Review Article

Lyme Disease Presenting as a Spontaneous Knee Effusion

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Abstract

Musculoskeletal complaints, which are frequently associated with Lyme disease, often prompt patients to see a physician. In particular, transient episodes of spontaneous knee effusion are common early in the progression of Lyme disease, and, if left untreated, 60% of patients diagnosed with the disease develop Lyme arthritis. This disease is easily treated with antibiotics; therefore, inclusion of Lyme disease in the differential diagnosis as a potential cause of a spontaneous knee effusion can prevent the development of more severe symptoms associated with the disease. However, the time required to receive test results and the inconsistencies between serum and synovial tests can complicate diagnosis of the disease.

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Lyme borreliosis, or Lyme disease, is the most common vector-borne illness in the United States.[1] However, variability in the presentation of the disease can make accurate diagnosis difficult. Approximately 30,000 new cases are reported to the Centers of Disease Control and Prevention each year, but preliminary data suggest that the actual infection rate may be up to 300,000 new cases annually.[2-4] In 2009, 95% of disease transmissions were reported from 12 states, specifically those clustered in the Northeast (from Maine to Maryland), Midwest (Wisconsin and Minnesota) and West (northern California and Oregon).[5,6]

Transmission occurs when an infected nymphal tick of the *Ixodes ricinus* species complex bites a human and remains attached for at least 24 hours[7] (Figure 1). This allows time for the *Borrelia burgdorferi* spirochetes to undergo phenotypic changes that cause them to migrate from the gut of the infected tick through the saliva and into human blood.[6] Most transmissions occur in the late spring and summer, but little seasonal transmission has been noted in patients who present without the hallmark symptom of early Lyme disease, the erythema migrans rash[5,8,9] (Figure 2).

Lyme disease has a bimodal age distribution, with peaks reported in patients aged 5 to 9 years and 55 to 59 years,[3] but the disease should be considered in the differential diagnosis of patients with potential exposure to ticks and symptoms of the disease.

Differential Diagnosis for Spontaneous Knee Effusion

Spontaneous knee effusions can present as traumatic, septic, or arthritic in appearance. If a spontaneous knee effusion is the result of Lyme disease, it may have a presentation similar to that of either a septic or arthritic knee, depending on the stage of disease (Figure 3).

Effusion Related to Trauma

Effusion can develop following osseous, ligamentous, or meniscal injury.

If no injury or traumatic event can be identified, the clinician should investigate the patient's knee alignment and consider the possibility of an overuse injury. Although osteoarthritis is usually characterized by a gradual onset, a flare-up may result in spontaneous knee effusion. Once traumatic and mechanical origins have been excluded, infectious and immunologic causes should be considered.

Effusion Related to Infection

Erythema and warmth can signify an infection. Osteomyelitis, several forms of arthritis (eg, bacterial septic, gonococcal, viral), tuberculosis, and endocarditis are potential causes of knee effusion. Common viruses that cause knee effusions include parvovirus, hepatitis B, hepatitis C, rubella, and alphaviruses.[10] Fungal arthritis is rare, but it should be considered as part of the differential diagnosis in immunocompromised patients. Effusion associated with seronegative reactive arthritis (Reiter syndrome), acute rheumatic fever (ARF), and poststreptococcal reactive arthritis (PSRA) is fairly common, as well. A recent history of gastrointestinal illness may indicate Reiter syndrome, whereas a pharyngeal infection would raise suspicion of ARF in the setting of two major Jones criteria (ie, arthralgia, prolonged PR interval, elevated erythrocyte sedimentation rate [ESR] and/or C-reactive protein level, and fever). If the criteria are not met, suspicion of PSRA is raised. In addition, ARF is associated with a polyarthritis, whereas PSRA more commonly presents as monoarthritis.[10]

Effusion Related to Crystalline-induced Arthritis

Gout and pseudogout are infiltrative diseases that frequently produce crystal-induced arthritis in adults, and the presentation is similar to that of septic arthritis. Risk factors for these diseases include a history of renal stones, increased alcohol consumption, a high purine diet, and the use of diuretics.[11] Hypersensitivity to penicillin or sulfa-containing drugs can cause a response similar to that of serum sickness. Fever, lymphadenopathy, rash, proteinuria, and arthralgia are more common symptoms, but knee effusion may occur.[10]

Figure 1

Photograph of a tick nymph after it attached to a human source for >24 hours. (Courtesy of the Centers for Disease Control and Prevention, Atlanta, GA.)

