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Case Reports and Series

Lyme Disease Manifestations in the Foot and Ankle: A Retrospective Case Series

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ABSTRACT

Lyme disease is the result of *Borrelia burgdorferi* bacterial infection after exposure from a tick bite. A pathognomonic finding in early-stage Lyme disease is an expanding, red macular ring known as erythema migrans. Lyme arthritis is a late-stage manifestation of this disease, affecting the large, weightbearing joints with intermittent pain and swelling. The existing data on Lyme disease and subsequent arthritis have reported manifestations in the lower extremity, primarily in the knee and ankle and less commonly the small joints of the foot. We present a retrospective case series of 11 cases of painful arthritis in the foot and ankle with confirmatory Lyme disease testing.

Surveillance of Lyme disease (LD) by the Centers for Disease Control (CDC) began in 1982. Since 1994, 10,000 to 30,000 new cases annually have been reported in the United States, making it the most common vector-borne disease in the United States (1,2). The northeastern and north central regions of the United States have the greatest prevalence of the *Ixodes scapularis* tick (also known as *I. dammini*) and a prevalence of the preferred host of the ticks, deer (1). Transmission occurs by a bite from an infected tick that has been attached for >24 hours (3). The saliva of the tick with the circulating *Borrelia burgdorferi* spirochete is injected into the host's skin, where an immune reaction precipitates. This allows for bacterial replication in the dermis and a subsequent inflammatory response that presents as an erythema migrans rash (4). Hematogenous dissemination of the spirochete follows, allowing for multiple organ systems to be affected (5).

Lyme arthritis is a late stage manifestation of LD. It most commonly presents in the large, weightbearing, synovial joints and is usually asymmetric. It is also usually pauciarticular or monoarticular and has a bimodal age distribution, with the most commonly affected age groups 5 to 9 and 55 to 59 years (7,8). Approximately 60% of patients with untreated LD will be affected (2). Responses include synovial hypertrophy, infiltration of mononuclear cells, vascular proliferation, and accumulation of cytokines, complement, immune complexes, and neutrophils in synovial fluid (9,10). Matrix metalloproteinase production from chondrocytes is increased, which is thought to lead to cartilage destruction (10).

Clinically, patients present with intermittent episodes of joint pain and swelling. This occurs weeks to months after the presentation of erythema migrans, if any had been documented. Persistent joint pain for months or years can occur in some patients after a series of attacks. An acute and a chronic phase of the arthritis have been described. The acute phase occurs earlier in the disease process and presents as more frequent, intense, and fleeting periods of inflammation. The chronic phase presents weeks to months later as pain that is self-limited, monoarticular, and, occasionally, treatment resistant (6,11). This chronic form is presumed to be an autoimmune response, rather than a prolonged infection of the affected joint (12). Theories include a cross-reaction between the host synovial proteins and anti-*Borrelia* antibodies or focal inflammation mediated by cytokines (12,13).

The published data have shown that the ankle is a commonly affected joint in pauciarticular Lyme arthritis; however, little

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documentation has been presented of involvement of the forefoot. We present the cases of 11 patients with foot and ankle pain of durations varying from 1 month to 1 year who were found to have positive testing results for LD. The areas of complaint varied greatly across multiple locations of the foot and ankle, including ankle edema, diffuse forefoot pain, and pain isolated to individual metatarsophalangeal joints.

Patients and Methods

A single-center, retrospective medical record review was performed using the senior authors' (J.R.M., L.J.C.) practice during a 3-year period (July 31, 2011 through August 1, 2014). The following clinical data were obtained from the private practice electronic database of the senior authors (J.R.M., L.J.C.). The data were identified and recorded for the investigation by 2 of the authors (J.R.M., K.W.D.), using the "International Classification of Diseases, version 9," code 088.81. All patients who had initially presented with lower extremity pain, were not currently being treated for LD, did not have a history of LD, and did have a documented diagnosis of LD with laboratory records available were included in the present study. In accordance with the LD 2-tier testing guidelines, the first required test is the enzyme immunoassay or immunofluorescence assay. If the first test yields a positive or equivocal result, 2 options are available: (1) if the patient has had symptoms for $\leq$30 days, an IgM Western blot is performed; or (2) if the patient has had symptoms for >30 days, the IgG Western blot is performed. The IgM test should not be used if the patient has shown signs or symptoms consistent with LD for >30 days. An IgM Western blot is considered positive when 2 or 3 of 3 bands are positive, and an IgG Western blot is considered positive with $\geq$5 of 10 bands are positive. Patients were only excluded from analysis if the testing was incomplete or yielded a negative result.

