Use MRI to Make Ankylosing Spondylitis Diagnosis

BY BRUCE JANCIN
Denver Bureau

PARIS — Earlier diagnosis of ankylosing spondylitis has emerged as a high priority, and MRI is vital in accomplishing it, according to Dr. Martin Rudwaleit.

The average interval between onset of symptoms of ankylosing spondylitis (AS)—chiefly inflammatory low back pain—and the time of diagnosis is 6-10 years.

Moreover, AS, a disease with an estimated prevalence of about 0.5%, has its onset predominantly in young adulthood. Symptoms occur by age 30 in 80% of cases and by age 45 in 95%. So the lengthy delays in diagnosis, which often involve extensive work absenteeism, take place during what would ordinarily be among the most productive years of life.

A major reason for the long delay in diagnosis is that the standard diagnostic criteria for AS used for nearly the past quarter century—the 1984 modified New York criteria—require unequivocal radiographic evidence of sacroiliitis. Because x-ray changes are a late disease manifestation, they typically don't appear until years after symptom onset.

Long before the classic radiographic findings are evident, however, active inflammatory lesions are present on MRI, stressed Dr. Rudwaleit, a rheumatologist at the University Hospital Charité, Berlin.

Bone marrow edema located periarticularly, adjacent to the sacroiliac joint space, indicates active inflammatory osteitis. This is the most important MRI finding in establishing the diagnosis of AS, he added.

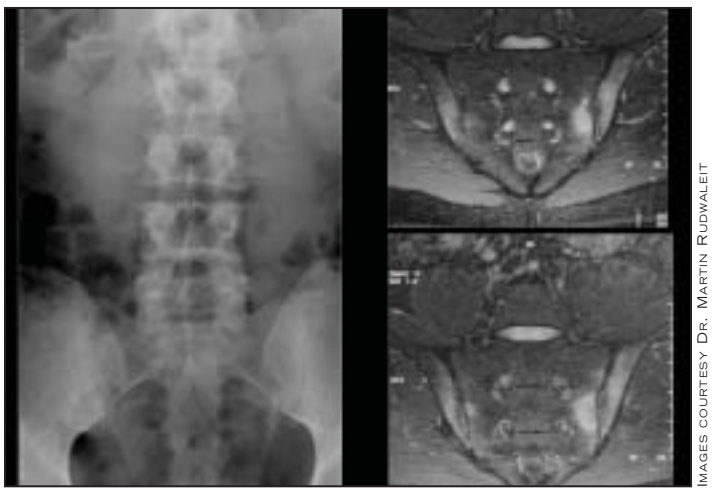
Another big reason for the long delay in diagnosis is that the core clinical features required under the modified New York criteria—namely, restricted spinal mobility and restricted chest expansion—are, like the radiographic changes, late disease manifestations. Similarly, the distinctive postural changes often considered pathognomonic for AS aren't apparent until the disease is well along.

Dr. Rudwaleit and coworkers have proposed a new diagnostic algorithm for AS. It focuses on identifying disease in the preradiographic stages and relies upon MRI and HLA-B27 testing (Ann. Rheum. Dis. 2004;63:535-43). The criteria are now undergoing minor alterations in a multicenter validation study, in which 650 patients with chronic low back pain have been enrolled to date.

"We think diagnosis of axial spondyloarthritis without radiographic changes is feasible in daily clinical practice," he said at the annual European Congress of Rheumatology.

As part of the effort to develop improved diagnostic criteria, he and his coworkers have devised a simpler method for differentiating inflammatory from mechanical low back pain. The distinction is critical because inflammatory low back pain is the earliest and most important symptom of AS. The diagnostic challenge arises from the fact that AS accounts for only 5% of chronic low back pain.

By analyzing the clinical histories of 101 patients with confirmed AS and 112 others with mechanical low back pain, Dr. Rudwaleit identified four parameters that best discriminated between the two: morning stiffness of more than 30 minutes' duration, improvement of back pain with exercise but not with rest, nighttime awakening due to back pain during only the second half of the night, and alternating buttock pain. When any two of these four criteria were met, the sensitivity and specificity for inflammatory back pain were 70% and 81%, respectively (Arthritis Rheum. 2006;54:569-78).



IMAGES COURTESY DR. MARTIN RUDWALEIT

STIR MRIs (right top and bottom) show inflammation adjacent to the sacroiliac joints (white areas) not seen on x-ray (left).

But the presence of inflammatory back pain doesn't suffice to make the diagnosis of AS; that requires additional criteria, ideally including a positive MRI, which has the greatest sensitivity and specificity of the various diagnostic criteria, according to Dr. Rudwaleit.

