported cases of septic arthritis caused by LM and the majority of patients were immunocompromised or had an underlying disease [6,15,17,18,25]. Concomitant underlying diseases and/or their therapeutic management can lead to alterations of the immune system which makes individuals more susceptible to infection [26]. There have been cases of infection caused by LM in patients with impaired cell-mediated immunity secondary to transplantation, lymphoma, or acquired immunodeficiency syndrome. Some reports state that increased susceptibility to LM occur in patients given methotrexate [27,28]. Methotrexate effects on neutrophil chemotaxis and lymphokines are possible mechanisms for altered immunity and increased susceptibility [28]. In the present case, we described a late PJI due to LM in a woman who had a TKA without any immunological abnormality.

The varied clinical presentation due to LM has been widely described. Listeriosis can clearly present as an isolated infection. Nieman and Lorber reported the first case of arthritis by LM in 1980 [29]. It can be indolent and patients may not be febrile, although they may have local reactions in the affected joint. Meningitis and bacteremia are the most common clinical syndromes described in the literature. Endocarditis, prosthetic valve endocarditis, and endophthalmitis are frequent too, but septic arthritis and PJIs are extremely rare [4-6,15-17,30-39]. PJIs are rare, but can lead to severe complications, including permanent joint removal. It is usually described as a late complication, manifesting itself months or years after the initial replacement [6,17]. That is why LM should be considered in all PJIs when the initial isolate is a gram positive bacillus. Of course, the surgeon must be aware of other gram-positive bacilli due to their clinical implications such as Bacillus species (spp), Corynebacterium spp, Clostridium spp, Propionibacterium spp, and Lactobacillus spp. When talking about PJIs due to LM, the hip is the most often affected, followed by the knee [4,5,7,15,17,30,32,34,36,38,39]. An important characteristic with this kind of organism is the long period of time between implantation of the prosthesis and the beginning of symptoms. The late manifestation suggests a subclinical bacteremia and hematogenous dissemination of the infection without association with the surgical procedure [4,5,15-17,30,32,34,36,38,39]. As in our case, the main symptoms are severe joint pain and fever. We believe that the infection was not secondary to the surgery, assuming that a low-

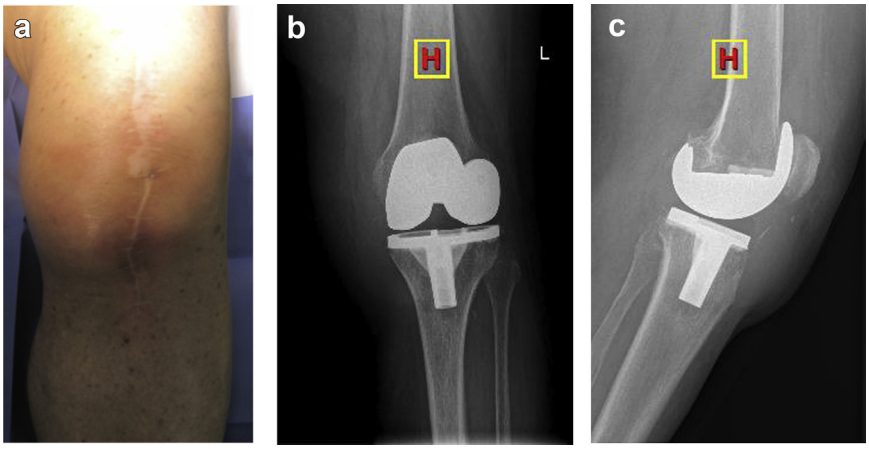

Figure 1. Clinical photograph (a) shows the knee incision site with effusion, tenderness, and erythematosus. Anteroposterior (b) and lateral (c) radiographs of the left knee showing no femoral or tibial component loosening.

