Abatacept Promising for Tx-Refractory Uveitis

Uveitis is an important source of morbidity in JIA patients, and 20% don't respond to other agents.

BY BRUCE JANCIN

EXPERT ANALYSIS FROM A SYMPOSIUM SPONSORED BY THE AMERICAN COLLEGE OF RHEUMATOLOGY

SNOWMASS, COLO. – Abatacept may be a safe and effective therapy for patients with juvenile idiopathic arthritis and severe uveitis that is refractory to anti–tumor necrosis factor agents.

Findings from a series of abatacept-treated patients recently reported by Italian investigators are encouraging because uveitis is an important source of morbidity in patients with JIA, and roughly 20% of affected patients do not respond to infliximab and adalimumab, Dr. Alexei A. Grom said.

The Italian series included seven patients with a mean uveitis duration of 11.6 years when they went on abatacept (Orencia) at 10 mg/kg per month. All had previously failed immunosuppressive therapy and two or more anti-TNF agents. All responded to abatacept, and six maintained a clinical remission after a mean of 9.2 months of therapy at 10 mg/kg per month.

The mean frequency of uveitis flares in the 6 months immediately prior to introducing abatacept was 3.7 episodes. In the first 6 months on the T-cell costimulation modulator, the mean frequency of flares was 0.7 episodes. There were no new ocular complications and no deterioration of preexistent ones. One patient withdrew from the study because of an arthritis flare and oral mycosis (Arthritis Care Res. 2010;62:821-5). The same investigators subsequently reported on two additional abatacept-treated patients with uveitis (Arthritis Care Res. 2011;63:308).

Up to one-quarter of all JIA patients will develop uveitis. Roughly 90% of cases occur in patients with oligoarticular-onset JIA. About 80% of uveitis cases are asymptomatic, but this complication can nonetheless be damaging. In one Midwestern case series, 30% of affected JIA patients had cataracts, 24% had band keratopathy, 27% had glaucoma, and 33% had permanently diminished vision.

"So, in most cases of JIA, what determines how we treat them is not the arthritis itself, but whether they have this complication or not," said Dr. Grom of Children's Hospital Medical Center, Cincinnati. Treatment typically begins with steroid eyedrops, but they should not be used alone for longer than 3 months. Even low-grade inflammation at 3 months is intolerable; if present, it's time to add systemic therapy, typically methotrexate. If that doesn't clear the inflammation, anti-TNF therapy is warranted, he continued.

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DR. GROM

There are no good clinical trials of anti-TNF therapy for JIA uveitis, only relatively small uncontrolled case series akin to the Italian abatacept report, but the clinical experience indicates that about 50% of patients will respond to etanercept (Enbrel), albeit with frequent flares.

The response rate to the anti-TNF monoclonal antibodies seems to be significantly better. About 80% of patients respond to infliximab (Remicade), although many require relatively high doses of 10-20 mg/kg and infusions every 4 weeks. Similarly, about 80% of patients respond to adalimumab (Humira), although weekly injections may be required, at least initially, Dr. Grom said.

He declared having no relevant financial relationships. ■

Accurate Diagnosis of Lyme Arthritis Improves Prognosis

BY DIANA MAHONEY

FROM THE JOURNAL OF THE AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS

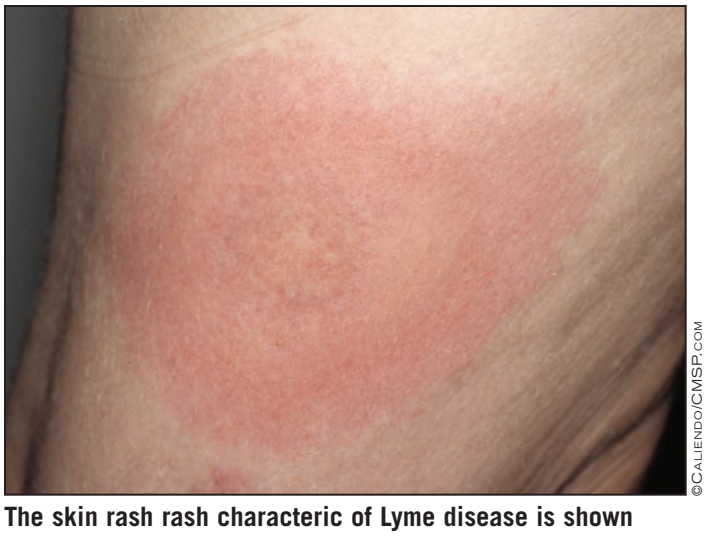
Most cases of Lyme arthritis are brief and can be managed successfully with oral antibiotics, according to a recent review article. A delayed or missed diagnosis, however, increases the likelihood that the inflammatory response triggered by infection with the tick-borne *Borrelia burgdorferi* spirochete will lead to permanent joint damage, according to Dr. Brian G. Smith of Yale University in New Haven, Conn., and colleagues. For this reason, they stressed, Lyme arthritis "should be considered in the evaluation of patients with monoarticular or pauciarticular joint complaints in a geographic area in which Lyme disease is endemic."

