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Knee Lyme Arthritis in Pediatric and Adolescent Patients May Be Associated With Meniscal Changes on MRI

Matthew D. Milewski, MD, Kirsten Ecklund, MD, Sang Won Lee, MSc, Ryan P. Coene, MS, Ryan M. Sanborn, BA, Emma C. Gossman , BS, Patricia E. Miller, MS, Benton E. Heyworth, MD, and Yi-Meng Yen, MD, PhD

Investigation performed at Boston Children's Hospital, Boston, Massachusetts

Background: Lyme arthritis is a common manifestation of late-stage Lyme disease in pediatric and adolescent patients. Patients with Lyme arthritis typically present with atraumatic knee effusion and may undergo magnetic resonance imaging (MRI) to aid in diagnosis. The incidence of meniscal pathology on MRI in association with Lyme arthritis is unknown. This study aims to evaluate the incidence of meniscal pathology on MRI in young patients with Lyme arthritis.

Methods: Patients (<18 years old) presenting with a unilateral knee effusion from 2009 to 2019 with a positive Lyme antibody serologic test, MRI within 2 weeks of the positive test, and ultimate diagnosis of Lyme arthritis were included in the study. MRI, which was performed to distinguish Lyme arthritis from other causes of knee effusion, underwent analysis by a pediatric musculoskeletal radiologist. Meniscal signal abnormality was graded as follows: grade 1 = globular, grade 2 = linear nonsurfacing, and grade 3 = surfacing tear.

Results: Eighty-seven patients (10.6 ± 3.9 years, 71.3% male, 67.8% White) were included. Fourteen (16%) patients had meniscal changes (grade 1: n = 4 [5%]; grade 2: n = 3 [3%]; grade 3: n = 7 [8%]). Thirteen of the 14 patients (93%) with meniscal changes on MRI were treated only with oral antibiotics, with resolution of knee symptoms and return to sports, whereas 1 patient (7%) underwent arthroscopic partial meniscectomy.

Conclusions: Of the 87 pediatric patients with serologically confirmed Lyme arthritis and MRI of their affected knee, 16% had a coexistent meniscal abnormality on MRI, but only 1 patient overall required surgical treatment related to the meniscus. Physicians should be aware of potential MRI meniscal changes in pediatric and adolescent patients who present with symptomatic knee effusion because of Lyme arthritis. Future research to evaluate the physiologic effects of Lyme arthritis on meniscal tissue is needed.

Level of Evidence: Level IV Case Series. See Instructions for Authors for a complete description of levels of evidence.

Introduction

Lyme disease is the most commonly reported tick-borne disease in the United States[1]. Although data since the COVID-19 outbreak have been limited, the prevalence of Lyme had been continuing to rise over time with more than 30,000 reported cases from 2008 to 2019[1,2]. Lyme disease is caused by the spirochete *Borrelia burgdorferi*, which is primarily transmitted through an Ixodes tick[3]. Lyme disease is a multisystem disorder, which affects dermatologic, neurologic, cardiac, and musculoskeletal systems[4]. Lyme arthritis is a common manifestation of late-stage Lyme disease in children and adolescents. Children have twice the likelihood of developing arthritis as adults and can present earlier in the disease course[5]. The knee is the most commonly affected joint in Lyme arthritis with 90% of cases in children involving this joint[6]. Patients are diagnosed with Lyme disease based on a combination of clinical findings, positive serologic testing, and exposure in Lyme endemic areas. Patients with Lyme arthritis typically present with symptomatic knee monoarthritis and may undergo additional testing, such as magnetic resonance imaging (MRI) to aid in diagnosis and to exclude other causes of acute monoarthritis.

Disclosure: The **Disclosure of Potential Conflicts of Interest** forms are provided with the online version of the article (http://links.lww.com/JBJSOA/A764).

MRI is used widely to assess traumatic, infectious, and inflammatory musculoskeletal disorders[4]. MRI is increasingly used to differentiate between septic arthritis and Lyme arthritis[4,7]. Ecklund et al. in 2005 identified MRI characteristics including myositis, popliteal adenopathy, and lack of subcutaneous edema suggestive of Lyme arthritis versus septic arthritis[8]. In addition to aiding with diagnosis, MRI provides additional information about articular and periarticular structures including the menisci.

Although the effect of Lyme arthritis on articular cartilage has been well studied, there is lack of data on its effect on the meniscus[3]. Given the paucity of data, the incidence of meniscal changes in association with Lyme arthritis is unknown. This study aimed to evaluate the incidence of meniscal pathology on MRI in young patients with Lyme arthritis.

