



Arthritis News

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GENETIC LINK MAY PLAY ROLE IN INCREASED RHEUMATOID ARTHRITIS JOINT DAMAGE

SAN ANTONIO, TEXAS—Rheumatoid arthritis patients with a genetic variation of a protein called TNF (tumor necrosis factor) may experience increased joint damage, according to research presented this week at the American College of Rheumatology Annual Scientific Meeting in San Antonio, Texas.

Previous research has shown that TNF in patients with rheumatoid arthritis can contribute to inflammation and joint damage. Therefore, agents such as etanercept, infliximab and adalimumab that block the action of TNF, are proving to be an important new class of therapy for the treatment of patients with rheumatoid arthritis and other systemic inflammatory diseases. Determining which genes regulate the production of TNF could further influence the treatment approaches in patients with rheumatoid arthritis.

Researchers studied 190 patients with early-stage (less than 14 months from the onset of symptoms) rheumatoid arthritis who had received no prior treatment with any arthritis specific drugs including TNF inhibitors. The patients were followed for an average of three years in an on-going observational study, which included X-rays of participants' hands and feet at the outset of the study and then annually. Genetic analysis of these patients showed that a particular variation in the TNF gene (that has previously been implicated in elevated production of TNF) is associated with higher progression of total X-ray damage over three years compared to patients without this TNF genetic variation. While further validation of these results is required, this initial study suggests a possible genetic association between the TNF gene and joint damage.

"These exciting preliminary results suggest an association of radiographic damage (that is, what can be seen in an X-ray) in rheumatoid arthritis and a particular TNF gene variation," said Dinesh Khanna, MD, currently an investigator at the University of Cincinnati who performed his work at the University of California in Los Angeles, Los Angeles, California. "However, these results should be considered preliminary until validated in different groups around the world."

The American College of Rheumatology is the professional organization for rheumatologists and health professionals who share a dedication to healing, preventing disability and curing arthritis and related rheumatic and musculoskeletal diseases. For more information on the ACR's annual meeting, see www.rheumatology.org/annual.

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Editor's Notes: Dr. Khanna will present this research during a scientific session at the ACR Annual Scientific Meeting from 2:45–3:00 PM CT (3:45–4:00 PM ET) on Monday, October 18, in Ballroom B of the Henry B. González Convention Center. He will be available for media questions during a briefing at 8:30 AM CT (9:30 AM ET) on Tuesday, October 19, in the on-site Press Conference Room, Room 218.

Association Between Tumor Necrosis Factor-alpha Polymorphism and Radiographic Progression in a Seropositive Rheumatoid Arthritis Inception Cohort

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Purpose: To determine whether the tumor necrosis factor gene (TNFA) -308 guanine to adenosine polymorphism is associated with disease activity parameters of rheumatoid arthritis (RA).

Methods: Early RA patients (within 14 months of symptom onset, n = 190) included in this study had active disease with no previous DMARD treatment and were seropositive for rheumatoid factor (RF). The -308 TNFA polymorphism was analyzed using PCR-pyrosequencing. RA disease status was measured using the disease activity score (DAS), functional capacity using the health assessment questionnaire-disability index (HAQ-DI), and radiographic progression using the Sharp score.

Results: The patients with -308 TNFA AA+AG genotypes had significantly higher progression rates in joint space narrowing (JSN) score (median scores 0.45 vs. 0.01 units per year, p=0.02) and total Sharp score (TSS=1.95 vs. 0.85 units/yr, p=0.03) compared to patients with the TNFA GG genotype. There was a trend for a higher erosion score (ES) progression rate in the patients with the AA+AG genotypes (0.84 vs. 0.49 units/yr) compared to the GG genotype (p=0.16). When the radiographic progression was evaluated categorically using a proposed classification criterion for progressive radiographic disease, a higher percentage of patients with the AA+AG genotypes (25/44 or 57%) were classified as having progressive disease as compared to those with the GG genotype (46/125 or 37%, p=0.02). In a multivariable linear regression model, the presence of the AA+AG genotypes was associated with a higher progression rate (p=0.013) after adjusting for the presence of DRB1*04 shared epitope, interaction of DRB1*04 and AA+AG genotype, DMARD use in patient years, and ethnicity.

There was no difference between patients with the AA+AG vs. GG genotypes in disease activity as measured by the EULAR or ACR response rates or in disability by HAQ-DI.

Conclusion: This study shows an association between the TNFA -308 polymorphism and progression of radiographic damage in early RA, RF positive patients. Further studies need to be conducted to validate these results in both longitudinal observational cohorts and randomized clinical trials.

Disclosure: D. Khanna, None; H. Wu, None; G.S. Park, None; V. Gersuk, None; R.H. Gold, None; G.T. Nepom, None; W.K. Wong, None; J.T. Sharp, None; K.J. Bulpitt, None; H.E. Paulus, None; B.P. Tsao, None.