Case Report

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Lyme Disease: A Potential Source for Culture-negative Prosthetic Joint Infection

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Abstract

The presentation of Lyme arthritis can mimic periprosthetic joint infection (PJI) caused by typical bacterial organisms. A patient with left total knee arthroplasty (TKA) and chronic Lyme disease presented to our institution with Lyme-associated PJI. He complained of pain, erythema, and fever for 3 days and met Musculoskeletal Infection Society criteria for PJI. Preoperative synovial fluid Lyme polymerase chain reaction (PCR) and serological tests were positive, whereas both preoperative aspiration and intraoperative cultures were negative. The patient underwent resection arthroplasty with insertion of an antibiotic spacer followed by intravenous ceftriaxone and oral doxycycline treatment for 6 weeks. He underwent reimplantation at 8 weeks after repeat synovial fluid PCR analysis was negative. At 1 year, the patient was asymptomatic with a painless, functional, revision TKA. It is essential to consider Lyme-associated PJI in the setting of culture-negative PJI, especially in regions with a high prevalence of Lyme disease.

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Lyme disease, which is caused by *Borrelia burgdorferi*, is one of the most common vector-borne illnesses in the United States and is transmitted by *Ixodes* tick species, which are prevalent in the East Coast and Midwest regions. Disseminated manifestations of Lyme disease, including fever or chills, erythema, joint pain, and joint effusion, can mimic the presentation of bacterial septic arthritis.[1] In patients who have previously undergone total joint arthroplasty (TJA), synovial fluid analysis may even fulfill many of the Musculoskeletal Infection Society (MSIS) criteria for periprosthetic joint infection (PJI), including increased erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level, white blood cell (WBC) count, and polymorphonuclear neutrophil percentage, although the synovial fluid culture is negative.[2] Traditionally, synovial fluid Lyme polymerase chain reaction (PCR) testing, in conjunction with Lyme antibody testing, has been used to confirm the diagnosis of Lyme arthritis in native joints because of the inability to culture *B burgdorferi*.[3] In regions with a high prevalence of Lyme disease, it may be important to consider the addition of Lyme PCR and Lyme antibody testing for those patients who have undergone TJA and whose presentation is consistent with a diagnosis of culture-negative PJI.

Figure 1

A and **B,** Preoperative AP and lateral radiographs of primary TKA before resection arthroplasty. **C,** Static cement spacer supported with an intermedullary humeral nail. **D,** Reimplantation was performed using revision TKA components. TKA = total knee arthroplasty

Case Report

The patient is an 83-year-old man from central Pennsylvania who underwent uncomplicated left total knee arthroplasty (TKA) at an outside institution approximately 6 years before presentation (Figure 1). The patient reported pain, erythema, and fever for 3 days and had a moderate effusion and limited range of motion on examination. Knee aspiration was performed during an emergency department visit that revealed a synovial fluid WBC count of 17,370 cells/μL, with a 92% neutrophil differential count and absence of crystals. The synovial fluid culture was negative for bacterial growth. The ESR and CRP level were 64 mm/h and 6.7 mg/dL, respectively. The patient was treated for presumed PJI, given that he fulfilled the MSIS criteria. The patient underwent resection arthroplasty with insertion of a static antibiotic spacer, as purulence and synovitis were noted intraoperatively.

When intraoperative cultures were confirmed as negative for bacterial growth, serum Lyme antibody testing and synovial fluid Lyme PCR were sent for analysis. A Lyme IgM/IgG screening was completed by chemiluminescence immunoassay using a LIAISON analyzer. The screening was positive, with an index value of >12.4 (reference range, <0.91). A reflex confirmatory Western blot was completed using the MarDx *B burgdorferi* Marblot Strip Test System and a TrinBlot processor. The Lyme IgM testing was negative, with only one of three significant bands (23 kDa) present. However, Lyme IgG testing was positive, with the presence of 8 of 10 significant bands, at 18, 23, 28, 30, 39, 41, 58, and 66 kDa. Nucleic acid extraction for Lyme PCR testing was performed using a MagNA Pure LC 2.0 instrument. Real-time synovial fluid PCR was completed on an ABI 7500 system using Scorpion primers and a Quest Diagnostics proprietary assay, which discriminates between *B burgdorferi*, *afzelii*, *andersonii*, and *garninii* species and has been validated according to the College of American Pathologists and Clinical Laboratory Improvement Amendments regulations.

A diagnosis of disseminated Lyme disease was made based on a positive Lyme IgG and synovial fluid PCR and negative Lyme IgM. Oral doxycycline was initiated for 2 weeks, after which the patient was transitioned to 4 weeks of intravenous ceftriaxone. Repeat aspiration was performed at approximately 8 weeks postoperatively from the date of resection, which revealed a negative synovial fluid PCR. He subsequently underwent removal of the antibiotic cement spacer and reimplantation using revision TKA components. At 1-year follow-up, the patient was asymptomatic with functional and painless TKA.