Materials and Methods

Patients

The study was conducted at a single, large pediatric hospital in a Lyme disease endemic region. After IRB approval for the retrospective study, a query of the institutional imaging database was conducted to identify all patients who presented with symptomatic knee effusion and underwent an MRI from February 2009 to October 2019. Inclusion criteria included patients <18 years of age, positive Lyme serologic test, and MRI within 2 weeks of the positive test. Exclusion criteria included lack of ipsilateral knee MRI or MRI performed after irrigation and debridement and patients <1.5 years of age because of low likelihood of Lyme arthritis. The resulting cohort consisted of 87 patients with serologically confirmed Lyme arthritis and MRI within 2 weeks of their serologies.

Patient Characteristics

Demographic, clinical, and laboratory data were retrospectively collected from patient's medical charts. Demographic data obtained included age at presentation, sex, race, and ethnicity based on the electronic medical record, height, weight, and presentation location. Clinical data obtained included maximum temperature, presence of fever, and ability to bear weight. Laboratory data obtained included the results of Lyme disease serology including enzyme-linked immunosorbent assay, immunoglobulin G, immunoglobulin M, and polymerase chain reaction for all patients with a Lyme arthritis diagnosis. Additional laboratory data obtained included first serum and maximum serum white blood cell (WBC) count, first serum and maximum serum C-reactive protein (CRP), first serum and maximum serum erythrocyte sedimentation rate (ESR), joint aspiration status, and joint fluid WBC count.

MRI Protocols and Analysis

All 87 patients underwent imaging of the involved knee on 1.5-T or 3-T MRI scanners (Siemens Medical Systems). Imaging protocol included sagittal and axial fluid-sensitive (T2 weighted with fat suppression or inversion recovery), sagittal proton density-weighted without fat suppression, and long axis T1-weighted sequences, although specifics of the protocols varied over the study period. MRI was reviewed by a pediatric musculoskeletal radiologist with >20 years of experience. To establish inter-rater reliability, a pediatric orthopaedic surgeon with >10 years of experience reviewed a random subset of 45 MRI scans. MRI was used to evaluate for presence of meniscus pathology. Meniscal signal abnormality was graded as follows using the classification system developed by Lotysch et al. and elaborated by Dillon et al.[9,10]. Grade 1 signal is a rounded or amorphous signal in the meniscus that does not disrupt an articular surface. Grade 2 signal is a linear signal that does not disrupt an articular surface and is subdivided into 2A, 2B, and 2C. Grade 2A signal is a linear signal not in contact with an articular surface, grade 2B signal is an abnormal signal in contact with an articular surface on a single image, and grade 2C is an extensive wedge-shaped signal abnormality not in contact with an articular surface. Grade 3 signal is a signal that disrupts an articular surface and indicates a meniscal tear[9,10].

Statistical Analysis

For demographic, clinical, laboratory, and imaging characteristics, categorical variables were summarized by frequency and percentage, whereas continuous variables were summarized by mean and SD. We used Wilcoxon rank-sum tests for continuous variables and Pearson's χ^2 tests for categorical variables in subgroup analysis.

Inter-rater reliability for meniscus changes was determined on a random subset of 45 deidentified knee MRIs read by 2 independent raters. Inter-rater reliability was assessed by estimating the S (concordance) statistic, along with a 95% confidence interval. Reliability estimates were interpreted based on definitions used by Fleiss[11] and Cicchetti and Sparrow[12]: <0.40 as poor, 0.40 to 0.59 as fair, 0.60 to 0.74 as good, and >0.74 as excellent.

Source of Funding

None of the authors received financial support related to this study.

Results

In total, 87 patients (10.6 ± 3.9 years, 68.9% male) fulfilled the inclusion and exclusion criteria and were analyzed in the study. Race and ethnicity of the patients included 67.8% White, 5.7% Black or African American, 4.6% Asian, 8.0% Other, and 13.8% Unable or Declined to Answer. The average patient height was 146.6 ± 22.0 cm, and the average weight was 38.9 ± 17.8 kg. Approximately 64% of patients presented to the emergency department, and the rest presented to an outpatient clinical setting. In terms of clinical symptoms, maximum temperature was 37.6 ± 1.4°C, 44% of patients had a fever, and 21% of patients refused to bear weight. Serum laboratory assessment revealed first and maximum WBC count ($\times 10^3$/mL) of 9.5 ± 2.6 and 9.8 ± 2.7, respectively. First serum and maximum serum CRP were 3.7 ± 4.1 and 4.3 ± 4.6 mg/L, and first serum and maximum serum ESR were 36 ± 23.1 and 44.4 ± 29.2 mm/hr. Furthermore, 61% of patients underwent joint aspirations and had a mean joint fluid WBC count ($\times 10^3$/mL) of 60.0 ± 3.9 (Table I).

