Clinical Response Tracked IgA RF

Rheumatoid Factor *from page 1*

6 patients dropped out, leaving 126 evaluable for analysis. The study results included the observation that in all patients, all three isotypes of RF decreased significantly with treatment.

"But the most impressive data related to IgA rheumatoid factor, which was low at baseline in responders and very high in nonresponders," said Dr. Montecucco, chair of rheumatology, University of Pavia, Italy.

Mean baseline IgA RF was 24.8 IU/mL among responders, compared with 130.4 IU/mL in nonresponders.

There also was a trend for lower levels of IgM RF in responders, but this was not statistically significant, he said.

Good clinical response, measured according to the European League Against Rheumatism's modified Disease Activity Score (DAS 28), was seen in 83 patients (66%), with only minor differences between the drugs.

Clinical responses also were analyzed according to level of baseline IgA RF, with 45 patients classified as IgA RF negative (below 20 U/mL), 38 as low positive (20-100 U/mL), and 43 as high positive (above than 100 U/mL). The 83 patients who were good responders all were either negative for IgA RF or had a low but positive level.

Conversely, the 43 high positives all showed poor responses, confirming that baseline IgA correlates with clinical response to treatment with anti–tumor necrosis factor (TNF)–α drugs, Dr. Montecucco said.

This strong clinical association between baseline IgA RF and response to anti-TNF therapy also was confirmed on multivariate analysis after adjustment for all possible confounding factors, including disease duration, C-reactive protein, and positivity for anti–cyclic citrullinated peptides (CCP), according to Dr. Montecucco. Response also was associated with male gender and lower baseline DAS and disability scores.

The correlation between gender and response to anti–TNF-α treatment has recently been reported from national registers in Italy and Norway, with a proposed explanation for the finding being that TNF inhibition may induce upregulation of aromatase. This could increase the level of anti-inflammatory androgens and improve outcome (Arthritis Rheum. 2006;54:2309-46).

Anti-CCP levels also were followed in the study. The effects of treatment on this marker have been controversial, with previous studies providing conflicting results. Some reports have suggested that anti-CCP levels fall with treatment, at least in early disease.

But in this cohort of patients with advanced disease anti-CCP levels did not decrease with therapy.

"While rheumatoid factor and anti-CCP antibodies share some important features, such as being present before disease onset, they appear to represent two distinct antibody systems that are differently induced and probably differently regulated in rheumatoid arthritis," Dr. Montecucco said.

Clinical experience has left no doubt that IgM RF is reduced with effective treatment, but until now, it has not been known whether serum IgA RF also decreases with treatment, Dr. Montecucco said. Nor has it been known if reduction in IgA titers would correlate with clinical response.

Until now there have been no reliable serologic markers to predict which patients are less likely or absolutely unlikely to benefit from treatment with TNF-α–blocking agents.

Approximately one-third of patients do not respond to treatment with these expensive and potentially toxic drugs.

Several lines of evidence suggest that rheumatoid factor IgA may be as important as IgM. For example, high titers of IgA isotope of rheumatoid factor are associated with early erosive disease. ■

High Temperature, Humidity May Increase Gout Attack Risk

BY JEFF EVANS
Senior Writer

WASHINGTON — High temperature and humidity appear to increase the risk of recurrent gout attacks independently of other known risk factors, Yuqing Q. Zhang, D.Sc., reported at the annual meeting of the American College of Rheumatology.

"Although the pathophysiology of gout is well understood and efficacious clinical therapies are available, many patients with gout still suffer from recurrent gout attacks" that are brought on by certain risk factors, said Dr. Zhang of Boston University.

Decreases in intravascular volume as a result of perspiration in hot and humid weather can result in high serum uric acid levels because of a reduction in uric acid excretion, Dr. Zhang said.

Only a handful of studies have examined the relationship between risk factors for dehydration and the risk of gout attack recurrence.

Dr. Zhang and his colleagues enrolled 197 patients with a median 5-year history of gout through an online advertisement.

The patients answered a "hazard period" questionnaire on a Web site that asked about risk factors for gout attacks during the 2-day period prior to their report of an attack.

