Lyme periprosthetic joint infection in total knee arthroplasty

Muriel Adrados, MD a,*, Daniel Howard Wiznia, MD a, Marjorie Golden, MD b, Richard Pelker, MD, PhD a

a Department of Orthopaedics and Rehabilitation, Yale University School of Medicine, New Haven, CT, USA
b Department of Infectious Disease, Yale University School of Medicine, New Haven, CT, USA

A B S T R A C T

Lyme arthritis, caused by the spirochete Borrelia burgdorferi sensu stricto, is a common tick-borne illness in New England and the upper Midwest. Most often, the disease affects the knee and has typically been reported as a cause of native joint infection. There has been only 1 case of Lyme periprosthetic joint infection (associated with a total knee arthroplasty) reported in the literature, and to our knowledge, no other reported cases of Lyme periprosthetic joint infections exist. In this article, we report on 2 patients diagnosed with prosthetic joint infections who were subsequently found to have Lyme prosthetic joint infections, with B burgdorferi as the infectious organism. We discuss the medical and surgical management of these patients.

Introduction

Lyme arthritis is common in New England and the upper Midwest. It typically presents with monoarticular pain and swelling, a clinical picture that is similar to a native septic joint. Before 2016, however, only 1 case of Lyme arthritis associated with a total knee prosthesis (PJI) had been reported in the literature [1].

Prosthetic joint infections are both a personally devastating and systemically costly complication of joint arthroplasty. The management of PJI frequently necessitates staged surgical procedures and prolonged antibiotic therapy [2]. Diagnosis of the condition can be challenging and is frequently made through indirect measurements of inflammatory markers, joint fluid cell counts in addition to microbiology cultures [2,3]. The American Academy of Orthopaedic Surgeons developed a clinical practice guideline [4] for the assessment of PJI, which include first screening procedures and prolonged antibiotic therapy [2]. Diagnosis of the condition can be challenging and is frequently made through indirect measurements of inflammatory markers, joint fluid cell counts in addition to microbiology cultures [2,3]. The American Academy of Orthopaedic Surgeons developed a clinical practice guideline [4] for the assessment of PJI, which include first screening procedures and prolonged antibiotic therapy [2].

Case report

Lyme arthritis is a tick-borne illness caused by the spirochete Borrelia burgdorferi sensu stricto. In New England and the upper Midwest, it is most often diagnosed in the knee joint, which can be a challenge to diagnose and treat. We report two cases of Lyme arthritis that were misdiagnosed as prosthetic joint infections (PJI). These cases highlight the importance of considering Lyme arthritis in the differential diagnosis of joint infections, especially in regions where it is endemic.

Case histories

Case 1

An 89-year-old woman with a past surgical history of a right total knee arthroplasty for degenerative joint disease 16 years...
Table 1
Musculoskeletal Infection Society consensus definition for periprosthetic joint infection.

1. There is a sinus tract communicating with the prosthesis; or
2. A pathogen is isolated by culture from at least 2 separate tissue or fluid samples obtained from the affected prosthetic joint; or
3. Four of the following 6 criteria exist:
   a. Elevated serum ESR and CRP
   b. Elevated synovial leukocyte count
   c. Elevated synovial neutrophil percentage
   d. Presence of purulence in the affected joint
   e. Isolation of a microorganism in a culture of periprosthetic tissue or fluid
   f. Greater than 5 neutrophils per high-power field in 5 high-power field

before presentation, presented to the Emergency Department with a 24-hour history of right knee pain, swelling, and stiffness. She denied fevers, chills, sweats, or other constitutional symptoms. She denied any recent trauma but did report a recent dental cleaning 1 month prior, which was performed without antibiotic prophylaxis. She had a past medical history significant for monocular gammopathia of undetermined significance, chronic kidney disease, duodenal ulcer, hypertension, a right bundle branch block, and glaucoma. She was an active independent woman who lived alone and ambulated with a walker with no prior problem with her right total knee arthroplasty.