TABLE I Patient Characteristics (n = 87)*

Characteristic	
Demographic	
Age at presentation (yr)	10.6 ± 3.9
Male sex	60 (69.0%)
Race	
White	59 (67.8%)
Black or African American	5 (5.7%)
Asian	4 (4.6%)
Other	7 (8.0%)
Unable or declined to answer	12 (13.8%)
Height (cm) (n = 70)	146.6 ± 22.0
Weight (kg)	38.9 ± 17.8
Presented to the emergency department	56 (64%)
Clinical symptoms	
Maximum temperature (°C) (n = 81)	37.6 ± 1.4
Had a fever (n = 86)	38 (44%)
Refused to bear weight	18 (21%)
Laboratory values	
First serum WBC count (×10^3/mL) (n = 82)	9.5 ± 2.6
Maximum serum WBC count (×10^3/mL) (n = 82)	9.8 ± 2.7
First serum CRP (mg/L) (n = 68)	3.7 ± 4.1
Maximum serum CRP (mg/L) (n = 77)	4.3 ± 4.6
First serum ESR (mm/hr) (n = 77)	36 ± 23.1
Maximum serum ESR (mm/hr) (n = 82)	44.4 ± 29.2
Underwent joint aspiration (n = 82)	50 (61%)
Joint fluid WBC count (×10^3/mL)	60.0 ± 3.9

*CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, and WBC = white blood cell.

Knee MRIs of the patients were evaluated for meniscal changes according to the classification system by Loytsch et al. and Dillon et al. outlined above[9,10]. Figure 1 shows MRI of a patient with typical features of Lyme arthritis and meniscus tear (Fig. 1). Table II summarizes the meniscus pathology noted in patients with Lyme arthritis. Fourteen (16%) patients had grade 1 or higher meniscal changes with 4 (5%), 3 (3%), and 7 (8%) patients having grade 1, grade 2, and grade 3 meniscal changes, respectively (Table II). Only 1 of the 14 patients with meniscal changes on MRI underwent surgical treatment (a partial meniscectomy) given concern for continued symptoms in association with significant meniscal tear and evidence of displacement. In a subgroup analysis, patients with meniscal pathology on the MRI had a significantly higher mean age (12.6 ± 2.7 years vs 10.2 ± 4.0 years, p = 0.05) compared with those without. There was no statistically significant difference between patients with and without meniscal abnormality on imaging in terms of sex (78.6% male vs 67.1% male, p = 0.59).

There was excellent inter-rater reliability based on a random subset of 45 deidentified knee MRIs for all variables assessed including lateral meniscus anterior horn, lateral meniscus posterior horn, medial meniscus anterior horn, and medial meniscus posterior horn (Table III).

Discussion

The aim of this study was to identify the incidence of meniscal pathology on MRI in children and adolescents with Lyme arthritis. Of the 87 pediatric patients with serologically confirmed Lyme arthritis and MRI of their affected knee, 16% had meniscal abnormality on MRI with 8% having grade 3 changes. The assessment by 2 independent raters demonstrated excellent inter-rater reliability. The one patient who underwent surgical intervention presented with increasing pain and swelling in the right knee, which was associated with a direct contact lacrosse injury. He was initially evaluated in an urgent clinic, but subsequent blood work was positive for Lyme disease and MRI showed popliteal lymphadenopathy and synovitis consistent with Lyme disease. MRI also showed a large medial meniscus tear with displacement associated with a parameniscal cyst. He was treated for Lyme disease with a month of doxycycline and underwent arthroscopic partial medial meniscectomy after completion of antibiotic treatment. Intraoperatively, medial meniscus was noted to have an unstable displaced degenerative tear extending from the midbody to the posterior horn with poor tissue quality. The meniscus was deemed unrepairable, and the inner 30% of the medial meniscus was removed. Although the incidence of meniscal abnormalities in children is unknown, these results indicate the coexistence of Lyme arthritis and meniscal abnormalities in the pediatric population. Meniscal signal changes by themselves do not necessarily indicate the presence of a tear, but this study underscores the usefulness of MRI as a diagnostic tool in pediatric patients who present with symptomatic monoarthritis. In addition to aiding in the diagnosis of Lyme disease, MRI can identify additional articular abnormalities such as meniscal disease.