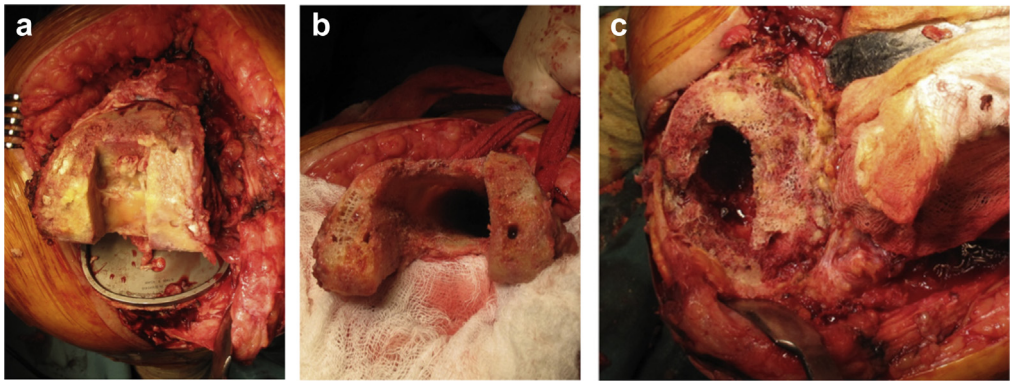

Figure 2. Intraoperative images. Femoral (a, b) and tibial (c) exposure after component removal and aggressive debridement.

grade LM infection occurred without relation with the initial replacement. With the evidence of the long interval between surgery and the onset of the symptoms, hematogenous inoculation is the most likely pathogenesis.

Clinical diagnosis is challenging, and radiological imaging may be useful as symptoms may be indolent. Culture and Gram's stain of the sample is critical for diagnosis and early treatment. Recognition in multiple samples increases the possibility of diagnosis [16,30]. Simultaneous infection with SA has been described, and LM could be underestimated as a consequence of the rapidly growing Staphylococcus [40]. Listeria has not been recognized as a contaminant and routine cultures may be negative. Molecular methods for diagnosis are useful when a rare microorganism is present or the results are obtained during ATB therapy [16]. This is really relevant because standard ATB treatment for SA may be inadequate for LM [41]. Different treatments have been described in the literature. Intravenous ATB treatment combined with surgical intervention typically results in complete symptom resolution. The most frequent is the combination of two-stage revision surgery and ATB therapy [6,17,32-34,39,42]. The second alternative in frequency is the administration of intravenous ATB; ampicillin and gentamicin followed by oral administration of trimethoprim/sulfamethoxazole or ampicillin [33,38]. In immunocompromised hosts, prolonged ATB administration is necessary [7,33,38,43]. Generally, the infection seems to be more indolent with high recurrence rate. That is why a 6-week duration of intravenous therapy followed by 3 months of oral administration is indicated [4,5,15,17,30,32-34,36,38,39]. The best ATB selection for PJI remains uncertain; ampicillin and gentamicin are usually the gold standard [4-6,15,30,32-34,36,39,43]. Penicillin or trimethoprim/sulfamethoxazole has also been used with ampicillin, although both agents are bacteriostatic [23]. On the contrary, gentamicin is bactericidal [23]. There is proven synergism between ampicillin or penicillin and gentamicin so co-administration of gentamicin is recommended [23,44-46]. In this patient, we performed a one-stage revision surgery of the left TKA combined with 6 weeks of intravenous ampicillin (2 g/4 hours), followed by trimethoprim/sulfamethoxazole (2 ampoule/12 hours), and finally amoxicillin orally for 7 months.

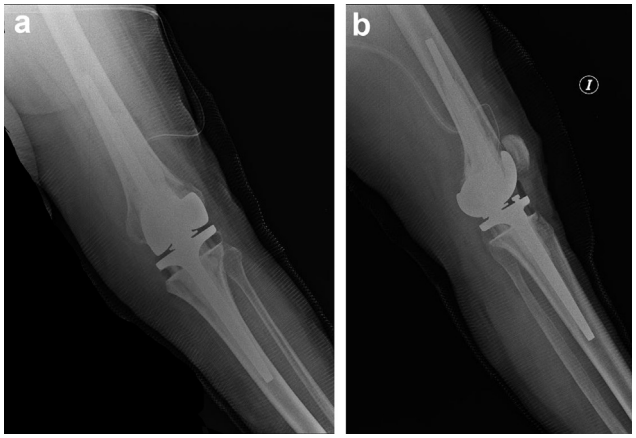

Figure 3. Immediate postoperative anteroposterior (a) and lateral (b) radiographs show one-stage revision surgery with a gentamicin-loaded rotating hinge prosthesis implantation.