Discussion

Lyme disease, caused by *B burgdorferi*, is an endemic illness in the East Coast and Midwest regions. In a patient with TJA, articular and systemic manifestations of Lyme disease may mimic the presentation of PJI.[1] Although synovial fluid analysis in cases of Lyme arthritis and bacterial septic arthritis is similar, the utility of culture to differentiate the two is limited. In cases of suspected articular involvement, synovial fluid PCR has been the gold standard for the definitive diagnosis of Lyme arthritis.[3] Because of their similar diagnostic test results, Lyme arthritis in a patient with TJA may be indistinguishable from culture-negative PJI on routine evaluation.[4] The preoperative workup may yield results supporting the diagnosis of PJI, based on the MSIS criteria, including elevated ESR and CRP level, synovial fluid WBC count, and neutrophil differential count.[2] However, in such cases, the synovial fluid culture and intraoperative cultures will not isolate an organism. Additional workup of synovial fluid PCR with serum Lyme antibody testing may be essential to differentiate between Lyme-associated PJI and culture-negative infections.

Although Lyme arthritis of native joints has been thoroughly described, there has been only one documented case of Lyme-associated PJI so far that presented in a patient with unicompartmental knee arthroplasty.[5] The patient originated from a region of high Lyme disease prevalence similar to the background of our patient. However, the patient was treated with intravenous 2 g ceftriaxone for 6 weeks without any surgical intervention. Repeat knee aspiration was performed at 18 days after cessation of intravenous treatment, which revealed the absence of *B burgdorferi* DNA by PCR analysis. The authors did not report on any short-term follow-up but did raise the question of whether this nonoperative treatment would yield similar outcomes in patients with a primary or revision total knee replacement. At our institution, we performed two-stage exchange arthroplasty with a static spacer and intravenous antibiotics for 6 weeks, given the chronicity of the disease. We were also concerned about the potential of *B burgdorferi* to produce biofilm formation similar to that of other common bacterial pathogens, in which case nonoperative treatment would be unsuccessful.

As *B burgdorferi* aggregates have recently been implicated in the formation of biofilms, it is important to consider this spirochete as an important and unrecognized pathogen in the setting of culture-negative PJI.[6,7] Studies on *B burgdorferi* pleomorphic forms have demonstrated formation of aggregates with biofilm-like properties in early growth phases, with increases in formation as a response to environmental stress, such as introduction of antibiotics, similar to what is observed in the more common bacterial pathogens.[7] These findings suggest a role for Lyme disease evaluation in both scenarios of localized and disseminated Lyme disease and in patients with painful TJA located in endemic areas. Consequently, aggressive surgical intervention would be warranted to physically decrease the biofilm burden in the joint, given the limited role of antibiotics in this scenario.

Treatment-refractory Lyme arthritis has had favorable and reliable outcomes when appropriate treatment is administered.[8] By contrast, culture-negative PJI is associated with significantly increased morbidity and mortality.[4] Early and definitive diagnosis of Lyme-associated PJI will allow for the timely initiation of targeted antimicrobial therapy, which will reduce the need for prolonged broad spectrum antibiotics, and thus may reduce the risk of antibiotic resistance. Irrigation and débridement with polyexchange for PJI have been reported to have a success rate of up to 40%, but there is a concern that it may jeopardize the outcomes of two-stage exchange arthroplasty performed on those who fail the procedure.[9] Resection arthroplasty with insertion of an antibiotic cement spacer followed by reimplantation has higher success rates in controlling infection but involves greater morbidity and mortality.[10] The optimal method for treating and eradicating PJI remains elusive. Going forward, as we identify more cases of Lyme-associated PJI, we may be able to define a standard of care for surgical intervention.

References

1. Smith BG, Cruz AI Jr, Milewski MD, Shapiro ED: Lyme disease and the orthopaedic implications of Lyme arthritis. *J Am Acad Orthop Surg* 2011;19:91-100.

2. Parvizi J, Zmistowski B, Berbari EF, et al: New definition for periprosthetic joint infection: From the Workgroup of the Musculoskeletal Infection Society. *Clin Orthop Relat Res* 2011;469:2992-2994.

3. Nocton JJ, Dressler F, Rutledge BJ, Rys PN, Persing DH, Steere AC: Detection of Borrelia burgdorferi DNA by polymerase chain reaction in synovial fluid from patients with Lyme arthritis. *N Engl J Med* 1994;330:229-234.

4. Berbari EF, Marculescu C, Sia I, et al: Culture-negative prosthetic joint infection. *Clin Infect Dis* 2007;45:1113-1119.

5. Wright WF, Oliverio JA: First case of Lyme arthritis involving a prosthetic knee joint. *Open Forum Infect Dis* 2016;3:ofw096.

6. Merilainen L, Herranen A, Schwarzbach A, Gilbert L: Morphological and biochemical features of Borrelia burgdorferi pleomorphic forms. *Microbiology* 2015;161(pt 3):516-527.

7. Sapi E, Bastian SL, Mpoy CM, et al: Characterization of biofilm formation by Borrelia burgdorferi in vitro. *PLoS One* 2012;7:e48277.

8. Steere AC, Angelis SM: Therapy for Lyme arthritis: Strategies for the treatment of antibiotic-refractory arthritis. *Arthritis Rheum* 2006;54:3079-3086.

9. Sherrell JC, Fehring TK, Odum S, et al: The Chitranjan Ranawat Award: Fate of two-stage reimplantation after failed irrigation and debridement for periprosthetic knee infection. *Clin Orthop Relat Res* 2011;469:18-25.

10. Kurd MF, Ghanem E, Steinbrecher J, Parvizi J: Two-stage exchange knee arthroplasty: Does resistance of the infecting organism influence the outcome? *Clin Orthop Relat Res* 2010;468:2060-2066.