Lyme disease is named after the town of Lyme, Connecticut, where it was first identified in 1977[13]. Lyme has a bimodal distribution with highest rates of Lyme disease in individuals 5 to 9 years of age and 55 to 59 years of age[1]. Prevalence of Lyme disease remains high among the endemic regions in the United States, which is not confined to the northeast region. States with high incidence of Lyme disease include Connecticut, Delaware, Maine, Maryland, Massachusetts, Minnesota, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont, Virginia, and Wisconsin[1]. Infection can occur year-round, but months with the highest number of cases are June, July, and August[14]. Lyme disease is no longer a disease of endemic regions with a recent estimate based on commercial insurance claims data suggesting close to 20% of the 476,000 patients diagnosed and treated with Lyme in the United States annually are from nonendemic states[15]. Patients presenting with Lyme arthritis are often treated with doxycycline therapy (100 mg for 28 days) with additional therapy based on

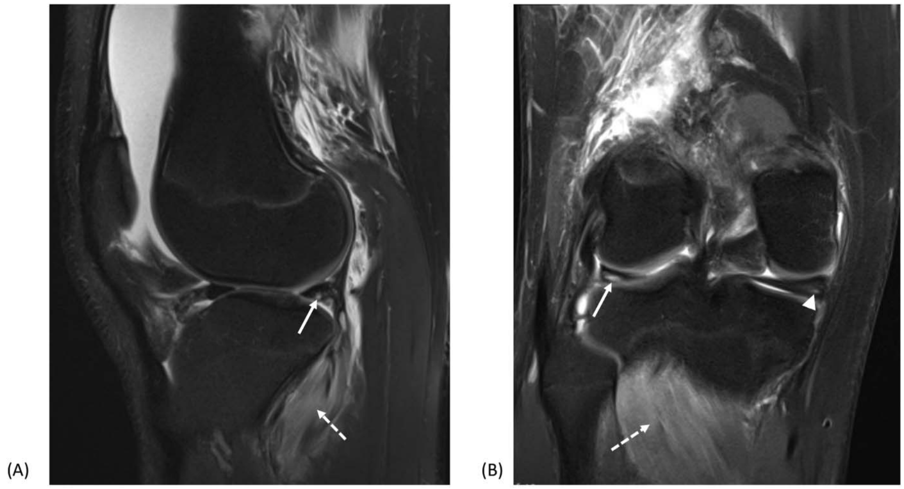

Fig. 1
Patient with Lyme arthritis and meniscus tear. Fourteen-year-old boy with Lyme arthritis of the right knee and posterior horn lateral meniscus tear as well as posterior horn medial meniscal signal abnormality. Sagittal T2-weighted magnetic resonance (MR) image with fat suppression (**Fig. 1-A**) and coronal proton density-weighted MRI with fat suppression (**Fig. 1-B**) show typical features of Lyme arthritis including large joint effusion with synovitis and myositis of the popliteus muscle (dashed arrow). Linear increased fluid signal in the posterior horn of the lateral meniscus extends to the inferior surface (solid arrow) indicating a tear. Globular signal abnormality in the posterior horn of the medial meniscus does not extend to the surface (arrowhead).

response[3]. For patients with refractory Lyme arthritis that does not improve with antibiotics, arthroscopic synovectomy can be considered. The effect of Lyme arthritis on meniscal pathology is thus far unknown, and a better understanding of the relationship may aid in treatment decisions in the future.

After the initial tick bite, Lyme arthritis can result from invasion of spirochete into synovial joints, triggering an inflammatory response in the synovial tissue[14]. Resulting synovial hypertrophy, vascular proliferation, and infiltration of mononuclear cells can induce accumulation of neutrophils, immune complex, complement, and cytokines in the synovial fluid, leading to acute arthritis[14]. Usually, Lyme arthritis is treated with antibiotics with excellent prognosis, but sometimes, the inflammatory process can last after the resolution of active infection, resulting in refractory Lyme arthritis[16]. Unlike bacteria that cause septic arthritis, *Borrelia burgdorferi* has not been shown to directly produce collagenases and other enzymes that destroy the joint extracellular matrix[17,18]. Instead, *Borrelia burgdorferi* causes chondrocytes to increase production of matrix metalloproteinases, which leads to degradation of extracellular matrix proteins, collagen, and proteoglycans, and contributes to cartilage damage[14]. Lyme disease is associated with articular cartilage damage in 25% of adult patients with chronic Lyme arthritis, most commonly in the knee joint and correlated with patient age[19,20]. As published in a case report by Tran and Milewski, authors of this article have previously noted poor quality meniscus tissue in a patient with Lyme arthritis, breaking down easily with arthroscopic intervention and requiring more extensive resection in the setting of a tear[3]. Furthermore, chondrocalcinosis can present in Lyme arthritis as fine, delicate, linear calcification of articular cartilage or as more extensive calcification of fibrocartilage on x-ray[20].

