In JIA and JDM, Fractures Start Before Steroids

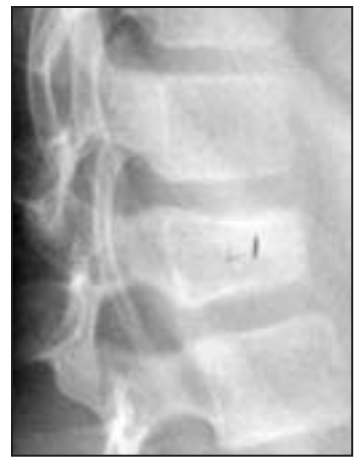
BY AMY ROTHMAN SCHONFELD

PHILADELPHIA — Vertebral fractures are present in a significant percentage of children with rheumatic diseases, and these fractures appear prior to prolonged glucocorticoid exposure, according to Dr. Leanne M. Ward.

"Vertebral fractures are an underrecognized complication of steroid-treated rheumatic disorders," said Dr. Ward, director of the Pediatric Bone Health Clinical and Research Programs at University of Ottawa. "But when do the fractures first occur—in the course of the disease or steroid treatment."

Investigators from the Canadian STOPP (Steroid-Associated Osteoporosis in the Pediatric Population) Consortium evaluated the spine health of 134 children (89 girls, median age 10 years) with rheumatic conditions. Thirty children had juvenile dermatomyositis (JDM), 28 had juvenile idiopathic arthritis (JIA) excluding systemic JIA, and 76 were diagnosed with other rheumatic disorders (systemic lupus erythematosus, systemic vasculitides, systemic JIA, and others). The children underwent thoracolumbar spine x-rays and lumbar spine areal bone mineral density (LS aBMD) evaluation within 30 days of beginning glucocorticoid therapy.

Seven percent of the group (9 of 134) had vertebral fractures; in these 9 children, 6 patients had a single vertebral fracture,



COURTESY DR. LEANNE M. WARD

Fracture (L1), seen in a girl on chronic steroids for JDM.

while 3 patients had between 2 and 5 fractures, for a total of 13 fractures. Three of the fractures (23%) were moderate, and the rest were deemed mild. Most fractures were located in the mid-thoracic and upper lumbar regions, said Dr. Ward, who presented the findings at the annual meeting of the American College of Rheumatology.

Although the mean LS aBMD scores for the group were lower compared with the norm (-0.6 plus or minus 1.22, $P<.001$), LS aBMD did not predict the development of vertebral fractures. The odds for fracture were increased 10-fold if the child reported back pain.

The STOPP Consortium was founded in 2003 as a Canadian national pediatric bone health working group of investigators from 12 tertiary children's hospitals. Its main focus is to track bone mineral accrual and incident spine fractures in glucocorticoid-treated children. The group plans to follow children for 6 years from the time treatment is initiated, allowing investigators to determine cumulative vertebral fracture rates and the potential for bone mass restitution and reshaping of fractured vertebral bodies.

Dr. Ward recommends children with rheumatic diseases undergo baseline spine radiographs at the time of diagnosis and then annually, or more frequently if they have new onset back pain. Children with vertebral fractures who are symptomatic (i.e., have back pain) may be candidates for bisphosphonate therapy, she said.

Dr. Ward reported having a business relationship with Novartis. ■

Serum Marker Identifies JIA Patients Most Likely to Flare

BY MITCHEL L. ZOLER

PHILADELPHIA — Extending methotrexate for more than 6 months after remission had no added benefit for preventing long-term flares in a randomized study of more than 300 patients with juvenile idiopathic arthritis.

The findings also showed that measuring serum levels of the inflammatory marker myeloid-related protein (MRP)8/14 predicted which patients in remission would experience flares off treatment and which would not.

Based on these results, MRP8/14 now is routinely used at the University of Muenster, Germany, to guide withdrawal of methotrexate from juvenile idiopathic arthritis (JIA) patients in remission, Dr. Dirk Foell said at the annual meeting of the American College of Rheumatology. More work is needed to refine use of prognostic, inflammatory markers in these patients, he added.

Some patients may reach an unstable remission on medication, giving them a status of clinical but not immunologic remission. "MRP8/14, a marker of phagocyte activity, indicates subclinical inflammation and identified patients with an increased risk of relapse in whom therapy may not be safely stopped," said Dr. Foell.

