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BRIEF REPORT

First Case of Lyme Arthritis Involving a Prosthetic Knee Joint

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Borrelia burgdorferi sensu stricto is the most common tick-borne illness in the United States. Arthritis is usually a manifestation of late disease but has not been associated with cases of periprosthetic joint infections. We report on a patient who was first diagnosed with periprosthetic joint infection and subsequently Lyme arthritis.

Keywords. *Borrelia burgdorferi*; Lyme arthritis; periprosthetic joint infections.

The bacterium *Borrelia burgdorferi* sensu stricto is the most common tick-borne illness in the United States [1]. Arthritis is usually a manifestation of late disease and occurs in an estimated 10%–24.8% of untreated patients, but it has not been associated with cases of periprosthetic joint infections (PJIs) [1]. We report on a patient who was first diagnosed with PJI and subsequently Lyme arthritis.

CASE REPORT

A 67-year-old male from central Pennsylvania presented to the orthopedic outpatient surgical office in November 2015 with a 3-month history of progressive left knee pain and swelling. His symptoms began in late August 2015, and there was no history of trauma, tick bite, or rash. No systemic symptoms or illnesses were reported either. In early November 2014, he had undergone a medial compartment unicompartmental joint arthroplasty of his left knee for advanced single compartment degenerative arthritis. There was no evidence of joint effusion, infection, or Baker's cyst prior to joint arthroplasty. He is an avid outdoorsman who enjoys hunting, hiking, and golf in a Lyme endemic region of the United States. The patient was functioning quite well and pain free the first 10 months after surgery. At his office visit, clinical examination revealed a moderate joint effusion but no erythema, warmth, instability, or significant pain with range of motion. The knee was aspirated, and synovial analysis of the turbid fluid revealed purulent pleocytosis (51 543 cells/μL; neutrophils 91.8%), positive human neutrophil elastase and α-defensin, elevated C-reactive protein, and detection of *B burgdorferi* deoxyribonucleic acid (DNA) by Qualitative, Real-Time polymerase chain reaction (PCR) (Roche Molecular Diagnostics, Branchburg, NJ). Synovial fluid Gram-stain and bacterial cultures were negative after 7 days of incubation. Serum laboratory results showed an erythrocyte sedimentation rate of 25 mm/h (range, 0–20 mm/h), C-reactive protein 0.7 mg/dL (range, 0.0–0.5 mg/dL), and *B burgdorferi* antibody enzyme immunoassay (EIA) screen >5.0 (reference range, <0.90) with all 10 immunoglobulin G (IgG) Western blot bands reactive. Twice daily 100 mg of oral doxycycline was initiated empirically prior to laboratory results; however, on testing results 1-week later, the patient was converted to daily intravenous 2 grams ceftriaxone for 6 weeks. Clinically, the patient had significant resolution of left knee pain and swelling without surgical incision and drainage or excision arthroplasty. Synovial fluid analysis 18 days after end of therapy demonstrated 540 total nucleated cells per microliter (38% neutrophils, 34% lymphocytes, and 28% monocytes), negative human neutrophil elastase, α-defensin, and C-reactive protein, and negative detection of *B burgdorferi* DNA by PCR. End-of-therapy synovial fluid Gram-stain and bacterial cultures were negative after 7 days of incubation. Serum laboratory results showed an erythrocyte sedimentation rate of 8 mm/h and C-reactive protein <0.2 mg/dL.

DISCUSSION

Borrelia burgdorferi sensu stricto infections such as that seen in this patient are unknown; therefore, a review of the published literature was performed by conducting a PubMed search. A search of past case reports or case series using Medical Subject Headings (MeSH) search terms "infectious arthritis", "*B burgdorferi*", "*Borrelia* infections", "Lyme disease", "metal-on-metal joint prostheses", "prostheses and implants", and "prosthesis implantation" demonstrated no related publications. Searching Lyme arthritis only with restrictions of English language, humans, adults greater than age 19 years, and clinical trial produced 8 relevant Lyme arthritis-related prospective studies among 93 publications [2–9]. Although these publications discussed musculoskeletal manifestations of Lyme disease, particularly arthritis, none reported cases in association with PJI.

Periprosthetic joint infection is a devastating complication following joint arthroplasty that causes significant morbidity with an estimated cumulative incidence of 1%–2% for both

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hips and knees [10, 11]. The Musculoskeletal Infection Society (MSIS) and Infectious Disease Society of American (IDSA) have recently issued consensus statements providing criteria to a uniformed definition of PJI for both research purposes and clinical practice (Table 1) [10, 11]. Although there was no communicating sinus tract or direct result from traditional microbiological culture, our patient met these criterion for PJI based upon elevated synovial fluid leukocyte count (>3000 cell/μL), elevated synovial neutrophil count (>65%), purulence, and evidence of a microorganism with identification to the level of genus and species.

Deirmengian et al [11] recently reported a prospective single-center trial to document performance characteristics of combined synovial fluid biomarkers, α-defensin, and C-reactive protein, in the diagnosis of PJI. A total of 149 evaluable patients were enrolled for evaluation and assignment to 2 groups based upon whether there was an aseptic diagnosis to prosthetic joint complication (n = 112) or MSIS defined PJI (n = 37). The α-defensin and C-reactive protein assays were optimized to a cutoff value of 5.2 mg/L and 3.0 mg/L, respectively. Overall, authors reported the combination of these biomarkers resulted in a sensitivity of 97.3% and specificity of 100%. These biomarkers were used in this case, and our patient also demonstrated synovial fluid α-defensin and C-reactive protein levels above these cutoff values, providing further support of PJI.

