MRSA Infections Are Seen in Patients on Anti-TNF Therapy

BY NANCY WALSH
New York Bureau

PARIS — Methicillin-resistant *Staphylococcus aureus* infections have been reported for the first time in patients with rheumatoid arthritis being treated with tumor necrosis factor inhibitors.

In a poster presented at the annual European Congress of Rheumatology, Dr. Jack Lichtenstein noted that he had observed that several of his patients receiving tumor necrosis factor (TNF) inhibitors developed severe methicillin-resistant *S. aureus* (MRSA) infections, so he undertook a review of medical records of all patients in his clinical practice being treated with these drugs between August 2003 and July 2006 to determine the overall incidence and severity of these infections.

Among 430 patients receiving infliximab, etanercept, or adalimumab, 15 developed MRSA infections, had to stop TNF inhibitor therapy and received intravenous antibiotics, reported Dr. Lichtenstein, a rheumatologist in group practice in Annapolis, Md.

In addition, 12 patients required hospitalization.

Concomitant immunosuppressive treatment included prednisone in 12 patients and methotrexate in 6. Clinical presentations included cellulitis in six, osteomyelitis in three, sinusitis in two, and septic arthritis, mastitis, pneumonia, and Fournier's gangrene with sepsis in one each.

More than half of the infections occurred within the first 6 months of treatment, but four developed after more than a year of therapy. Six were seen in patients on infliximab, five in those on etanercept, and four in those on adalimumab.

Another 10 patients developed methicillin-sensitive *S. aureus* (MSSA) infections, 5 of which were cellulitis, 4 of which were septic arthritis, and 1 osteomyelitis. Seven of these required hospitalization and nine were given intravenous antibiotics.

Other bacterial infections seen in anti-TNF-treated patients included gram-negative bacterial cellulitis in four, severe *Clostridium difficile* infections in three, and tuberculosis with fatal pneumonia, *Mycobacterium marinum* joint infection, and *Nocardia* pneumonia in one each.

Other infections for which no bacterial agent was cultured included cellulitis in nine, pneumonia in six, and diverticulitis in two.

MRSA and MSSA infections were more common than were other bacterial infections in this group of anti-TNF-treated patients, according to Dr. Lichtenstein, who noted that MRSA infections may have a protracted course and may not respond to available treatments.

Attempts to restart TNF inhibitors after control of the MRSA infections led to recurrent infection in seven patients, and only two patients were able to resume TNF inhibitor therapy after the infection was controlled.

Dr. Lichtenstein wrote that he would no longer continue the use of TNF inhibitors in patients with MRSA or MSSA infections.

About one-third of Americans are carriers of MSSA and 0.8% carry MRSA, and infections with these organisms are expected to be common in immunocompromised patients such as these.

This study was wholly funded by the investigators and had no pharmaceutical, institutional, or financial support. ■

High Coffee Intake Kicks Up the Risk Of Developing Rheumatoid Arthritis

BY NANCY WALSH
New York Bureau

PARIS — Heavy coffee drinking was associated with progression of undifferentiated arthritis to rheumatoid arthritis in an analysis of data from a Norwegian early arthritis clinic.

The study included 280 patients aged 18-75 years with arthritis of at least one joint. The mean age was 45.7 years, median disease duration was 23 days, and 55% were women, Dr. Maria D. Mjaavatten said at the annual European Congress of Rheumatology.

Data were collected from a structured patient history. Examinations included swollen and tender joint counts, measurement of C-reactive protein and erythrocyte sedimentation rate, and patient-reported health status.

At baseline, 130 patients had monoarthritis, 96 had oligoarthritis, and 54 had polyarthritis. At 1 year, 30 of these patients (10.7%) had developed rheumatoid arthritis (RA). Multivariate analysis showed the strongest predictor of RA development was a positive titer of anti–cyclic citrullinated peptide (CCP) at presentation, with an odds ratio of 73.23.

But drinking 10 or more cups of coffee daily also was associated with an elevated risk (OR, 22.50), Dr. Mjaavatten of the department of rheumatology, Diakonhjemmet Hospital, Oslo, wrote in a poster.

The link of coffee intake with RA also was seen in earlier studies. In the Mini-Finland Health Survey, carried out between 1978 and 1980, the odds ratio for RA was 14.80 in those with a daily coffee intake of 11 or more cups. After adjustment for confounders including age, sex, smoking, alcohol intake, body mass index, and serum cholesterol, the relative risk was 2.20 for those drinking four or more cups of coffee daily (Ann. Rheum. Dis. 2000;59:631-5).