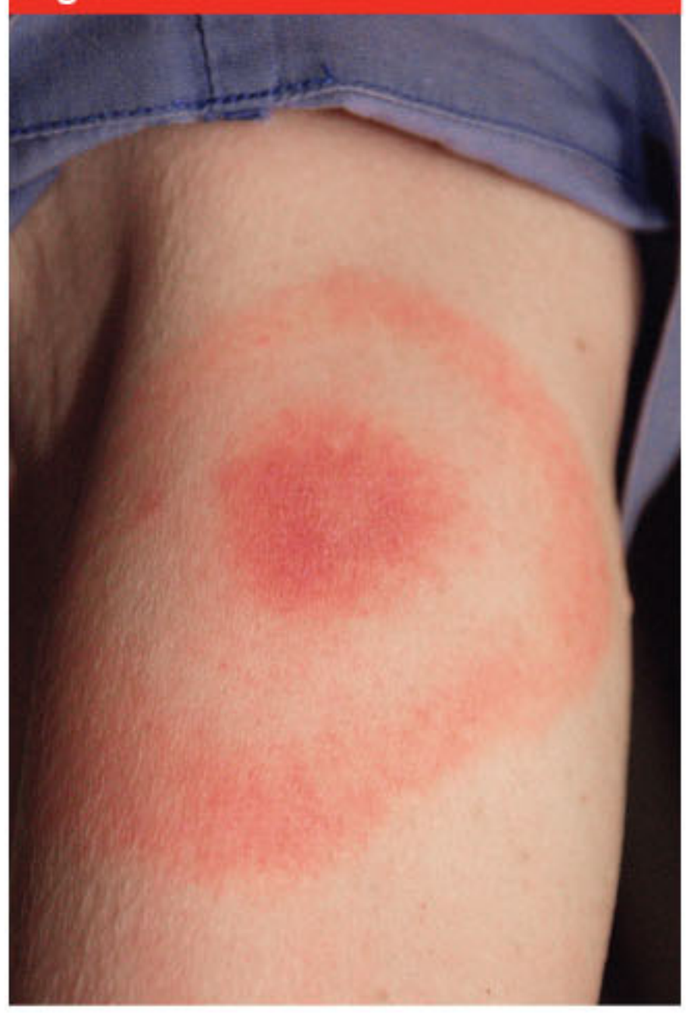
Effusion Related to Vascular Conditions and Neoplasms

Vasculitis (notably Henoch-Schönlein purpura and Wegener granulomatosis), bleeding disorders, and vascular fragility caused by a vitamin C deficiency can cause hemarthrosis.[10,11] In the setting of effusion with a hematologic origin, the joint is typically painful and warm, similar to a septic joint. Synovial hemangiomas and pigmented villonodular synovitis can recur as a nontraumatic hemarthrosis of the suprapatellar pouch.[10] Familial Mediterranean fever or recurrent polyserositis has reportedly caused massive knee effusions in Sephardic Jews and those of Armenian, Turkish, or Arab descent.[10]

Patients with hemophilia may present with a spontaneous knee effusion that has an appearance similar to that of an effusion related to infection. Although trauma most likely precipitated bleeding into the joint, it was likely so minor that the patient or parent may not recall the event. Hemophilia A, or factor VIII deficiency, is the most likely form of the disease to present as a hemarthrosis, and it is typically diagnosed in children younger than 3 years.[10]

Certain benign tumors and neoplasms, including leukemia, lymphoma, Ewing sarcoma, osteosarcoma, synovial sarcoma, and metastatic disease, may present with a knee effusion before other abnormalities are detectable. If night sweats, night pain, fever, and unintentional weight loss accompany the effusion, further oncologic workup should be done.[11]