On examination, she had a right knee effusion with range of motion limited by pain to a 10-40 degree flexion arc. The skin overlying the knee was moderately warm and intact without drainage. All vital signs were within normal limits. Laboratory data included a serum white blood count of 13.4 × 10^9/L, 74% neutrophils, CRP of 101.0 mg/L (normal 0.1-3), and ESR of 19 mm/h (normal 0-20). A urinalysis was remarkable for pyuria and bacteriuria. An arthrocentesis of the right knee demonstrated 66,100 cells (WBC)/µL, 93% granulocytes. The aspirate was also sent for culture and sensitivities. No organisms were seen on gram stain. A moderate number of calcium pyrophosphate crystals were also noted.

The patient was admitted to the hospital and started on vancomycin, ceftriaxone, and colchicine for treatment of presumed prosthetic joint infection, urinary tract infection, and concomitant pseudogout. The following day, she was taken to the operating room for a right knee irrigation and debridement and liner exchange for presumed PJI. During the surgery, a small amount of intra-articular purulence and a brinuous exudate with greater than 5 neutrophils per high-power field observed from histologic analysis of periprosthetic tissue at ×400 magnification. The excursion arc. The skin overlying the knee was moderately warm and intact without drainage. All vital signs were within normal limits. Laboratory data included a serum white blood count of 13.4 × 10^9/L, 74% neutrophils, CRP of 101.0 mg/L (normal 0.1-3), and ESR of 19 mm/h (normal 0-20). A urinalysis was remarkable for pyuria and bacteriuria. An arthrocentesis of the right knee demonstrated 66,100 cells (WBC)/µL, 93% granulocytes. The aspirate was also sent for culture and sensitivities. No organisms were seen on gram stain. A moderate number of calcium pyrophosphate crystals were also noted.

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At 6-week follow-up, 2 weeks after completion of her antibiotic treatment, the patient’s knee pain and swelling had completely resolved. The patient missed further follow-up appointments. She expired 5 months after this hospitalization from heart disease. No autopsy was performed.

Case 2
An 80-year-old woman with hypertension and atrial fibrillation underwent an uncomplicated right knee arthroplasty for osteoarthritis 4 months before presenting to her surgeon’s outpatient orthopaedic office with anterior proximal tibia erythema and tenderness. The patient denied fevers, chills, sweats, or constitutional symptoms. She denied trauma to the leg, and she stated that she had a pedicure 6 weeks before presentation. In the office, she was prescribed oral cephalaxin. Over the following 4 days, the erythema resolved; however, she experienced an increase in right knee pain and swelling. She underwent an arthrocentesis of the right knee, which revealed 87,830 WBC/µL, 93% polys with a negative gram stain. She was admitted to the hospital for a presumed acute prosthetic joint infection.

On arrival to the hospital, the patient had normal vital signs, a serum white blood count of 8.8 × 10^9/L, ESR of 108 mm/h, and CRP of 161 mg/L. IV cefazolin was started, and she was brought to the operating room on hospital day 3 for presumed PJI. Exploration of the prosthetic knee revealed well-fixed components with a small amount of intra-articular purulence and fibrinous exudate with minimal synovial hypertrophy. The polyethylene liner was exchanged, additional fluid and tissue samples were sent for analysis, and the wound was irrigated with bacitracin solution. Lyme PCR was performed on the synovial fluid obtained during the surgery, and this was found to be positive. Subsequent Lyme ELISA performed on serum was also strongly positive at 4.65 units (normal <0.9). Western blot IgM and IgG were negative. The patient was diagnosed with Lyme disease and switched to ceftriaxone. All preoperative and intraoperative cultures were negative for growth at end of a 7-day incubation period.

