CRP Predicts Drug Efficacy in Psoriatic Arthritis

Another factor that contributed to infliximab's efficacy was absence of hip or knee involvement.

BY DIANA MAHONEY
New England Bureau

The absence of large joint involvement, higher serum C-reactive protein levels, and lower disability scores at treatment initiation may be predictors of a good therapeutic response to infliximab in refractory psoriatic polyarthritis, an open-label study has shown.

The efficacy of infliximab in psoriatic arthritis patients has been demonstrated in several placebo controlled and open label trials, but the high cost and potential risks associated with the anti–tumor necrosis factor–α (TNF-α) agent warrants careful selection of patients who are most likely to benefit from this treatment, wrote Dr. Jordi Gratacós of Parc Taulí University Hospital in Barcelona, and colleagues.

To this end, the investigators sought to identify variables associated with a good clinical response in psoriatic arthritis patients being treated with the drug (Ann. Rheum. Dis. 2007 Jan. 25 [Epub doi: 10.1136/ard.2006.060079]).

The multicenter study included 69 patients with active psoriatic arthritis who showed no clinically significant response to at least 8 weeks of treatment with 15 mg of methotrexate weekly. Per study criteria, patients had to have peripheral polyarthritis—defined by the presence of five or more swollen and tender joints—and at least one of the following criteria: morning stiffness lasting more than 45 minutes, an erythrocyte sedimentation rate (ESR) of more than 30 mm per first hour, or a C-reactive protein (CRP) level greater than 15 mg/L. Patients testing positive for rheumatoid factor were excluded from the investigation.

In addition to their stable doses of methotrexate, study participants received 5mg/kg of infliximab every 8 weeks.

In an intent-to-treat analysis conducted at 38 weeks of active treatment, 30 of the 69 patients (44%) experienced a major clinical response, defined as an improvement of at least 50% of the initial American College of Rheumatology (ACR) composite index, the authors reported. With use of the ACR20 and ACR70 measures, 44 and 18 patients, respectively, were identified as responders.

The results of a univariate analysis based on an ACR50 response at 38 weeks as the main outcome showed that involvement of large joints (hip or knee) and a high level of disability, defined as a score of 2 or higher on the validated Health Assessment Questionnaire (HAQ) at the start of treatment "were both predictors of smaller response to infliximab than in patients with no involvement of the large joints and an HAQ less than 2," the authors wrote.

When the univariate analysis was performed at 14 weeks, the results were similar except for associations with CRP and age.

In the 14-week analysis, the presence of a CRP of at least 10 mg/L at the start of treatment "was associated with a significantly high rate of response," reported the authors. And patients who achieved an ACR50 were younger (mean age 39 years), compared with those who did not respond (mean age 45 years), they wrote.

In a multivariate logistic regression model, CRP values and the absence of arthritis in the hip or knee or both were independent predictors of an ACR50 response.

Severe disability was not a significant predictor, but there was a trend toward an association, the authors reported.

While the results of this study suggest that some variables may significantly influence the treatment response to infliximab among patients with psoriatic arthritis, "the data reported here cannot be used as a definitive guide for deciding which patients should be given anti-TNF treatment," the authors stressed, noting the study's small size and focus on patients with the most severe and refractory disease usually seen in clinical practice. "Large studies supporting our data will be needed in order to prove our statistical model and to establish more accurately the predictive factors for clinical response to infliximab in patients with [psoriatic arthritis]," they concluded. ■

Image of the Month

Radiographs obtained of both hands showed similar changes in multiple phalanges. In particular, the lesions had a lacy, punched-out appearance that suggested osseous sarcoidosis, said Dr. Sterling G. West, a professor of medicine in the division of rheumatology at the University of Colorado at Denver.

The lesions reflect granulomatous involvement of the phalangeal shafts.

Notably, the lesions are not associated with periostitis or sequestra helping to separate sarcoid bone involvement from chronic osteomyelitis.

Sarcoidosis can have a number of manifestations, though pulmonary involvement is present in more than 90% of patients with the disease. Symptoms of pulmonary involvement include dyspnea and dry cough, as in this patient.

Patients tend to have well-established sarcoidosis by the time that bone involvement is present, said Dr. West. Bone involvement tends to occur more frequently in African Americans.