Figure 2

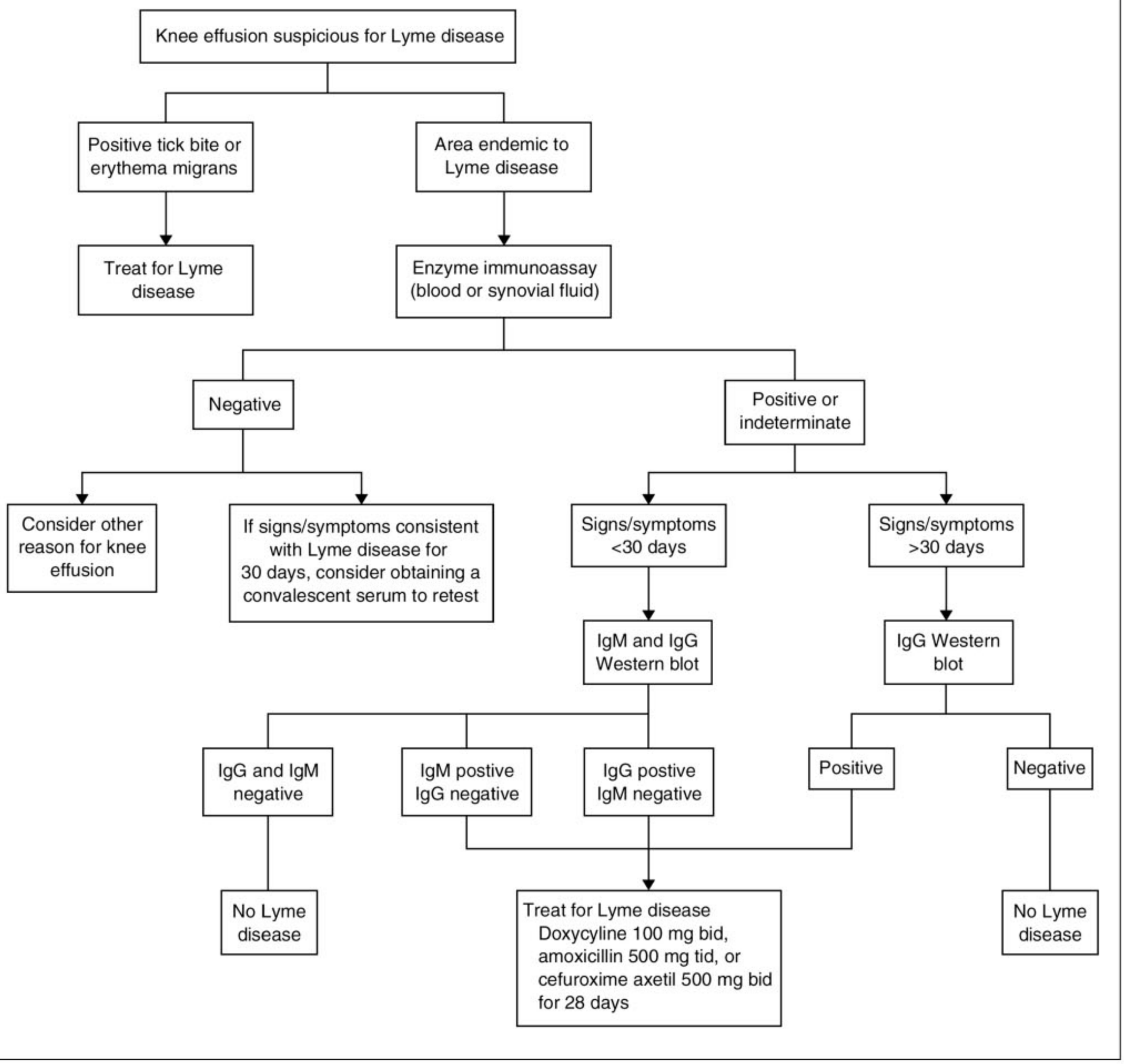


Photograph of the arm demonstrating an erythema migrans rash, which is the hallmark feature of patients with early Lyme disease. (Courtesy of the Centers for Disease Control and Prevention, Atlanta, GA.)