In North America, Lyme disease can involve several organs and is caused by the tick-borne bacterial pathogen *B burgdorferi* sensu stricto [1]. Although arthralgia and myalgia frequently accompany early Lyme disease, late-onset Lyme arthritis typically arises 6–12 months after infection acquisition [1, 2]. Late-onset Lyme arthritis affects large, weight-bearing joints, with knee involvement nearly universal at some point, although other articulations may be involved [1, 2]. Criteria for the diagnosis of late-onset Lyme arthritis are based on exposure within an endemic area as well as the presence of brief, intermittent attacks of monoarticular or oligoarticular arthritis, Centers for Disease Control and Prevention-defined antibody response on enzyme-linked immunosorbent assay, and exclusion of other forms of arthritis [1, 8]. Serologic testing is particularly important, because 100% of patients with late-onset Lyme arthritis have strongly reactive 2-tier testing with a positive total-antibody screen (EIA or immunofluorescence assay) and a positive IgG immunoblot [1, 2]. In a prospective evaluation by Steere et al [2] of 55 patients with Lyme arthritis, the majority of patients were reported to have moderate inflammation on synovial fluid analysis with 2400–34 600 white blood cells/μL and 30%–91% polymorphonuclear leukocytes. A positive synovial fluid *B burgdorferi* sensu stricto DNA Qualitative, Real-Time PCR test provides adjunctive evidence implicating the pathogen [8, 9]. Our patient fulfilled these criteria to support the diagnosis of Lyme arthritis. In addition, PJIs are typically classified as "early" (those occurring within 3 months of implantation), "delayed" (3–12 months after implantation), and "late" (more than 12 months after implantation) [10]. Early and delayed infections are thought to be due to organisms introduced at the time of surgery, whereas late infections are more likely to be hematogenously acquired [10]. Although not quite 1 year from the time of surgery did this patients symptoms first present, it is still most plausible that disseminated Lyme disease with hematogenous seeding provides the best possible explanation of how the organism gained access to the prosthetic joint. Furthermore, Sapi et al [12] recently reported that *B burgdorferi* sensu stricto demonstrates several hallmark features of biofilm production (eg, aggregate superstructures, production of alginate, and adherence to abiotic and biotic surfaces) that may have aided in the establishment of this patient's infection.

Treatment strategies for PJI often necessitates surgical incision and drainage, staged excision arthroplasty, and prolonged intravenous and oral antimicrobial therapy because typical microorganisms causing these infections are usually living in a biofilm to harbor resistance leading to increased risk of chronicity and recurrence [10]. The IDSA PJI guidelines currently recommend "four to 6 weeks of pathogen-specific intravenous or highly bioavailable oral antimicrobial therapy" for organisms not traditionally associated with infections [10]. Lyme disease guidelines published by the IDSA indicate that late "Lyme arthritis can usually be treated successfully with antimicrobial agents administered orally" (eg, doxycycline, amoxicillin, or cefuroxime) for 28 days in adult patients without evidence of neurologic disease [1, 3, 4, 6]. Previous studies have also been published demonstrating the efficacy of once daily ceftriaxone (2-gram dose) for 14 or 28 days in the treatment of late Lyme disease [4–7]. However, this evidence is presumed to be based

Table 1. MSIS and IDSA Criteria for Periprosthetic Joint Infection (PJI)[a]

(A) Major Criteria
1. A sinus tract that communicates with the prosthesis
2. Isolation of a virulent pathogen (eg, *Staphylococcus aureus*) on 2 separate tissue or fluid culture samples obtained (perioperative aspirate and/or intraoperative) from the affected prosthesis
(B) Minor Criteria
1. Purulence within the affected joint
2. Erythrocyte sedimentation rate >30 mm/h and C-reactive protein level >10 mg/L
3. Synovial fluid leukocyte count >3000 cells/μL
4. Synovial fluid neutrophil percentage >65%
5. Isolation of a virulent pathogen on 1 separate tissue or fluid culture sample obtained (perioperative aspirate and/or intraoperative) from the affected prosthesis
6. Greater than 5 neutrophils per high-powered field in 5 high-powered fields observed on histological analysis of periprosthetic tissue at 400× magnification
Definite PJI
1. One major criterion
2. Four of 6 minor criteria
Possible PJI
1. The presence of PJI is possible even if the above criteria are not met; the clinician should use his/her clinical judgment to determine whether this is the case after reviewing all the available preoperative and intraoperative information

Abbreviations: IDSA, Infectious Disease Society of American; MSIS, Musculoskeletal Infection Society.

[a] References [10, 11].

upon infection of native joints. Based upon these limitations, once daily intravenous ceftriaxone (2 grams) monotherapy was continued for 6 weeks. Furthermore, based upon the history of a unicompartment knee arthroplasty and mild presenting symptoms, this patient did not undergo any orthopedic surgical intervention. Clinically, the patient had cessation of his knee pain, resolution of joint effusion, normalization of synovial infection and inflammatory parameters, and negative end-of-therapy detection of *B burgdorferi* DNA by PCR. Although this patient's clinical outcome was achieved without the need for surgical incision and drainage or staged excision arthroplasty procedure, it is unclear whether this same strategy would produce similar results in patients with other types of joint arthroplasties. Finally, it is unclear whether these results could also be achieved with any of IDSA-recommended oral antimicrobial agents.

CONCLUSIONS

To the best of our knowledge, this report describes the first patient with late *B burgdorferi* sensu stricto arthritis-related prosthetic joint infection. This case highlights how early prompt diagnosis and adequate antimicrobial therapy may obviate the need for additional aggressive orthopedic surgical intervention. Clinicians in all regions of Lyme endemic areas should be aware of this infection. This case also highlights the value of an aggressive need to further investigate and interpret unexpected findings in clinical practice. Finally, more cases are needed to develop optimal management strategies.

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