Antibiotics, DMARDs Quell Lyme Arthritis

BY DIANA MAHONEY
New England Bureau

BOSTON — Antibiotic therapy decreases the duration of persistent joint inflammation in Lyme arthritis, and disease-modifying antirheumatic drugs can reduce its severity in individuals with antibiotic-refractory disease, Dr. Alan Steere reported at a rheumatology conference sponsored by Harvard Medical School, Boston.

Antibiotics remain the cornerstone of treatment for Lyme arthritis, with most patients responding to a 1-month course of oral doxycycline or amoxicillin, said Dr. Steere of Massachusetts General Hospital, Boston. In patients with mild, residual joint swelling, the oral antibiotic regimen is repeated for an additional 30 days. When joint swelling is moderate to severe, an additional month of intravenous antibiotic therapy with ceftriaxone, cefotaxime, or penicillin is a standard course, he said.

To assess postantibiotic treatment strategies in refractory patients and to compare disease course in antibiotic-responsive and -refractory patients, Dr. Steere and his colleagues reviewed the outcomes of 117 patients seen from November 1987 through May 2004. Of the study group, 50 were antibiotic responsive and 67 had antibiotic-refractory Lyme arthritis.

All patients met Centers for Disease Control and Prevention criteria for Lyme arthritis as well as the Infectious Diseases Society of America guidelines for antibiotic treatment. The antibiotic-refractory patients tended to receive intra-articular steroids more often than the antibiotic-responsive patients did, but "the majority of the refractory patients were not given this medication," he said.

"In patients with antibiotic-responsive arthritis, a 1-month course of oral doxycycline was usually successful, while patients with refractory arthritis tended to have persistent disease even after 2 months of oral antibiotics and 1 month of IV ceftriaxone," Dr. Steere said.

Of the 67 patients with refractory arthritis, 22 were treated with NSAIDs or intra-articular corticosteroids. If arthritis persisted for 12-24 months, they underwent arthroscopic synovectomy. In the remaining 45 patients, DMARD therapy (primarily hydroxychloroquine) was added to the regimen if polymerase chain reaction (PCR) testing was negative for *Borrelia burgdorferi*. If the arthritis persisted, patients received oral methotrexate for 3-4 months, or two to four infusions of intravenous infliximab, after which arthroscopic synovectomy was offered, if needed.

Data on 20 of the 22 patients treated with NSAIDs or intraarticular corticosteroids showed that 11 had complete resolution of arthritis within a median of 11 months after the start of antibiotic therapy, and 9 underwent arthroscopic synovectomies. "Arthritis resolved in the all of the patients within a median of 14 months," Dr. Steere said.

Follow-up data on 42 patients treated with DMARDs showed that 34 had resolution of arthritis within a median of 8 months after the start of antibiotic therapy, 3 of the remaining 8 patients who did not respond to treatment with hydroxychloroquine elected to have arthroscopic synovectomies, which was successful in only 1 patient.

The two patients with failed synovectomies, plus the remaining five with unresolved arthritis, received methotrexate or intravenous infliximab. Both drugs induced responses, he said, but "infliximab resulted in particularly marked reductions in joint inflammation."

Overall, arthritis persisted in the 42 patients who received DMARDs for a median of 9 months. One of these patients had a breakthrough case of persistent infection.

Based on these findings, a "reasonable management plan" for Lyme arthritis that persists after 60 days of antibiotics (including 30 days of intravenous therapy) should include an additional month of oral antibiotic therapy if PCR testing for *B. burgdorferi* DNA is still positive; treatment with NSAIDs if PCR results for *B. burgdorferi* DNA are negative; and the addition of 200 mg oral hydroxychloroquine twice daily if arthritis still persists. If arthritis persists for 3-6 more months, arthroscopic synovectomy should be considered, Dr. Steere said.

Because Lyme arthritis eventually resolves even without antibiotic therapy, he and his colleagues also sought to determine whether antibiotic therapy altered the natural course of the disease in patients with antibiotic-refractory arthritis.

They compared the current findings to those of 21 patients treated for Lyme arthritis in the late 1970s "before the etiologic agent of Lyme disease was known," he said.

Those patients received NSAIDs and intra-articular steroids, but not antibiotics, and had episodes of arthritis for a median of 43 months. For the antibiotic-responsive patients and the antibiotic-refractory patients in the current study, the median total time of arthritis episode was 4 and 16 months, respectively. ■

THE EFFECTIVE PHYSICIAN

Lyme Disease Prevention and Treatment

BY WILLIAM E. GOLDEN, M.D., AND ROBERT H. HOPKINS, M.D.

Background

The Infectious Diseases Society of America recently updated its guidelines on identification and management of Lyme disease and other zoonoses associated with bites from *Ixodes* ticks.