Rheumatologic Causes of Effusion

Rheumatologic causes of effusion, specifically the spondyloarthropathies of childhood, psoriatic arthritis,

Figure 3



Diagnosis and treatment algorithm for patients who present with a knee effusion suspicious for Lyme disease.

reactive arthritis, and those causes associated with gastrointestinal diseases (eg, irritable bowel syndrome, uncontrolled celiac disease) should be included in the differential diagnosis. Systemic lupus erythematosus causes polyarthritis and also leaves patients more susceptible to bacterial infection. Approximately one half of patients with Behçet disease have arthritis, which commonly presents in the knee.[12] Knee effusions associated with juvenile idiopathic arthritis (JIA), especially in the pauciarticular form, are easily confused with those associated with Lyme disease in young children. It should be noted that, in areas of the United States where Lyme disease is endemic, the prevalence of Lyme arthritis in children who present with a spontaneous joint effusion is 31% to 45%.[13]

Clinical Presentation of Lyme Disease

The progression of Lyme disease can be divided into four stages: early localized, early disseminating, late

disseminating, and posttreatment syndrome. The typical presentation occurs 3 to 30 days after infection and includes fatigue, chills, fever, headache, muscle and joint aches, and swollen lymph nodes with or without an erythema migrans rash.[14] If left untreated, Lyme disease can progress to include severe cardiac, neurologic, and musculoskeletal symptoms.[15]

Early symptoms are not always observed. In a study of 104 patients, approximately 20% of patients with Lyme disease never found a rash and, in another study of 55 patients, 84% did not recall a tick bite.[8,16] For many patients, even when they experience early localized flu-like symptoms, they do not consider them significant enough to justify a doctor's appointment. Therefore, they wait to seek treatment until the more acute symptoms of early disseminating or late disseminating Lyme disease occur.

Knee effusion may appear in the early disseminating stage of the disease, weeks to months after infection or as part of Lyme arthritis in the late disseminating stage of the disease (Figure 4). Knee pain may begin as migrating arthralgia, with swelling affecting one or two large joints at a time.[17] The knee is one of the most common places for a tick bite, which may explain why knees are symptomatic early in the progression of the disease.[15,18] Overall, the knee is by far the most commonly affected joint, and episodes of effusion can last from a few days to years if untreated.[19,20] The effusion tends to grow large, with pain that is out of proportion.[17,18] It may be accompanied by Baker cysts that are easily ruptured.[17,21] Suspicion of Lyme arthritis is more likely in children than in adults. However, Daikh et al[22] compared the presentation and treatment of the condition in children and adults and found no significant difference between the two groups in terms of joint swelling or erythema at presentation. The duration of symptoms at presentation tends to be shorter in children than in adults. Daikh et al[22] compared the presentation of Lyme arthritis in 29 adults and 52 children and found that 46 children (88%) presented within 2 weeks of symptom onset versus 15 adults (52%); 9 children (18%) versus 8 adults (28%) waited ≥6 weeks to seek medical attention.

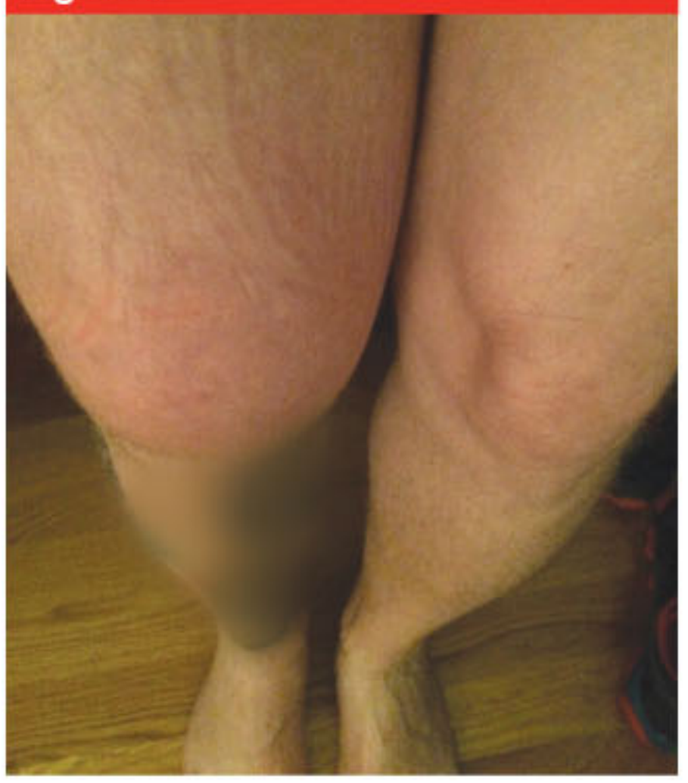
If left untreated, 60% of patients with Lyme disease eventually develop Lyme arthritis, with the most severe cases leading to permanent joint damage.[5] In an early study of 25 patients with Lyme arthritis, Lawson and Steere[23] found that 15 patients had knee effusions, 3 had soft-tissue swelling, 6 had infrapatellar fat pad edema, 5 had enthesopathy, and 6 had a loss of cartilage. The authors also observed cartilage calcification in two patients and calcification of the meniscus in one patient. As the disease progressed, juxta-articular osteoporosis, cartilage loss, and bone erosion were observed. In addition to direct joint destruction, Lyme arthritis has been identified as a risk factor for the later development of degenerative arthritis.[21]

