BENDING THE VALUE CURVE

Septic Arthritis Versus Lyme Arthritis: A Case of Diagnostic Difficulty

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A 12-year-old female softball player with a history of type 1 diabetes mellitus presented to the pediatric emergency department of a tertiary care hospital after 1 day of right knee pain and swelling. The pain was described as 6 to 7 out of 10 in severity, worse with activity, and better with rest. Associated symptoms included fever, chills, decreased appetite, and fatigue. There was no history of trauma, recent travel, or tick bites. Earlier in the day she had been seen by her primary care physician, who prescribed cephalexin for bilateral ingrown toenails. Initial vital signs were as follows: temperature of 36.8°C, heart rate of 130 beats per minute, respiratory rate of 18 breaths per minute, blood pressure of 138/65 mm Hg, and oxygen saturation of 100% on room air. On physical examination, the patient was in no acute distress. Her right knee had a moderate effusion with overlying warmth but no erythema. There was minimal tenderness to palpation. Knee range of motion was limited to 0 to 90°. She could bear weight but walked with a limp. She also had evidence of healing bilateral ingrown toenails without surrounding erythema.

Screening laboratory tests were significant for a serum white blood cell (WBC) count of 5.2 K/μL (reference range: 4.0–10.5 K/μL), with 51% neutrophils, 38% lymphocytes, and 10% monocytes, C-reactive protein (CRP) of 12.92 mg/dL (reference range: <1.0 mg/dL), and erythrocyte sedimentation rate of 76 mm/hour (reference range: 0–20 mm/hour). A radiograph of the knee showed no evidence of acute fracture. Joint aspiration was performed by the Orthopedic Surgery service and revealed a synovial fluid WBC count of 66 280 per mm^3 (58% neutrophils, 32% lymphocytes, and 10% mononuclear cells). A Gram-stain showed 3+ WBCs and no organisms. The patient was subsequently diagnosed with septic arthritis of the right knee; her ingrown toenails were thought to be a potential source of infection. She was admitted to the pediatric inpatient floor by the Orthopedic Surgery service and then taken to the operating room for surgical debridement of the right knee a few hours later. The removal of nail beds from bilateral great toes was performed by the Podiatry service at the time of surgery. The Infectious Disease service was consulted for antimicrobial recommendations, and the Pediatrics service was consulted for the management of type 1 diabetes mellitus. On postoperative day 1, the Pediatrics service took over primary responsibility with consultation from the Orthopedic Surgery, Podiatry, and Infectious Disease services.

The patient was initially started on intravenous clindamycin. CRPs trended down from 12.92 to 5.89 mg/dL over the first 6 days and then stayed at ~6 mg/dL. The results of blood cultures and joint aspirate cultures remained negative. However, the patient continued to spike fevers almost daily, with temperatures ranging from 36.4 to 39.8°C. An extensive laboratory workup was conducted and included urine *Chlamydia trachomatis* and *Neisseria gonorrhoeae* RNA, serum Lyme disease DNA polymerase chain reaction (PCR), antinuclear antibody, rheumatoid

www.hospitalpediatrics.org
DOI:https://doi.org/10.1542/hpeds.2017-0142

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HOSPITAL PEDIATRICS (ISSN Numbers: Print, 2154-1663; Online, 2154-1671).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

Dr Keane drafted the initial manuscript and edited subsequent versions; Drs Top and Burbridge critically reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

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factor, and various synovial fluid studies including bacterial and fungal detection PCR. The results of all of these were negative. On hospital day 6, clindamycin was switched to linezolid for better coverage of methicillin-resistant *Staphylococcus aureus* given local resistance of methicillin-resistant *S aureus* to clindamycin. On hospital day 8, ceftriaxone was added for coverage of Gram-negative organisms, specifically *Kingella kingae*, although suspicion for this was low. On hospital day 10, the result of an MRI that was obtained to rule out osteomyelitis and bone abscess was negative. The patient was still intermittently febrile, and the results of cultures were negative. During her hospitalization, the patient required multiple changes to her insulin regimen because her blood glucose levels were difficult to control.

On hospital day 11, a pediatric orthopedic surgeon not previously involved in this case was asked by his colleagues to evaluate the patient. His impression was that she had a diagnosis of reactive arthritis, not septic arthritis. He recommended that the Pediatrics service obtain serum Lyme enzyme-linked immunosorbent assay (ELISA) with reflex to Western blot, then discharge the patient with close follow-up. She was discharged on oral clindamycin; 4 days later, her Lyme test resulted positive, so clindamycin was stopped and doxycycline was begun. The patient completed a 28-day course of doxycycline for the treatment of her Lyme disease, recovered uneventfully, and returned to playing softball.