They also filled out a control period questionnaire every 3 months for 1 year to provide data about time intervals during which gout attacks did not occur.

The questionnaires asked about use of dehydrating medication (such as diuretics), alcohol use, food intake (especially foods rich in purine or with little purine), and details of gout attacks when they occurred.

The Weather Underground Web site (www.wunderground.com) provided weather information from more than 1,600 airports in the United States based on date and zip code. Each particular type of weather was divided into quintile groups to determine its impact on the risk of gout attack.

As temperature during the 2 days prior to a gout attack increased from the lowest quintile (0-53°F) to the highest quintile (87-105°F), the relative risk of a gout attack doubled.

The dose-response relationship between temperature and recurrent gout attacks seemed to suggest a threshold effect such that when the temperature reached 85°F, the risk of recurrent gout attacks increased dramatically, according to Dr. Zhang.

The relationship between the level of humidity during the 2 days prior to a gout attack and the risk of recurrent attacks followed the pattern for temperature very closely.

High humidity appeared to be the strongest predictor for recurrent gout attacks, but very cold and dry weather also slightly increased the risk of recurrent attacks.

The findings remained significant after controlling for medication use (especially diuretics), alcohol consumption, and purine-rich food intake.

Recurrent gout attacks were not associated with barometric pressure or precipitation.

"In hot and humid weather, subjects with gout may need to increase fluid intake to counteract volume depletion and to prevent a recurrent gout attack," Dr. Zhang concluded. ■

IMAGE OF THE MONTH

"The first thing you think of when a patient [like this one] walks into your office is medial meniscal tear just because meniscal lesions are so common in a patient in this age group," said Dr. Hollis G. Potter, chief of magnetic resonance imaging at the Hospital for Special Surgery in New York. "You might also suspect that she might have some early medial osteoarthritis."

"There wasn't anything glaring in her presentation that directed them to think that she had an inflammatory arthropathy," said Dr. Potter.

Upon magnetic resonance imaging (MRI), the patient was found to have severe synovial expansion with an inflammatory synovitis. "It was pretty clear that even if her meniscus had been torn—which it wasn't—that wouldn't be the cause of her pain. The cause was really the fact that she had an inflammatory synovitis," said Dr. Potter.

The synovial proliferation extended into the medial and lateral gutters (see arrows in first image). The patient also had early marginal bony erosion (see arrow in second image) affecting the medial tibial plateau. Together, the synovial proliferation and bony erosion indicated rheumatoid arthritis (RA).

The images were obtained using a cartilage-sensitive sequence used for evaluating articular cartilage.

"We do this for all patients routinely," said Dr. Potter. The technique allows physicians to noninvasively evaluate the morphologic integrity of the cartilage. "When we find articular lesions, I find it drives patient management more than anything else."

"It's always been my sense that the purpose of MRI is to find what physicians are not clinically suspecting," said Dr. Potter, who is also a professor of radiology at Cornell University, New York.

"I find that if the MRI doesn't in fact change the management or affect the management in some way, it's a very expensive test that really hasn't helped anybody at all," Dr. Potter told RHEUMATOLOGY NEWS in an interview.

Based on the imaging findings, the patient underwent serologic testing and was placed on appropriate clinical management. This patient was identified with RA early in the disease progression when disease-modifying antirheumatic drugs can make a big difference in slowing disease progression.

Synovial expansion with an inflammatory synovitis (arrows) suggests RA.

Marginal bony erosion (arrow) suggests RA. There is no evidence of meniscal tear.

PHOTOS COURTESY DR. HOLLIS G. POTTER

Dr. Potter and her colleagues have found another use for MRI in rheumatology: They are investigating synovial recruitment patterns in patients with early, clinically suspected, inflammatory RA—patients who meet the American College of Rheumatology criteria for inflammatory arthritis. In an ongoing, prospective pilot study, they are using MR angiography with a contrast agent to assess neovascularity in areas of inflammatory synovium. The hope is that work like this will help better define patients who are good candidates for therapy with biologic agents, said Dr. Potter.

—Kerri Wachter