Other Causes of Knee Effusion

Septic Arthritis

Early differentiation between Lyme and septic arthritis is critical because the latter is a medical emergency. In a matter of days, enzymatic release by both invading bacteria and host synovial cells and chondrocytes rapidly degrades articular hyaline cartilage, destroying the joint. Although the Kocher criteria (ie, inability to bear weight, history of fever ≥101.3°F [38.5°C], white blood cell [WBC] count ≥12,000 cells × 10^3 per mL, and ESR ≥40 mm/h) were originally developed for the pediatric hip, it may be helpful in identifying patients at high risk of septic

Figure 4



Photograph of the lower extremities demonstrating a spontaneous knee effusion.

arthritis.[13,24,25] The disproportional relationship between swelling and self-reported pain is the most characteristic presentation of a knee affected by Lyme disease. However, patients with septic arthritis typically refuse to bear weight and are more likely to present with a fever ≥101.3° F (38.5°C) than are patients with Lyme arthritis.[13,24] Erythema in the setting of a warm, swollen joint with limited range of motion is more likely the result of septic arthritis than Lyme disease.[10,20]

Pauciarticular Onset Juvenile Idiopathic Arthritis

Before Lyme disease was described in the literature, an aberrant number of children in Lyme, Connecticut, were diagnosed with JIA, which can present in several forms, including pauciarticular (fewer than five joints affected), polyarticular (five or more joints affected), or systemic. The pauciarticular form is most important for Lyme disease comparison because of the similarities in presentation.[10] JIA most commonly occurs in children aged 2 to 3 years and is rarely diagnosed in those older

than 10 years; this is younger than the average age of patients diagnosed with Lyme disease. The duration of symptoms is another distinguishing characteristic. For diagnosis of JIA, symptoms must persist for a minimum of 3 months in the setting of monoarthritis or 6 weeks if multiple joints are affected. Synovitis, effusion, soft-tissue swelling, and osteopenia are all potentially visible on radiography.[10] In the pauciarticular form, children generally do not appear sick, but patients with JIA can present with iridocyclitis, which is not associated with Lyme disease.[20]

Diagnostic Tests

Blood

The current standard of care is a two-tier blood test, specifically with an enzyme-linked immunosorbent assay (ELISA) and an immunoblot analysis for confirmation. The ELISA provides an objective estimate of *B burgdorferi* antibody concentration, but it lacks sufficient specificity to be used as a stand-alone test.[2,26] Western blot analysis is considered positive if either two immunoglobulin (Ig) M or five IgG bands for specific *B burgdorferi* are present; however, because of the lack of automation, the results are too subjective and yield too many false-positives to be considered a primary test.[2,6] For early Lyme disease, the two-tiered test has a sensitivity, specificity, and positive predictive value of 48%, 99.5%, and 66%, respectively.[27]

Other tests may be helpful for differentiating between Lyme disease and other causes of knee effusion. Barring coinfection, patients with Lyme disease have a normal WBC count, packed cell volume to hemoglobin concentration, and platelet count, thereby ruling out acute leukopenia and leukemia.[6,10] However, 35% of Lyme patients may have elevated liver function levels during the early-stage.[6] ESR and C-reactive protein level are frequently tested to rule out noninflammatory sources of effusion, but results of these tests are similar in the setting of septic arthritis and Lyme disease.[13] In patients with Lyme disease, the ESR is frequently elevated but rarely >88 mm/h.[6] Testing for the presence of antinuclear antibodies can rule out systemic lupus erythematosus and may be helpful in identifying JIA, but caution is warranted because this test has a low sensitivity and specificity for diagnosis of JIA.[10]