A study from Iowa implicated decaffeinated coffee. Researchers reported that subjects who drank four or more cups a day had a relative risk of 2.58 for RA, suggesting that exposure to the solvents used for extracting caffeine before the mid-1970s might have played a role (Arthritis Rheum. 2002;46:83-91).

A case-control study in Denmark between 2002 and 2004 found that subjects who were shared epitope carriers and smoked, drank more than five cups of coffee each day, or used oral contraceptives were at high risk for anti-CCP–positive RA.

The researchers cited the hypothesis that exposure to environmental stimuli might be a primary triggering event for RA, with tobacco smoke being the prototype because it induces the presentation of citrullinated autoantigens in the lungs in genetically predisposed persons, which activates the adaptive immune response. They suggested coffee also might operate in this citrullination process, contributing to anti-CCP–positive RA (Arthritis Rheum. 2007;56:1446-53).

Further investigation of coffee intake in RA development is needed, Dr. Mjaavatten said, noting her results should be interpreted with caution, because the RA incidence was low in this cohort. ■

In Older Adults, Running Is Not Linked to Knee OA

BY MARK S. LESNEY
Senior Editor

Long-distance running among older adults has no effect on the development of radiographic osteoarthritis, according a small, prospective study comparing a population of runners with community-matched controls.

The study looked at 45 runners and 53 controls who were at least 50 years of age. After almost 12 years of observation, the runners did not exhibit more severe radiographic osteoarthritis (OA) or replaced knees than the controls.

As a result of these findings, "long-distance running or other routine vigorous activities should not be discouraged among healthy older adults out of concern for progression of knee OA," the investigators reported.

The question of whether strenuous weight-bearing exercise can lead to increased OA had not been conclusively answered before this study.

The researchers assembled a set of runners 50 years of age or older from the Fifty-Plus Runners Association and a set of demographically matched controls from the Stanford Lipid Research Clinics Prevalence Study.

Bilateral anteroposterior weight-bearing radiographs of the knees were taken serially in 1984, 1986, 1996, and 2002. A total of 45 runners (64.4% men) and 53 matched controls (69.8% men) completed at least two sets of radiographs that were used for the analysis.

The mean age for both groups was around 60 years at the first radiograph. Digitized radiographic films were read for narrowing, sclerosis, and osteophytes (each graded on a scale from 0 to 3) in the medial and lateral compartments of each knee by two readers blinded to group assignment, according to Dr. Eliza F. Chakravarty and colleagues from the Stanford (Calif.) University.

The primary outcome measure was the total knee score (TKS), which is the sum of each of the scores from the digitized radiographs mentioned above, from the medial and lateral compartments of both knees.

The secondary measure was the worst joint space width (JSW) in millimeters among the four compartments, which represented the knee with the worst OA. The lower the score, the worse the condition. A joint that was fully replaced was arbitrarily assigned a JSW of zero.

At baseline, runners had a significantly higher TKS than controls (1.29 vs. 0.40, respectively). The JSW of the worst knee was significantly lower in runners (4.54 vs. 4.84).

The prevalent radiographic OA expressed in percent was not significantly different between groups, although it was higher in runners (6.7% vs. 0% in the controls).

Runners also had a greater prevalence of knee injuries than controls, although this difference was not statistically significant. Runners had a lower body mass index (BMI) than controls, higher minutes per week of vigorous exercise and of running, and higher current runner status.

By the end of the study, the last radiograph showed that significant differences remained only in BMI, running minutes a week, minutes of vigorous exercise a week, and current runner status. TKS and JSW were no longer significantly different. Prevalent radiographic OA percent was still not significantly different, though the actual relationship of the values had flipped: 20% of runners compared with 32.1% of controls (doi:10.1016/j.amepre.2008.03.032).

"In this analysis, long-distance running was not associated with accelerated incidence or severity of radiographic OA," the investigators reported. "Over the prolonged period of observation (mean 11.7 years) and despite more prevalent OA and worse radiographic scores at the baseline, runners did not have more severe OA or replaced knees than controls. Although there were some suggestions that runners may have less OA than controls, these did not meet statistical significance."

The authors suggested that larger studies are needed to determine if running has a positive effect on preventing OA development.

The authors pointed out that the strength of their study was its prospective nature and the length of follow-up; the weaknesses were lack of analysis of clinical symptoms in the radiographic OA evaluation, and the fact that the runners were a self-selecting group of individuals (they chose to run and join a runners' group) who were healthy and continued running into their 6th decade of life.

Dr. Chakravarty and her colleagues stated there were no conflicts to disclose with regard to this study. ■