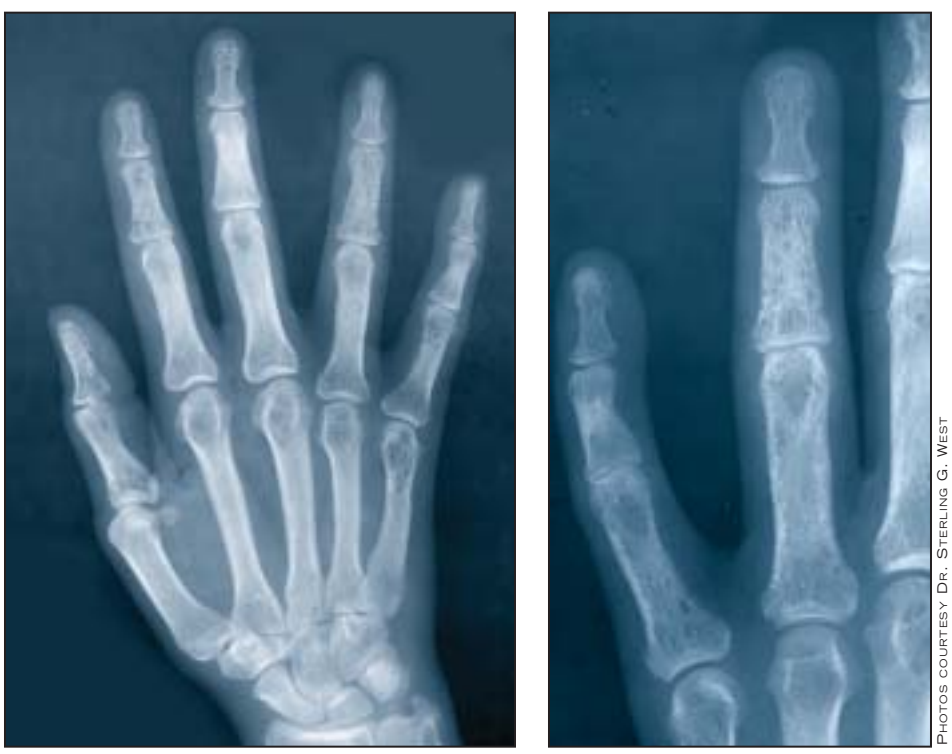
Cystic lesions have a predilection for the phalanges of the hands and feet. Soft tissue swelling can occur over the lesions. Sarcoidosis is the major cause of unidigital clubbing. When sarcoid bone involvement is associated with lupus pernio, the prognosis is generally poor.

Uveitis is another common manifestation of sarcoidosis and is usually bilateral. Dr. West recommends that all sarcoid patients get an eye screening.

Many patients with sarcoidosis undergo spontaneous remission, while some remit with steroids. Others may have a chronic course. Signs of poor prognosis include the involvement of three or more organs, disease onset after age 40, African American race, and symptoms lasting more than 6 months.

Osseous sarcoid typically indicates advanced sarcoidosis, which requires treatment with high-dose prednisone and additional agents such as azathioprine, methotrexate, or biologic agents—particularly infliximab to control all the sarcoidosis manifestations and prevent progression. This patient was initially treated with prednisone and azathioprine. Later, infliximab was added helping to stabilize his disease.

—Kerri Wachter



Photos courtesy Dr. Sterling G. West

Osseous sarcoid lesions affected multiple phalanges (hand, above left). These bony changes typically have a lacy, punched-out appearance (detail, above right).

Molecular Weight Guides Hyaluronic Acid Choice

BY ROBERT FINN
San Francisco Bureau

San Francisco — Because there are at least six commercial products available for viscosupplementation with hyaluronic acid, it can be hard to determine which to use, according to Dr. Anthony Luke, who provided tips and clinical pearls at a conference on sports medicine sponsored by the University of California, San Francisco.

Viscosupplementation with hyaluronic acid derivatives is FDA approved for treatment for mild knee osteoarthritis. However, available hyaluronic acid products differ in molecular weight, concentration, and suggested dosing, said Dr. Luke of the university.

The molecular weight of hyaluronic acid in synovial fluid is 6,000-7,000 kd, so one would expect that products at 6,000 kd, the closest in molecular weight to the natural substance, might perform best, Dr. Luke said. However, one study suggests that high–molecular weight injections result in better pain relief than low–molecular weight injections (Clin. Ther. 1999;21:1549-62), and another determined that the effect of hyaluronic acid on osteoblasts increased with molecular weight (Bone 2003;33:703-10).

On the other hand, low–molecular weight preparations may achieve higher concentrations in the desired tissue, he said. A recently published randomized controlled trial demonstrated that two hyaluronic acid preparations of different molecular weights were both more effective than placebo, but there was no statistically significant difference between them (Rheumatol. Int. 2006;26:325-30).

Studies have shown that viscosupplementation is similar to steroid injections in success in reducing pain in mild osteoarthritis, he said. But viscosupplementation appears to have a more prolonged effect than corticosteroids.

Dr. Luke said that he prefers a superolateral approach with a 1.5-inch needle, finding it to be more accurate than the bent-knee approach. If the patient's knee has an effusion, it should first be drained with a 22-gauge needle to avoid diluting the hyaluronic acid.

Dr. Luke said that he occasionally uses the treatment in patients with severe osteoarthritis of the knee who can't take steroids. ■