Synovial Fluid

Synovial fluid testing for Lyme disease is somewhat controversial given the lack of FDA-standardized testing procedures and the potential for nonspecific results. Nonetheless, synovial testing can help to confirm a diagnosis of Lyme disease or rule out other causes of spontaneous knee effusion.[8,10,28,29] An arthrocentesis may temporarily alleviate some symptoms as fluid is removed. Normal synovial fluid is acellular, clear, and viscous, with a protein concentration resembling plasma, but the glucose concentration is one third of that normally seen in plasma.[10] Samples are typically sent for culture and Gram stain as well as chemical tests to check the levels of lactate dehydrogenase, protein, and glucose as well as the WBC count. The presence of abnormal cells, including crystals or malignancies, is examined microscopically.[10]

Polymerase chain reaction (PCR) tests have been used to detect *B burgdorferi* DNA to confirm a diagnosis of Lyme disease, but the sensitivity of PCR tests is relatively low.[29] A Western blot test can also be used to check the synovial fluid for anti-Borrelia IgG antibodies, but no studies to date have proven the clinical accuracy of this test for diagnosis of Lyme disease. In seronegative patients, banding may occur in the test secondary to the sticky nature of the immunoblot fluid or the immunopathogenesis of another process.[28]

The WBC count can aid the clinician in differentiating between the origins of effusion with similar presentations. Lyme disease typically presents with a significantly higher WBC concentration than does aseptic arthritis and a significantly lower concentration than that associated with septic arthritis.[8] In the setting of Lyme disease, joint aspirate typically has a cell count of 1,000 to 50,000 WBC cells/μL and is primarily composed of neutrophils, but the Gram stain may be negative.[9,10] A normal cell count is <500 cells/mm^3 and, in patients with osteoarthritis or septic arthritis, the counts are typically <2,000 cells/mm^3 and >100,000 cells/mm^3, respectively.[9] The odds ratio for septic arthritis increases from 2.9 to 28, with cell counts of 25,000 cells/μL and >100,000 cells/μL, respectively.[10] Gout, pseudogout, and other inflammatory diseases have cell counts similar to those of Lyme disease, ranging from approximately 2,000 cells/mm^3 to 100,000 cells/mm^3, but these counts are usually in the tens of thousands.[9] When the diagnosis cannot be determined by the cell count alone, clinical features and radiography can help the clinician distinguish between potential causes of effusion (Table 1).

Other Tests

Imaging can help the clinician assess the extent of joint destruction at presentation and monitor disease progression. Radiography may be used to assess for deformity of the joint surface, osteopenia, evidence of trauma, or indications of infection.[30] MRI is useful for identifying changes in the synovium and bone, and ultrasonography can be used to assess the

Table 1

Blood and Synovial Fluid Analysis Results for Conditions Presenting With Spontaneous Knee Effusion

Condition	Blood Analysis	Synovial Analysis
Normal	ESR <20 mm/h CRP level <1 mg/L Hematocrit 36% to 51% Platelets 150–350 × 103/μL Leukocytes 4.00–11.0 × 10^9/L	Acellular, clear, viscous,1/3 glucose concentration of plasma <500 WBCs/mm^3 <25% PMNs
Lyme disease	Positive ELISA and positive immunoblot (2 IgM or 5 IgG bands present) Elevated ESR up to 88 mm/h CRP level >10 mg/L Normal leukocytes, hematocrit, and platelets	1,000–50,000 WBCs/mm^3 >50% PMNs Negative Gram stain Normal glucose
Osteoarthritis	Normal platelets, hematocrit, ESR, leukocytes, and CRP level	Yellow, transparent, slightly decreased viscosity <2,000 WBCs/mm^3 <25% PMNs Normal glucose Normal complement
Septic arthritis	ESR >40 mm/h CRP level >10 mg/L	>100,000 WBCs/mm^3 >75% PMNs 3–5 g/dL protein Low glucose
Acute leukopenia and leukemia	Leukocytes <4 × 10^9/L	None
Gout, pseudogout	Uric acid levels may be normal or elevated, but are not correlated with severity of an attack and are not routinely checked.	2,000–100,000 WBCs/mm^3 Monosodium phosphate or calcium pyrophosphate dehydrate crystals are present. Low viscosity 90% PMNs