PJI rates after primary TKA ranges from 0.4% to 2% [47]. Principal methods used for the treatment of chronic PJI include one-stage revision surgery [48,49] and two-stage resection arthroplasty and reimplantation [50-52]. Two-stage revision surgery includes an interval use of ATB-loaded cement spacers, intravenous ATBs, and the use of ATB-loaded cement for prosthesis fixation at reimplantation [53]. This approach has become the gold standard treatment for many authors, with infection-free survival rates of 80%-100% [50-52]. Nevertheless, it requires at least 2 procedures, more time with limited mobility and more possibility for perioperative complications and morbidity [54,55]. Most authors state debridement, antibiotics, irrigation, and implant retention (DAIR) is an attractive, low-cost, low-morbidity option for acute PJI, within 4 weeks of index surgery, which involves a sensitive microorganism, or occurs as an acute metastatic infection where DAIR is performed within a few days of symptoms [49,56,57]. Current literature has reported a divided opinion on the difference in success rates and outcome of two-stage revision TKA for PJI in patients with a prior DAIR. Sherrell et al [58] reported a high failure rate of 34% in 83 TKAs undergoing two-stage revision after a failed DAIR as the initial treatment for PJI. Perhaps indicating DAIR as the initial treatment may compromise the success of two-stage reimplantation. However, Nodzo et al [59] reported similar success rates among patients undergoing a previous DAIR (82.2%) and those treated with direct two-stage revision surgery (82.5%). Rajgopal et al [60] reported a reinfection rate of 23.86% (21/88) in TKA that had undergone prior failed DAIR and 15.62% (15/96) in patients undergoing direct two-stage revision. According to this study, patients undergoing prior failed DAIR had almost 2 times higher risk of failure as compared to direct two-stage surgery. Gardner et al [61] reported a failure rate of 42% in 19 patients, who underwent a repeat two-stage debridement after a failed DAIR.

There is also strong evidence published by the ENDO-Klinik where they stated that better results could be achieved by choosing the one-stage approach only for highly selected patients with intact soft tissues, and susceptible microorganisms as in our

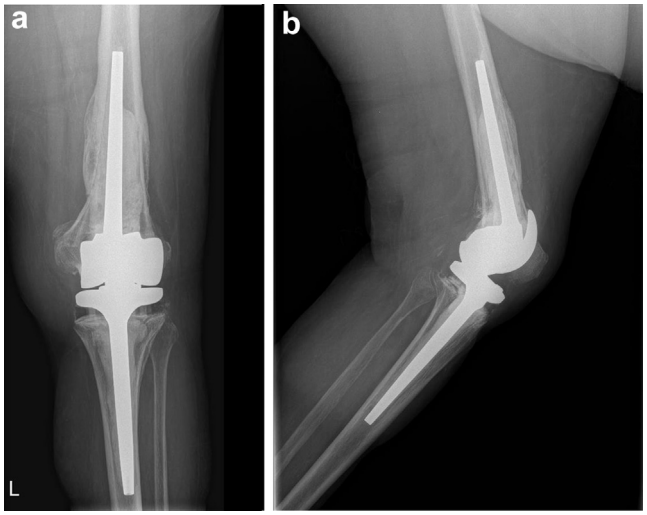

Figure 4. Anteroposterior (a) and lateral (b) radiographic views of the same patient's knee at 2 years of follow-up evidencing no signs of stem loosening, the patient being completely asymptomatic.

case [62]. Some studies have shown possible advantages of one-stage revision surgery for selected patients, including the need for only one procedure, shorter hospitalization time, reduced ATB therapy, reduced overall costs, and improved patient satisfaction. In addition, an increasing number of publications have reported high success rates with this only intervention. According to the ENDO-Klinik experience, one-stage exchange procedures should follow the same standardized surgical protocol. Aggressive debridement is indicated to remove all infected soft tissues including a complete synovectomy. The technique in 2002 included the excision of the collateral ligaments and the posterior cruciate ligament (PCL) to completely expose the posterior capsule, which was excised as well. Nowadays, the collaterals are detached and debrided rather than excised. Finally, fixed implants are explanted with osteotomes or small power saw blades. Due to the debridement of the collateral ligaments and PCL, patients may have symptomatic instability and a fully constrained implant like a hinged prosthesis is needed [62]. This device has been reserved principally for revision surgery. It is an option for a small number of patients with bone metaphyseal deficiency and/or gross ligamentous instability [63,64].