The patient was discharged on postoperative day 3. Pain and swelling rapidly resolved. She was maintained on ceftriaxone for the following 4 weeks and was then switched to oral doxycycline, which she took for an additional 4 weeks. Three months after the procedure, ESR and CRP serum levels had normalized, and the patient's pain had resolved.

She underwent an uncomplicated contralateral, left knee replacement 18 months later. At 24-month follow-up, the patient remained asymptomatic without further problems with her right knee.

Discussion
Lyme disease is endemic to the United States, concentrated around the Northeast and upper Midwest, with as many as 30,000 cases reported annually [8]. The disease is caused by the spirochete Borrelia burgdorferi sensu stricto, delivered through the bite of an Ixodes tick and is concentrated in regions where human populations coexist with white-tailed deer populations [9]. The classic initial presentation involves a target lesion (erythema migrans) centered on the tick bite. The bacteria then disseminates hematogenously. Patients may present with multisystem involvement, resulting in fatigue, headaches, myalgias, and arthralgias [10,11]. Arthritis is often a late sign of Lyme disease and manifests in a majority of untreated cases [12].

Although common, the pathophysiology of Lyme arthritis is not fully understood but thought to be a product of hematogenous dissemination to the synovial tissue. Once in the synovium, the organism likely stimulates an immune response that includes recruitment of inflammatory cells, immune complexes, cytokines,
and complements [13]. Lyme arthritis is a late manifestation of Lyme disease and often develops months after the tick bite. Lyme arthritis can present classically as episodic synovitis, which parallels inflammatory arthritides, or as an acute pauciarticular form or pseudoseptic form, which is commonly mistaken for acute septic arthritis [14].

Because of the difficulty in culturing *B. burgdorferi*, actual isolation of the spirochete is rarely attempted in clinical practice and is reserved for research purposes [15]. In general, serologic testing is used to establish a diagnosis of Lyme arthritis. The Centers for Disease Control and Prevention recommend a two-step process when testing blood for Lyme antibodies. The first step is the highly sensitive, ELISA or enzyme-linked immunofluorescence assay, which measures the antibody to the bacteria that causes Lyme disease. If the screening test is positive, the result is confirmed with the IgM and IgG Western blot. This second test is highly accurate [8]. PCR amplification of serum and tissue has also been explored for detection of Lyme, with several different reported sensitivities and specificities. Because of the difficulty in interpretation, PCR is not often used in clinical practice [15].

The pseudoseptic form of Lyme arthritis has many of the same hallmarks as septic arthritis; a large joint effusion, pain, fever, synovial hyper trophy, and a large number of WBC accumulating in the synovial fluid. Lyme arthritis also causes elevated ESR and CRP levels that are indistinguishable from septic arthritis [16]. Unlike septic arthritis, however, Lyme arthritis progresses more slowly and does not cause the rapid destruction of articular hyaline cartilage as seen in septic arthritis. Patients with this presentation remain a diagnostic challenge across the Northeast United States, where patients with acute Lyme arthritis can present to the emergency department with the clinical and laboratory signs of septic arthritis [17]. Unlike bacterial septic arthritis, however, Lyme arthritis of native joints can usually be successfully treated with a course of oral antibiotics without acute irrigation and debridement, the standard of care for septic arthritis. Refractory cases of Lyme arthritis with persistent synovitis despite appropriate antibiotic treatment have been shown to benefit from eventual synovectomy [18].

Both Lyme arthritis and PJJIs are relatively common problems encountered by orthopedic surgeons, but it is rare for these 2 problems to intersect and cause Lyme PJJIs. The 2 cases detailed here add to a prior publication by Wright et al. [1] who reported a patient who presented with a clinical picture of septic arthritis. The patient had an effusion in a prosthetic knee with a fluid aspirate with a high white blood count and high neutrophilic ratio (51,543 cells/μL; neutrophils 91.9%). No causative bacteria were ever isolated despite multiple aspirations. The diagnosis of Lyme disease was made with a positive qualitative real-time PCR from synovial fluid, and positive serum enzyme immunoassay followed by confirmatory Western blot. For both of our patients and the case described by Wright and Oliverio, multiple intraoperative cultures and tissues samples failed to yield bacteria growth. It was only when the diagnosis of Lyme was considered that appropriate testing was performed. Both serologic and Lyme PCR studies yielded the diagnosis.