Conclusions

Ixodes scapularis ticks can carry and transmit the organisms responsible for causing Lyme disease, human granulocytic anaplasmosis (HGA), and babesiosis.

Lyme disease is caused by infection with the spirochete *Borrelia burgdorferi*; it is the most common tick-associated infection in North America and is endemic in the Northeast, the upper Midwest, and Northern California. There have been no proven locally acquired cases of Lyme disease south of Maryland.

HGA, caused by a *Rickettsia* species that infects neutrophils, has a geographic distribution like that of Lyme disease. The clinical illness—fever, chills, headache, myalgia, leukopenia, thrombocytopenia, and elevated liver enzymes—is much more common in adults than in children.

Babesia, a genus of intraerythrocytic protozoa, causes an illness similar to malaria. *Babesia microti* are endemic in coastal southern New England, New York, New Jersey, Wisconsin, and Minnesota; other pathogenic *Babesia* species are found in California, Washington, and Missouri.

Bites from the Lone Star tick in the southern United States have been associated with an erythema migrans–like lesion; this southern tick-associated rash illness, abbreviated as STARI, is not thought to be caused by *Borrelia* infection.

Implementation

The best way to prevent tick-borne infections is to avoid tick bites by wearing protective clothing, using insect repellent containing DEET, and checking frequently for ticks; if found, they should be removed quickly.

Skin disinfection alone is recommended if removal of an embedded tick leaves residual mouthparts in the skin; complete removal does not reduce the risk of developing Lyme disease.

An erythematous skin lesion that develops while the tick is still attached (or within 48 hours of removal) is most likely a tick-bite hypersensitivity reaction. These are typically smaller than 5 cm in diameter and should improve within 48 hours.

Routine antimicrobial prophylaxis or serology for Lyme disease is not recommended after tick bites. However, single-dose doxycycline prophylaxis may be considered when an engorged *I. scapularis* tick (in a Lyme disease–endemic area) is removed after attachment for 36 hours or longer and the prophylaxis can be administered within 72 hours of tick removal.

Protective immunity should not be presumed following a previous case of mild Lyme disease or prior administration of the recombinant Lyme disease vaccine, which is no longer available.

Persons who reside in endemic areas should seek medical attention promptly if they develop a rash or viral-type illness up to 1 month following tick removal.

The clinical features of erythema migrans—an expanding ovoid erythematous lesion greater than 5 cm in diameter that develops 7-14 days after a tick is detached—are sufficient to make a clinical diagnosis of early Lyme disease. But clinical features alone are not sufficient to diagnose extracutaneous Lyme, HGA, or babesiosis. If there is uncertainty about the diagnosis, the CDC recommends two-stage testing of acute and convalescent sera for Lyme disease.

Oral doxycycline, amoxicillin, or cefuroxime are recommended for adults with early Lyme disease without specific neurologic syndromes or high-grade atrioventricular block. Macrolides are recommended only in cases where the first-line agents cannot be used. The same antibiotics are recommended for the treatment of late Lyme arthritis.

Ceftriaxone is recommended for early Lyme disease only if the patient has advanced atrioventricular block, meningitis, or radiculopathy. Patients with symptomatic myopericarditis or advanced heart block associated with Lyme disease should be hospitalized and monitored, and temporary cardiac pacing may be required until the atrioventricular block resolves. Late neurologic Lyme disease should also be treated with ceftriaxone.

Coinfection with HGA or babesiosis should be considered when a patient has more severe initial symptoms or does not improve as expected with appropriate initial antibiotic therapy, and the patient lives or has traveled in geographic areas where these infectious agents are endemic.

Acute and convalescent sera are the most sensitive tests for the diagnosis of HGA. Doxycycline is recommended for treatment, which should be initiated without waiting for serology results. If fever persists for more than 48 hours after initiation of antibiotics, an alternative diagnosis or coinfection with babesia should be considered.

Thin blood smear examination for parasites and babesia DNA polymerase chain reaction are the best tests for babesiosis in symptomatic patients. Acute and convalescent sera may be used to confirm the diagnosis. Antimalarials (atovaquone plus azithromycin, or clindamycin plus quinine) are used for the treatment of babesiosis. Patients with severe cases may require partial or complete RBC exchange transfusion.

Reference

Wormser, Gary P., et al. The Clinical Assessment, Treatment, and Prevention of Lyme Disease, Human Granulocytic Anaplasmosis, and Babesiosis: Clinical Practice Guidelines by the Infectious Diseases Society of America. Clin. Infect. Dis. 2006;43;1089-134.

DR. GOLDEN (right) is professor of medicine and public health and DR. HOPKINS is associate director of the medicine/pediatrics residency program at the University of Arkansas, Little Rock. Write to Dr. Golden and Dr. Hopkins at our editorial offices or imnews@elsevier.com.