Timely diagnosis of Lyme arthritis is often hampered by the fact that the clinical presentation – including recurrent episodes of joint swelling, typically in large joints such as the knee, but also possibly in the ankle, wrist, hip, or elbow; large effusions that may be out of proportion to patients' complaints; and, occasionally, fever – can be similar to that of inflammatory arthritides or acute bacterial septic arthritis, especially in children, the authors wrote (J. Am. Acad. Orthop. Surg. 2011;19:91-100).

In patients with acute symptoms, rheumatologists or orthopedic surgeons "may be asked to evaluate a child who presents to the emergency department with an acutely swollen, tender joint as well as other Lyme disease–related symptoms that may be indicative of bacterial septic arthritis, such as malaise or irritability with or without fever and limited weight bearing." Joint-fluid analyses in patients with both diseases frequently reveal "strikingly elevated joint leukocyte counts," occasionally leading to unnecessary surgical joint debridement in patients erroneously diagnosed with septic arthritis, they stated.

Because of the similar and overlapping presentations and the fact that an accurate, reliable rapid test for Lyme disease is not widely available, "clinical and laboratory variables should be used as tools in the diagnostic armamentarium," the authors wrote. Although these variables have not been definitively established, the findings of a retrospective comparison of the clinical indications and laboratory results of children who presented to the emergency department with serologically confirmed Lyme arthritis and those who presented with septic arthritis identified a negative history of fever, knee involvement, and normal C-reactive protein (CRP) levels as important predictors of Lyme arthritis (Pediatrics. 2009; 123:959-65).

More recently, the authors of the current study conducted a review of children who presented to their institution with joint effusion, and determined that – relative to patients with septic arthritis – those with Lyme arthritis "had a lower average peripheral white blood count, lower percentage of neutrophils in the differential, were less likely to present with a temperature [greater than] 101.5[° F], and were less likely to refuse to bear weight on the affected extremity," they wrote. "No statistically significant difference existed between the two groups with regard to erythrocyte sedimentation rate and CRP level" (J. Bone Joint Surg. Am. 2011;93:252-60).



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The skin rash rash characteric of Lyme disease is shown here on the thigh of a 59-year-old woman.

Following an accurate diagnosis, "Lyme arthritis has an excellent prognosis with appropriate management," the authors stressed. In adults without neurologic involvement, this includes a 28-day course of 100-mg doxycycline twice daily, 500-mg amoxicillin three times daily, or 500-mg cefuroxime axetil twice daily. The recommended treatment for children is a 28-day course of 50-mg/kg amoxicillin divided into three doses daily, 30-mg/kg cefuroxime axetil divided into two doses daily, or – for patients aged 8 years or older – 4-mg/kg doxycycline divided into two doses daily, they wrote.

Patients with mild persistent or recurrent synovitis after the initial therapeutic course should repeat the 28-day antibiotic course, whereas those with moderate to severe persistent arthritis should begin a 2-week or 4-week course of parenteral antibiotics, the authors wrote, noting that those with persistent symptoms after two treatment courses should undergo polymerase chain reaction (PCR) testing. Patients with positive PCR results should repeat the oral antibiotic regimen for 28 days, whereas those with negative PCR results may be treated with NSAIDs and intra-articular corticosteroids, they stated. Hydroxychloroquine, which may have antispirochetal and anti-inflammatory effects, may be used in the negative PCR patients, and "there may be a role for certain disease-modifying antirheumatic agents in the management of chronic Lyme arthritis, but experience with their use in this setting is limited," they said.

For patients with antibiotic-refractory Lyme arthritis, "arthroscopic synovectomy is a reasonable treatment option," the authors wrote, alluding to small case series demonstrating marked resolution of joint inflammation and maintained improvement follow the surgical procedure in treatment-refractory patients.

Increased awareness of the symptoms and risk factors associated with Lyme disease is needed to improve detection and treatment of Lyme arthritis, and further research is warranted to better distinguish between Lyme arthritis and other types of arthritis in symptomatic patients because the management approaches are inherently different, the authors concluded.

Dr. Smith disclosed a financial relationship with Stryker. Study coauthor Dr. Eugene D. Shapiro, also of Yale University, disclosed affiliations with the American Board of Pediatrics' Board on Infectious Diseases, and the American Lyme Disease Foundation. ■