There are no established guidelines for the treatment of Lyme periprosthetic joint arthritis. In both of our described cases, the diagnosis of Lyme arthritis was made after surgical intervention. Given the very limited experience with Lyme prostatic joint infections, we can only speculate as to whether medical therapy alone would have been adequate and recommend surgical irrigation and debridement with polyethylene exchange given that our 2 patients underwent irrigation and debridement and did well. The patient described by Wright and Oliverio did well with 6 weeks of antibiotics and no surgical intervention.

Given the limited reports of Lyme PJJ, no definitive recommendations can be made about optimal therapy. All 3 cases received different antibiotic regimens. In both our patients, once the diagnosis of Lyme arthritis was made, the patient was switched to oral doxycycline for 28 days. This is the standard treatment duration for patients with Lyme disease affecting native joints who are responding well to therapy. Infectious Disease Society of America guidelines recommend that clinicians consider retreatment for another 2–4 weeks if joint swelling persists after treatment, either with another course of oral therapy or with IV ceftriaxone [19]. The second patient received IV ceftriaxone for 4 weeks and then was switched to oral doxycycline for another 28 days. In the case described by Wright, the patient was treated with IV ceftriaxone for 6 weeks. All patients were ultimately treated successfully, and the patients were asymptomatic at their latest follow-ups.

Given that the presentation of Lyme PJJIs is atypical, we recommend obtaining serologic testing in patients who live in endemic areas for Lyme disease and who have a PJI in which a specific bacterium has not been isolated. If a bacterial pathogen has already been identified, with either positive blood cultures or prior arthrocentesis growing a causative organism, testing for Lyme is unlikely to be of benefit. Likewise, testing in nonendemic areas is of low predictive value.

The first patient presented was also found to have concomitant pseudogout. Because pseudogout itself is a rare reason for prosthetic joint pain and swelling [20], and the patient's clinical presentation and laboratory values were so remarkable (over 60,000 WBC/μL on aspirate, 93% granulocytes), the patient was given a presumed diagnosis of PJJ and was thus indicated for surgery. Similarly, the second patient’s aspiration yielded over 80,000 WBC/μL, and surgery was expedited. Neither patient received the diagnosis of Lyme until after their surgeries for presumed PJJ.

The acute presentation of both cases in this report was the main factor influencing the decision to proceed with expedient irrigation and debridement with prosthetic retention. In both of our cases, the symptoms were present for less than 2 weeks, the implants were deemed to be well positioned with good soft-tissue coverage, and there was no evidence of a virulent organism. Both patients were medically stable. Although some literature has challenged hardware retention even in acute cases of presumed PJJ [6], expedient debridement with liner exchange is an established practice that aims to minimize the morbidity of a multistage revision. It is indicated when the symptoms of the PJJ are less than 3 weeks, the components are well fixed, and the overlying soft tissues and skin are healthy without wounds or sinus tracts [7].

Summary

As the incidence of Lyme disease continues to climb and the number of patients undergoing joint replacement surgery increases, Lyme arthritis affecting prosthetic joints is likely to be seen more commonly. The 3 cases now described show that this infection can occur in recently as well as remotely placed prostheses. Lyme arthritis is most commonly seen in knees, so it is not surprising that this is the only site where Lyme PJJ has been identified to date. More studies are needed to understand pathogenesis of Lyme PJJ, role of biofilm, and optimal management. It is certainly plausible that Lyme PJJ can be cured with medical therapy alone, but given our successful treatment with irrigation and debridement, we currently recommend surgery.

References


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