Several factors can cause instability following TKA. The aggressive ligament release can be one of them. Our patient required an aggressive debridement to remove all infected soft tissues, including a complete synovectomy, the excision of the collateral ligaments, the PCL, and the posterior capsule. As a consequence, a gross ligamentous instability was assessed. Revision surgery in this scenario represents a surgical challenge. It must correct mechanical axis of the limb; balance flexion and extension gaps; assess ligament integrity, and have availability of constrained implants as necessary [65]. Perhaps, the fail-safe option remains knee fusion. Standard condylar knee arthroplasty has been found to have an unacceptable early failure due to imbalance, instability, and component subsidence.

The main indications for a rotating-hinge revision arthroplasty are medial or lateral collateral insufficiency, massive bone loss including the femoral condyles and the insertions of the collateral ligaments, and severe flexion gap imbalance. It seems that a rotating-hinge prosthesis is a good option for ligamentous deficiencies in revision surgery in elderly patients [66,67]. The reported rate of aseptic loosening of a rotating-hinge prosthesis is quite variable. Zahar et al reported 7 (11.9%) revision surgeries due to aseptic complications after one-stage exchange with a rotating-hinge prosthesis after 10-year follow up. There were 6 cases of aseptic loosening and 1 patient suffered a periprosthetic fracture. The average time to revision surgery was 5.1 years. A significant improvement of Hospital for Special Surgery Knee score was found, from a mean preoperative value of 35 to a mean postoperative score of 69.6 at latest follow up [62]. Gehrke et al [68] found a survivorship rate of 90% in 141 patients at 13 years in primary TKA. Excellent results for the Hospital for Special Surgery Knee score were also reported in 64% of the patients (100 to 70 points). Bistolfi et al [69] reported a survival rate of 79% in 32 patients with a hinged prosthesis used for revision TKA at a mean of 12 years of follow up. The main reason for revision was aseptic loosening in 4 cases. Unfortunately, current literature regarding one-stage revision surgery and loosening of rotating-hinge prostheses in this special situation remains scarce. However, a higher aseptic loosening rate is expected in hinged prostheses due to the increased constraint transfer to the bone-implant interface; rotating hinge implants may moderate this effect [70].

As far as we are concerned, this is the first case in the literature of one-stage revision surgery of a TKA due to LM in an immunocompetent patient. We believe that this type of infections with unusual organism treated with one-stage revision surgery can be more effective and can decrease patient's morbidity when compared to other surgical procedures, such as a two-stage revision surgery or a DAIR.

Key factors for the successful treatment of one-stage revision surgery for chronic PJI in TKA are the preoperative diagnosis, known susceptibility of the microorganism, aggressive debridement after a standardized surgical protocol, and the combination of local and systemic ATB therapy. This report suggests that there is indeed a role for one-stage approach. However, the tissue and the immune status of the patient must be considered, which in this particular case was not compromised. This is a single case and although one-stage approach seemed to have worked, it should not be recommended on the basis of a single report. Further studies with a multicenter prospective and comparative approach are needed to validate the results and to compare different procedures.

Summary

Gram-negative bacteria and other unusual pathogens are becoming increasingly recognized in immunocompromised hosts. Septic arthritis due to LM is extremely rare and most reported cases have occurred in immunocompromised patients. PJIs due to LM are rare, but can lead to severe complications, including permanent joint removal. It is usually described as a late complication, manifesting itself months or years after the initial replacement. Different treatments have been described in the literature. The most frequent is the combination of two-stage revision surgery and ATB therapy.

Acknowledgments

The study was performed at the Italian Hospital of Buenos Aires, Argentina.

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