CRP = C-reactive protein, ELISA = enzyme-linked immunosorbent assay, ESR = erythrocyte sedimentation rate, PMN = polymorphonuclear neutrophil, WBC = white blood cell

extent of joint effusion, synovial thickening, and cartilage damage.[10,21] It is rare to find evidence of permanent joint changes unless the patient has late-stage disease.[31]

If septic arthritis is suspected, especially in an adolescent, clinicians should consider ordering a urinalysis. *Neisseria gonorrhea* is the leading cause of bacterial septic arthritis in adolescents.[10] Additionally, pyuria can be present in reactions that resemble serum sickness or in the setting of urethritis, and microscopic hematuria can be a sign of kidney disease or vasculitis.[10]

Limitations of Testing

The length of time before laboratory results become available is one of the drawbacks of tests used to diagnose Lyme disease. When septic arthritis is included in the differential diagnosis, treatment must begin immediately while the clinician awaits the results of the serum study for Lyme disease. However, this can subject patients to risks secondary to unnecessary procedures and delays in the start of treatment for Lyme disease.

The lack of a sensitive and specific test for early Lyme disease is also troublesome; delaying treatment has been associated with a higher risk of permanent joint damage and other chronic complications of the disease, even after treatment.[32] Because the two-tier blood test relies on the presence of antibodies, patients with recent tick exposure will test negative. In a prospective study of 104 patients with early Lyme disease, Rebman et al[16] found that only 35.6% of patients tested positive during acute presentation, and a total of 60.6% tested positive by the 3- to 4-week follow-up. Interpretation of the test also depended on timing; if symptoms persisted for <30 days, a positive IgM or IgG result was sufficient to confirm diagnosis. However, if symptoms persisted for >30 days, a positive IgG was required to confirm the diagnosis.[16] Determining how long symptoms persisted can be difficult if the patient does not know the timing of tick exposure and if erythema migrans is not the presenting symptom.

Only 7.4% of patients had a positive IgG test at either time point in the study by Rebman et al.[16] Despite these shortcomings, in the early stage of the disease, the two-tier test is extremely accurate for diagnosis of late-stage Lyme disease, at which time patients are more likely to present with a spontaneous knee effusion. Branda et al[27] and Barclay et al[28] reported that the two-tier blood test has a sensitivity of 100% for detection of late-stage disease.

Reports of seronegative Lyme arthritis, with detectable *B burgdorferi* DNA in synovial fluid or tissue, have been documented in the literature. Some patients have shown only a T-cell response to *B burgdorferi* on a lymphoproliferation assay.[33-35] The cause of seronegativity is not yet understood. It is possible that the antibodies are complexed and not detectable on ELISA or that early antibiotic exposure left patients permanently seronegative, even if the antibiotics were insufficient to cure symptoms.[15,33]

Future Tests

The low sensitivity and positive predictive value of the two-tier blood test for detection of early-stage Lyme disease has prompted the development of alternative testing modalities. In particular, attention has been paid to the C6 peptide of the *B burgdorferi* variable major protein-like sequence-expressed lipoprotein.[27,29] Branda et al[27] found that the test had a sensitivity and specificity of 64% and 98.4%, respectively, but the positive predictive value was only 43%. However, using a two-tier approach to the C6 ELISA yielded the same sensitivity (64%) and a slightly higher specificity (99.5%) compared with the traditional two-tier test, with a positive predictive value of 70%, which is better than both the single-tier and traditional two-tier values.

Recently, Halpern et al[2] developed and tested a hybrid antigen immuno-PCR test. The authors reported that the test had a sensitivity of 69% and a specificity of 98%, both higher than the reported sensitivity and specificity for the two-tier test, 59% and 97%, respectively. More studies are needed to determine how titers change over time and whether the antigens will be able to specify specific stages of the disease.

Management

Lyme disease is readily treatable with antibiotics; 99% of patients diagnosed during the early localized infection period and 90% of patients with Lyme arthritis respond to therapy.[7,36] The Infectious Disease Society of America recommends a 28-day course of doxycycline (100 mg twice daily), amoxicillin (500 mg three times daily), or cefuroxime axetil (500 mg twice daily) if there is arthritis but no neurologic symptoms.[37] For children older than 8 years, amoxicillin (50 mg/kg daily in three doses), cefuroxime axetil (30 mg/kg daily in two doses), or doxycycline (4 mg/kg daily in two doses) can be administered.[37] NSAIDs can be used concurrently to treat orthopaedic symptoms. Joint swelling may not resolve immediately. If it does not resolve within several months of treatment, another 4-week course of oral antibiotics or a 2- to 4-week course of intravenous ceftriaxone is recommended. If this additional course of antibiotics does not resolve symptoms and a synovial PCR test result is negative, symptomatic therapy may be used, including NSAIDs, intra-articular corticosteroid injections, or antirheumatic drugs, such as hydroxychloroquine, sulfasalazine, or methotrexate.[9] For patients with advanced musculoskeletal Lyme disease resulting in persistent synovitis that limits function or causes significant pain, an arthroscopic synovectomy is indicated to reduce inflammation.[31,37]