TABLE II Meniscal Pathology (N = 87)

Characteristic	
Meniscal pathology (all)	14 (16%)
Grade 1	4 (5%)
Grade 2	3 (3%)
Grade 3	7 (8%)
Surgery	
Partial meniscectomy	1 (1%)

Review of the literature reveals a few reports on the association between Lyme arthritis and meniscal pathology. Schoen et al. in 1991 described arthroscopic synovectomy as treatment for refractory Lyme arthritis by studying 20 patients 10 to 60 years of age. Of the 20 patients, they found that 6 patients, including 4 with chondromalacia, had partial tears of medial or lateral meniscus[21]. Tran and Milewski in 2017 reported on a case of refractory Lyme arthritis in an adolescent patient who was found to have a concomitant medial meniscal tear extending from the midportion of the body to the posterior horn[3]. In addition, although not directly commenting on meniscal pathology, Lawson and Steere in 1985 studied 25 patients with Lyme arthritis and noted calcifications in both the lateral and medial menisci of a knee in one patient[22].

MRI can be used to identify meniscal tears and meniscal signal changes in pediatric patients with Lyme arthritis. Future longitudinal studies in patients with Lyme disease and coexistent meniscal pathology may aid in understanding the relationship between meniscal abnormalities and Lyme arthritis and perhaps prevent the need for an unnecessary surgical

TABLE III Inter-rater Agreement Summary for a Subsample of 45 Radiographs Read by 2 Independent Raters*

Measurement	S (95% CI)
Lateral meniscus anterior horn	1.00 (1.00-1.00)
Lateral meniscus posterior horn	0.86 (0.67-0.001)
Medial meniscus anterior horn	0.91 (0.77-1.00)
Medial meniscus posterior horn	0.81 (0.63-0.95)

*CI = confidence interval, and S = concordance statistic.

intervention. Although MRI is an expensive modality and may require sedation in very young children, it can be used in children to aid in diagnosis and to reveal further pathology.

This study has several limitations. Given the retrospective design of the study and involvement of a single institution, this study is limited by the available sample size. This study only completed inter-rater reliability testing for meniscal signal abnormality. The study findings are also restricted to pediatric patients, given that adult patients are more likely to have coexisting or pre-existing meniscal pathologies including degenerative changes.

Physicians should be aware of potential meniscal changes in young patients who present with symptomatic knee effusion because of Lyme arthritis. The presence of meniscal pathology in Lyme arthritis may be an important consideration in further management particularly in the setting of refractory Lyme arthritis. Future clinical and in vitro research to evaluate the effect that Lyme arthritis has on meniscal tissue should be considered. Usage of MRI to identify incidences of meniscal pathology in young patients with Lyme arthritis presents an interesting diagnostic tool that should continue to be evaluated.

Conclusion

Patients with Lyme arthritis have a notable rate of meniscal signal changes on MRI. Management of these patients will need to consider the possible coexistence of meniscal pathology in addition to treatment of their Lyme arthritis. ■

Matthew D. Milewski, MD[1,2]
Kirsten Ecklund, MD[2,3]
Sang Won Lee, MSc[1,2]
Ryan P. Coene, MS[1]
Ryan M. Sanborn, BA[1]
Emma C. Gossman , BS[1]
Patricia E. Miller, MS[1]
Benton E. Heyworth, MD[1,2]
Yi-Meng Yen, MD, PhD[1,2]

[1]Department of Orthopaedic Surgery–Division of Sports Medicine, Boston Children's Hospital, Boston, Massachusetts

[2]Harvard Medical School, Boston, Massachusetts

[3]Department of Radiology, Boston Children's Hospital, Boston, Massachusetts

E-mail address for M.D. Milewski: Matthew.Milewski@childrens.harvard.edu

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