He and his coworkers have developed a method of calculating AS probability derived by multiplying the likelihood ratios (LRs) of the individual AS parameters. For example, a positive MRI carries an LR of 9.0 based upon its high sensitivity and specificity. If a patient has a positive MRI plus inflammatory back pain, which has an LR of 3.1, plus heel pain, with an LR of 3.4, and elevated acute phase reactants, with an LR of 2.5, the resultant LR product is 237, indicating a greater than 90% probability of AS.

Dr. Rudwaleit considers a clearly positive MRI to be a prerequisite for anti–tumor necrosis factor therapy. Anti-TNF agents have proved highly effective in AS. There is hope that their early use can prevent or at least retard disease evolution.

The definitive evidence for this isn't in yet, but it's an exciting possibility that has added further impetus to efforts to diagnose AS earlier. ■

EXPERT OPINION

Monoclonal Antibodies for RA

Excluding those classified as orphan drugs, only one monoclonal antibody, rituximab (Rituxan), currently is used to treat rheumatoid arthritis.

Exposure of the embryo and fetus should be expected whenever this antibody is used in pregnancy. Although its molecular weight is very high, rituximab is known to cross the placenta in humans. The transplacental passage of the other antibodies has not been studied, but endogenous IgG crosses the placenta. Moreover, the long elimination half-lives ranging from about 2 to 19 days will place these antibodies at the maternal-fetal interface for prolonged periods. Studies in pregnant animals with Rituxan suggested low risk for humans.

BY GERALD G. BRIGGS, B.PHARM, FCCP

Rituxan may cause severe, infusion-related toxicity, including hypotension. Although premedication is used to lessen this effect, this toxicity could have deleterious effects on placental perfusion, resulting in harm to the embryo and fetus.

Six pregnancies have been exposed to Rituxan, including two in the first trimester. No structural anomalies were noted, and all infants appeared to be healthy at birth. One had depletion of B lymphocytes, but B-cell counts returned to normal at about 4 months of age. No increase in infectious disease was noted in any of the infants.

A full assessment of the risk of Rituxan and other monoclonal antibodies during pregnancy is not possible because of the very limited or absent human pregnancy data, including a lack of long-term evaluation of exposed offspring.

Nevertheless, these agents are used for life-threatening diseases and, if indicated, usually should not be withheld from a pregnant woman.

Exposure to monoclonal antibodies during human lactation has not been studied, but their excretion into human milk is likely. ■

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Predictors of DMARD-Free Remission Are Identified

BY DOUG BRUNK
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A fully sustained, disease-modifying-antirheumatic-drug–free remission occurred in 15% of patients using conventional, nonbiologic therapy, according to results from a large 10-year study.

"We were surprised by the high number of patients who achieved remission," Dr. Diane van der Woude of Leiden University Medical Centre (Netherlands), and the study's lead author, said in an interview. The data was reported at the annual European Congress of Rheumatology. "The patients we studied were enrolled between 1993 and 2003, a time when there were no biological agents available and disease activity was not strictly monitored. That 15% of patients treated with conventional therapy achieved remission is a useful number to keep in mind as a reference when reading reports of remission percentages after treatment with novel agents."

She looked at 454 RA patients. Patients were treated with a delayed or early treatment strategy with chloroquine, sulfasalazine, or methotrexate. They defined DMARD-free remission as absence of synovitis without concomitant use of disease-modifying antirheumatic drugs (DMARDs) for more than 1 year. Average follow-up was 8 years. Of the 454 RA patients, 69 (15%) achieved DMARD-free remission.

Univariate analysis revealed that the following were significantly associated with achieving DMARD-free remission: negative family history (hazard ratio of 1.8), short duration of complaints before presentation (HR 1.08 per month), nonsmoking (HR 1.8), low C-reactive protein at baseline (HR 1.01 per mg/L), absence of IgM rheumatoid factor and anti-CCP antibodies (HR 5.9 and 11.6, respectively), and absence of HLA shared epitope alleles (HR 2.1).

Multivariate analysis revealed that low C-reactive protein at baseline and absence of anti-CCP antibodies were significant independent predictors for DMARD-free remission.

"We are currently working on replication of these data in another large [non-Dutch] early arthritis cohort, also consisting of patients treated with conventional antirheumatic therapy," Dr. van der Woude said in an interview. "It will be interesting to see if we and our collaborators will find a similar prevalence of DMARD-free remission and similar predictive characteristics," she added. ■