Dr. Foell and his associates proposed a MRP8/14 cutoff of 690 ng/dL because they found it combined the best level of specificity and sensitivity for predicting relapse. But they recognize that the cutoff is a statistical number that is not ideal for all cases.

A multicenter collaboration of the Paediatric Rheumatology International Trials Organization (PRINTO), randomized 364 JIA patients with clinical remission on methotrexate. (The average age of the patients was 11 years, about two-thirds were girls, nearly 90% were white, and their median disease duration at enrollment was 3 years). The researchers took patients off of their methotrexate regimen after either 6 or 12 months of remission. They took serum specimens just before methotrexate stopped to measure MRP8/14, which is very stable in the serum. Specimens came from 188 of the patients (52%). Follow-up continued for at least 12 months following the withdrawal.

In an intention to treat analysis, the rate of relapse flares during the first year of follow-up was virtually identical in the two treatment arms: a rate of 40.2 flares/1,000 patient-months of follow-up in 183 patients withdrawn after 6 months, and 40.3 flares/1,000 patient-months in 181 patients withdrawn after 12 months. During 2 years of follow-up, the rates were 33 flares/1,000 patient-months and 29 flares/1,000 patient-months, respectively, also not a statistically significant difference.

An analysis of patients based on their MRP8/14 levels showed a dramatic difference in flare rates. Those with a level of less than 690 ng/dL just before cessation of methotrexate had a flare rate of 26/1,000 patient-months during the first year of follow-up, and 20/1,000 patient months through 2 years of follow-up. Patients with a MRP8/14 level of 690 ng/dL or more had rates of 57 flares/1,000 patient-months and 48 flares/1,000 patient-months, respectively, a statistically significant difference between the two arms, according to the investigators.

Dr. Foell said that he has been a scientific adviser to Wyeth, Regeneron Pharmaceuticals Inc., and CisBio International. ■

Golimumab May Reverse Joint Damage in Psoriatic Arthritis

BY MITCHEL L. ZOLER

PHILADELPHIA — Treatment with golimumab reversed structural joint damage in patients with psoriatic arthritis in a placebo-controlled, phase III study with about 400 patients.

The structural joint benefit from golimumab in this analysis complemented clinical improvements previously reported from the same study. Those benefits led the Food and Drug Administration to give marketing approval to golimumab for psoriatic arthritis (PsA). The results showed structural improvement with golimumab after 24 weeks of treatment independent of methotrexate co-treatment. The benefit continued through 52 weeks of follow-up, Dr. Arthur F. Kavanaugh said at the annual meeting of the American College of Rheumatology.

Structural improvement was seen with golimumab after 24 weeks, independent of methotrexate.

DR. KAVANAUGH

The GO-REVEAL (Golimumab—A Randomized Evaluation of Safety and Efficacy in Subjects With Psoriatic Arthritis Using a Human Anti-TNF Monoclonal Antibody) study enrolled 405 patients at 58 sites in the United States, Canada, and Europe. Enrolled patients had active disease despite treatment with disease-modifying drugs or nonsteroidal anti-inflammatory drugs. Their average age was 47 years, their average duration of PsA was 8 years, 60% were men, 97% were white, and 48% were on methotrexate treatment.

Patients received subcutaneous injections of 50 mg golimumab (146 patients), 100 mg golimumab (146 patients), or placebo (113 patients) at week 0, and then every 4 weeks through week 20. Starting at week 24, all patients received golimumab.

The new analysis used total Sharp/van der Heijde score to measure structural joint damage. At baseline, average scores were 18 in placebo patients, 24 in the 50-mg group, and 23 in the 100-mg group.

After 24 weeks, the scores changed by an average of +0.27 in the placebo patients (a worsening), –0.16 in patients getting 50-mg doses, and –0.02 in those on 100-mg doses. The difference between the 50-mg group and placebo patients was statistically significant. The difference between the 100-mg and placebo group did not reach statistical significance, said Dr. Kavanaugh, of the University of California, San Diego. The difference in average Sharp/van der Heijde scores between the placebo patients and those in both golimumab groups continued through 52 weeks of treatment, even though the placebo patients switched to golimumab treatment after 24 weeks.

The percentage of patients with clear progression on their Sharp/van der Heijde score tallied 8% in the placebo group and 2% in the 50-mg group, a significant difference.

Centocor Ortho Biotech Products LP, the company that markets golimumab (Simponi), sponsored the study. Dr. Kavanaugh and five of his associates on the study were research investigators for Centocor. Another five associates on the study are Centocor employees. ■