In retrospect, it is clear that our patient underwent an arguably unnecessary surgery and had a prolonged hospitalization for a medical diagnosis that was ultimately incorrect. The following discussion highlights several decision points that may have led to the outcomes in this case.

The first decision point was the premature diagnosis of septic arthritis in the emergency department when the synovial WBC count was nondiagnostic and Lyme testing was not initially performed. Traditionally, it is thought that a synovial WBC count $>50\,000$ per mm^3 with a neutrophil predominance of at least 90% is suggestive of septic arthritis.[1] However, in a retrospective cohort study conducted by Deanehan et al,[2] the authors demonstrated that in Lyme endemic areas, there were no significant differences in the synovial WBC count and percent neutrophils for children with Lyme and septic arthritis. Other shared features of Lyme and septic arthritis include presence of fever and elevated inflammatory markers.[3] These 2 diagnoses must be distinguished from each other because treatment and prognosis vary greatly; in endemic areas, Lyme testing should therefore be performed on all patients presenting with acute monoarticular arthritis.[3] In our case, unfamiliarity with Lyme testing led to the second problematic decision point.

Lyme arthritis was considered relatively early in our patient's hospital course, but initial testing was ordered incorrectly; serum *Borrelia burgdorferi* DNA PCR was ordered instead of Lyme ELISA with reflex to Western bot. Notably, the Centers for Disease Control and the Food and Drug Administration recognize that some commercial laboratories conduct inadequately validated tests for Lyme disease, including serum *B burgdorferi* DNA PCR.[4] The recommended 2-step testing for evidence of antibodies against *B burgdorferi* is ELISA followed by Western blot only if the ELISA is positive or equivocal.[5] Ordering the correct Lyme test is paramount to establishing the diagnosis with certainty and must be given careful consideration.

The 2 previous decision points led to the third overarching problem of diagnostic anchoring. The results of the serum Lyme PCR were falsely reassuring, and the fact that it was an incorrect test was missed by almost all members of the health care team. Nonetheless, the diagnosis of Lyme arthritis should not have been so easily dismissed, especially in a patient with knee involvement and little pain with movement. The persistence of fevers and CRP elevation likely contributed to the thinking that septic arthritis was to blame. Subsequently, more aggressive treatment was pursued, leading to increased patient morbidity and overuse of health care resources.

In a recent study by Baldwin et al[6] titled "Predictive Factors for Differentiating Between Septic Arthritis and Lyme Disease of the Knee in Children," the authors retrospectively reviewed the records of patients <18 years of age who presented to the emergency department of a large tertiary care children's hospital between 2005 and 2013 with knee effusions and in whom arthrocentesis was performed. Of significance, 46 (33%) of 140 patients who were ultimately diagnosed with Lyme disease underwent surgical incision and drainage on the basis of a presumed diagnosis of septic arthritis.[6] The variable that was shown to be most consistent with receiving surgical incision and drainage in the setting of Lyme arthritis was, not surprisingly, an elevated synovial WBC.[6] This illustrates that our case is not unique; it could be argued that operative management in children with Lyme arthritis needs to be done more judiciously. However, this decision is difficult because the alternative diagnosis of septic arthritis has the potential to permanently damage a joint.

Although it is unclear whether the well-known Kocher criteria influenced our patient's initial diagnosis or anchoring, it should be noted that it has not been validated in the knee. The Kocher criteria consist of 4 high-risk predictors of septic arthritis: fever >38.5°C, inability to bear weight on the affected joint, serum WBC $\geq 12\,000 \times 10^3$ cells per mL, and an erythrocyte sedimentation rate ≥ 40 mm/hour.[7] They were originally developed to differentiate septic arthritis from transient synovitis in children undergoing hip arthrocentesis but have been widely used and liberally applied, including to children with knee arthritis and those living in Lyme-endemic areas.[7] It is necessary for medical providers to be aware that the Kocher criteria were not intended to distinguish between septic arthritis and Lyme disease and have not been validated for the knee.[6]

CONCLUSIONS

Lyme arthritis should be included in the differential diagnosis of knee pain and effusion in pediatric patients living in

Lyme-endemic areas and should be evaluated appropriately. If an arthrocentesis is performed as part of a diagnostic workup, clinicians must view an elevated synovial WBC count as supportive, not indicative, of septic arthritis. If the synovial WBC count is high enough, arthroscopy is inevitable, but Lyme arthritis must remain on the differential diagnosis and be evaluated in accordance with evidence. There should be measures in place at each institution to ensure that providers order appropriate Lyme testing. Our institution may take steps in implementing a septic arthritis order set and discontinuing Lyme PCR completely. Perhaps most importantly, clinicians should use this case as a reminder to consider alternative diagnoses, especially when a patient does not improve as expected.

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Hospital Pediatrics 2018;8;170
DOI: 10.1542/hpeds.2017-0142 originally published online February 21, 2018;

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AN OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

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