

Lyme Disease, Initially Misdiagnosed as Rheumatoid Arthritis, Successfully Treated with Long-Term Azithromycin

Guy A. Buonincontro, D.O.

Lyme Disease Treatment and Research Center, Berlin, New Jersey

A 59-year-old white male with a 10-year history of migratory and fixed joint pains, was initially diagnosed and treated as having rheumatoid arthritis (RA). When the patient failed to respond to nonsteroidal anti-inflammatory drugs (NSAIDs), he was placed on hydroxychloroquine sulfate (Plaquenil) and maintained on this for 8 more years, despite nonimprovement. He was eventually diagnosed with Lyme disease and treated with 5 months of azithromycin (Zithromax). He has remained symptom free for 2 years.

Lyme disease is a multisystem disorder caused by the spirochete *Borrelia burgdorferi*. The organism is transmitted to humans and animals mostly by ticks of the *Ixodidae* complex (1-5). In the endemic areas of the northeast and north central United States, the vector is *Ixodes scapularis* (formerly *I. dammini*) (6). *Ixodes pacificus* is the vector in the western states and British Columbia (7-9).

Lyme disease (LD) is often characterized by an expanding skin rash (erythema migrans) and constitutional symptoms such as fever, headache, fatigue, and malaise (10).

If the disease is untreated or treated inappropriately, cardiac, neurologic or joint abnormalities may also occur (7, 10-12). There is also evidence that even properly treated cases can develop these complications.

The diagnosis of LD depends upon the physician's assessment of clinical findings, epidemiological data, and laboratory testing (10, 13). Laboratory confirmation may be difficult with present testing options (14, 15).

CASE REPORT

A 59-year-old white male presented with a 10-year history of migratory joint pain, which had started in the feet and progressed to the lumbar and cervical spines. Eventually, the knees and shoulders became involved. In the last 8 years, the hands had become swollen and painful. These symptoms were associated with fatigue, memory loss, sleep disturbances, and frontal headaches.

In 1984, despite negative serological testing for rheumatoid arthritis (RA), three different rheumatologists recommended treatment for RA. It is not known what clinical criteria were used for this diagnosis. After 2 years of nonresponse to nonsteroidal anti-inflammatory drugs (NSAIDs), the patient was placed on hydroxychloroquine sulfate (Plaquenil), with little response. He remained on Plaquenil and Naprosyn for an additional 8 years.

When first evaluated in our office in August 1992, the patient gave a strong history of tick exposure. He has been also living in an endemic area of Lyme disease (Princeton, NJ). He was unable to close his hands without pain and awoke frequently during the night because of hand, neck, and shoulder pain. Swelling of his fingers (interphalangeal (IP) and metacarpophalangeal (MCP) joints) and limited range of motion of

the cervical spine and shoulders were the only objective physical findings.

Laboratory studies showed a slightly elevated titer of *B. burgdorferi* antibodies (10.9 with neg. 0.0 to 9.0). He had evidence of antibody activity against proteins 39, 41, and 60 kd on western blot IgG.

Sedimentation rate, RA factor, C-reactive protein, and antinuclear antibody (ANA) were all negative. Complete blood count, chemistry profile and thyroid testing were all normal.

In September 1992, the patient was started on azithromycin (Zithromax) 250 mg daily. When evaluated 4 weeks later, the patient was sleeping through the night without pain. His morning stiffness and swelling were gone, and his pain had diminished by 50%. Antibiotics were continued for another month and then decreased to one capsule 3 times a week (Monday, Wednesday, and Friday). This dose was maintained for 3 more months.

The patient experienced no problems with the antibiotics and was able to discontinue both the Naprosyn and hydroxychloroquine sulfate shortly after starting the azithromycin.

The patient was symptom free on March 24, 1993, and remains so today, more than 2 years after stopping azithromycin.

DISCUSSION

Several recent articles have suggested that some physicians have a tendency to over-diagnose and over-treat Lyme disease (13, 15, 16). In May 1994, Schoen stated his opinion as "At the present time, most individuals presenting to physicians with complaints about late Lyme disease do not have Lyme disease!" He quoted a study published by Sigal evaluating the first 100 patients seen at a Lyme disease referral center in central New Jersey (16).

Is it not possible that since 1991, our diagnostic ability has improved to the point where we can better detect cases that were missed earlier?

In 1994, using cytological techniques, Schubert and Greenebaum identified the Lyme spirochete in the vitreous fluids of patients with choroiditis and vitriitis despite the negative serology testing before and after treatment (17). This case would not have been counted by Sigal as a legitimate case of LD as it comes under the heading of argued "seronegative" LD.

Many physicians may not have treated this "rheumatoid arthritis" patient based on positive history alone. Fewer would

have treated him on physical findings alone. Even with a completely negative serology, this patient should be given the benefit of the doubt and given a short course of antibiotics.

The other question this case presents is the treatment for chronic Lyme arthritis.

Lyme arthritis is a late complication of Lyme disease. Chronic Lyme arthritis is defined as 1 year or more of continuous joint inflammation. This occurs in just 10% of Lyme arthritis cases, usually starting during the second or third year of the infection (18-21).

Steere et al. (20) recommended treatment of Lyme arthritis with oral amoxicillin (with probenecid) or oral doxycycline. They prefer the latter since the former does not cross the blood-brain barrier very well. They also state that the main drawback of oral antibiotic therapy is that patients with Lyme arthritis may have latent or active neuroborreliosis, which may be inadequately treated with oral antibiotics. The possible use of IV ceftriaxone for an additional 2 to 4 weeks is recommended in those patients who do not respond to the oral regimen.

CONCLUSIONS

It is frequently suggested that if patients with LD do not respond to conservative therapy, that the diagnosis is incorrect. This principle should apply to all diagnoses. We should not assume diagnosis correct if the patient does not respond after a reasonable trial period of treatment.

All alternative diagnoses should be considered, even if the suggestion comes from the patient. Egos and prejudice should not deter us from including all possible diseases in our differential diagnoses.

Macrolides such as azithromycin have had reported success in treating Lyme disease in Europe and in the United States. Formalized research should be conducted to determine their value in the treatment of LD in all stages.

Reprint requests: Guy Buonincontro, D.O., Berlin Family Practice, 23 Harter Av., Berlin, NJ 08009.

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