Eleven consecutive patients were available in accordance with the selection criteria. All the patients underwent a thorough history and physical examination. In addition to collection of the demographic data, all the patients were queried regarding a complete review of systems and whether the patient could recall tick exposure or a rash consistent with erythema migrans (Table).

Results

Of the 11 patients reviewed, 8 (72.7%) were female and 3 (27.3%) were male. All the patients were permanent residents (>3 years) of the metropolitan-Philadelphia, Pennsylvania, area (endemic region). The symptoms had been present from 1 month to 1 year before the laboratory diagnosis, and the forefoot and ankle shared a similar prevalence of manifestations, 6 (54.5%) and 5 (45.5%), respectively. Only 2 patients (18.2%) recalled an inciting tick bite, and 5 (45.5%) described a rash consistent with erythema migrans. No patients underwent surgical intervention as a result of their LD-associated lower extremity manifestations. After diagnosis, all the patients were promptly referred to local physicians who specialize in the treatment of LD. Five patients (45.5%) were lost to follow-up after referral. The eventual resolution of symptoms after antibiotic treatment was documented in the remaining 6 patients (54.6%) by the senior authors (J.R.M., L.J.C.) with monitored follow-up. The mean average follow-up duration was 24.2 $\pm$ 19.7 (range 8 to 60) weeks.

Discussion

In 1977, LD was originally described after an investigation performed on a group of children living in Lyme, Connecticut, who complained of arthritis. At least 88% of LD cases in the United States reported in any single year occur within only 10 of the 50 states. Those areas highly endemic to LD presentation are represented by Connecticut, Delaware, Maryland, Massachusetts, Minnesota, New Jersey, New York, Pennsylvania, Rhode Island, and Wisconsin (7). Physicians in these highly endemic areas should not only be aware of the propensity for Lyme arthritis presentations, but also should make it a priority to always include LD in their arthritides differential diagnosis.

Table
Patient characteristics

Patient No.	Age (y)	Gender	Lower Extremity Manifestation	Systemic Symptoms (Review of Systems)	Duration (mo)	History of Tick Bite or Rash	Physical Findings	Treatment
1	52	Female	Forefoot	None	1	No/no	Hallux valgus, second hammertoe, pain at first, second, third MTPJs	PO doxycycline for 5 wk; treated with resolution
2	58	Female	Forefoot	Fevers, chills, headaches	1	No/yes	Hallux limitus, generalized forefoot pain	Lost to follow-up
3	11	Female	Ankle	Unilateral paresthesia	2	No/no	Mobile flatfoot, ankle pain throughout range of motion	Lost to follow-up
4	50	Female	Forefoot	Headaches	12	No/no	Generalized forefoot pain	Lost to follow-up
5	51	Male	Ankle	None	12	No/yes	Ankle pain at end range of motion	PO doxycycline for 8 wk; treated with resolution
6	52	Female	Forefoot	None	1	No/no	Short first ray, second hammertoe, generalized forefoot pain	PO doxycycline, azithromycin for 4 wk; treated with resolution
7	63	Male	Ankle	Unilateral paresthesia	3	No/yes	Ankle pain at end range of motion	Lost to follow-up
8	35	Female	Ankle	None	2	Yes/yes	Ankle pain at end range of motion	PO doxycycline for 4 wk; treated with resolution
9	14	Female	Forefoot	Fevers, chills, headaches, changes in vision, nausea, vomiting	12	No/no	Painful effusion at fourth MTPJ	IV metronidazole, azithromycin, ceftriaxone for 6 wk; treated with resolution
10	66	Female	Forefoot	None	1	Yes/yes	Hammertoes 2 to 5, pain at first, second, third MTPJs	Lost to follow-up
11	44	Male	Ankle	None	3	No/no	Ankle pain at end range of motion	PO doxycycline for 4 wk; treated with improvement, continued intermittent pain with eventual resolution

Abbreviations: IV, intravenous; MTPJ, metatarsophalangeal joint; PO, oral.