Lyme disease can be treated prophylactically with a single 200-mg dose of doxycycline or 4-mg/kg dose in children aged >8 years, but prophylactic treatment is only recommended if four specific conditions are met. The tick must be positively identified as being a nymph or adult *Ixodes scapularis* tick that has been attached for ≥36 hours (based on engorgement or known exposure time). The local Lyme disease infection rate must be ≥20%, and the patient must not have any contraindications to doxycycline. Prophylaxis must begin within 72 hours of tick exposure. Prophylaxis is not recommended in all cases in which a tick has been found attached to a person's skin because it is rare that a tick is able to stay attached long enough to infect the host; thus, the transmission rate for deer ticks is 1% to 3%.[26] Although the success rate of prophylactic therapy was found to be 87%, the confidence interval ranged widely, from 25% to 98%, calling into question the value of this treatment.[37]

Even with treatment, 10% to 20% of patients experience lingering symptoms, including arthritis, neurologic deficits, and cardiac issues, commonly known as posttreatment Lyme disease syndrome.[38] Patients with this condition may have a genetic variation that could cause an autoimmune response, prolonging inflammation and Lyme disease symptoms.[31,38] Because the symptoms of posttreatment Lyme disease syndrome mimic those of Lyme disease, clinicians evaluating a patient with a spontaneous knee effusion should find out whether the patient has a history of Lyme disease.

Senior Author's Experience

In areas with a high prevalence of Lyme disease, the disease should

always be considered in the differential diagnosis in patients presenting with a spontaneous knee effusion. In states with a low incidence of Lyme disease, the clinician should ask if the patient has traveled to an area where the disease is endemic. Blood or synovial fluid analysis can aid the clinician in the diagnosis of Lyme disease.

Summary and Future Directions

Lyme disease can affect any age group and is most frequently observed in children and middle-aged adults. The best prevention includes wearing long sleeves and pants when outdoors (especially in areas with high grass), reapplication of a DEET-based insect repellent every 1 to 2 hours, and prompt examination of the skin and clothes for ticks after returning inside. However, even with these precautions, ticks can be overlooked. If the physician suspects Lyme disease is the underlying cause of a spontaneous knee effusion, treatment of the disease should be initiated. Antibiotics, preferably doxycycline, can be started after a positive laboratory result. Timely recognition of Lyme disease is important because a delayed diagnosis is associated with increased duration and severity of symptoms during and after treatment, and the potential exists for symptom exacerbation by treatments for other potential causes of knee effusion.

Increased awareness of spontaneous knee effusion as a primary symptom of Lyme disease can aid diagnosis. Additional research on the distinction between Lyme-induced spontaneous knee effusion, which can occur as soon as the early disseminating stage of the disease, and Lyme arthritis (a late-stage manifestation) could help physicians diagnose the specific stage of Lyme disease. This would allow for better assessment of the patient's risk of complications and better symptom management.

As testing modalities improve in accuracy and speed, diagnosis of Lyme disease will become less challenging. The current amount of time required to obtain test results leads to the use of unnecessary and invasive tests and treatments for other causes of knee effusion (eg, septic arthritis). Finally, as our understanding of the *B burgdorferi* spirochete improves, revisiting the development of a vaccine for those living in areas where Lyme disease is endemic will considerably decrease its prevalence.

References

Evidence-based Medicine: Levels of evidence are described in the table of contents. In this article, references 2, 13, 16, 19-21, and 27 are level II studies. References 8, 22, 24, 28, and 31 are level III studies. References 5-7, 9-11, 15, 18, 23, 26, 29, 30, 32, 33, 37, and 38 are level IV studies. Reference 17 is level V expert opinion.

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