Fibrous Dysplasia Lesions Appear Early, Hurt Later

By Miriam E. Tucker
Senior Writer

Fort Lauderdale, Fla. — Although the majority of fibrous dysplasia lesions are established early in childhood, many patients don’t experience pain until later in life, Dr. Michael T. Collins reported at a meeting sponsored by the Paget’s Foundation for Paget’s Disease of Bone and Related Disorders.

Since many patients with fibrous dysplasia (FD) don’t present early enough for prevention of lesions, efforts should focus on therapies directed toward management or regression of existing lesions, and awareness and appropriate treatment of pain. Bisphosphonates have been shown to be effective in relieving pain, said Dr. Collins, who heads the Skeletal Clinical Studies Unit at the National Institute of Dental and Craniofacial Research (NIDCR) of the National Institutes of Health, Bethesda, Md.

The new findings are among the latest to come from ongoing research conducted within the NIDCR’s Skeletal Clinical Studies Program. Over the last 4 years, the group has published a series of papers on the clinical and metabolic aspects of FD, a rare congenital disorder of bone metabolism in which normal bone and bone marrow are replaced with abnormal fibrous tissue.

Elizabeth Hart, a medical student and trainee with the NIDCR program, presented a poster on her onset/disease progression study, which included 44 FD patients who were screened over 32 years and who had at least two 99mTc-methylene diphosphonate bone scans. The median number of scans was four; the median age at first scan was 10 years and the median follow-up 4 years.

The bone scans were scored for location and extent of FD lesions using a validated FD-scoring tool—and also developed by the NIDCR group—that captures the extreme variability of FD’s mosaic nature by incorporating the extent of disease in each of 11 skeletal segments (J. Bone Miner. Res. 2005;20:219-26).

More than 90% of skeletal lesions were established before age 15 years. Craniofacial lesions were established earliest, followed by long bone, and then axial lesions. New lesions were rarely established later in life (after age 25), Ms. Hart reported.

Paradoxically, even though children experience more new lesions and more fractures, they report less pain than do adults. That finding, presented in a second poster by Marilyn H. Kelly, R.N., and Beth Brallante, R.N., came from a population of 33 children aged 5-18 years and 43 adults aged 23-62 years.

Pain was reported by 65% of the group, but the proportion among children was just 45%, compared with 81% of the adults. The lower extremities were the sites most likely to be painful (56% of children and 89% of adults), while the sites most commonly associated with FD were the head (94% of children and 86% of adults) and the lower extremities (97% of children and 86% of adults).

The spine, which was the only site at which there was a significant increase in FD involvement over time (45% of children vs. 71% of adults), was not a significant source of overall pain morbidity, Ms. Kelly and her NIDCR associates reported.

The mechanism of bone pain in FD and its increase in adulthood are unknown and warrant further study, the functionalists said.

A previous study led by Ms. Kelly revealed that mental, emotional, and psychological function among both adults and children with FD is often normal, despite diminished physical function (Bone 2005;37:388-94). “In the all-important areas of relationships, education, and career, patients with FD are normal,” Dr. Collins noted in his overview presentation.

“…The parents’ emotional state is the one most dramatically affected by the diagnosis. ‘Parents of children with this disease suffer…. One of our goals is that by educating parents that their children’s life expectancy is not affected, and that their ability to achieve social and emotional health is not affected, parental emotional pain can be eased,’ he remarked.

Another earlier finding from the NIDCR program was the one that had reversed previous thinking about the clinical management of FD in whom the optic nerve becomes encased. Optic neuropathy is a major concern in FD, because the optic nerve passes through the skull base, which is affected in more than 90% of FD patients. As skull involvement increases over time, the optic nerve becomes encased in almost all patients.

The prevailing belief had been that it was necessary to prophylactically decompress the nerve in all patients to avoid progressive vision loss. However, the NIDCR group was able to show that in fact 91% of completely encased optic nerves were asymptomatic and that only 5% progressed to vision loss. Therefore, prophylactic nerve decompression was not indicated (N. Engl. J. Med. 2002;347:1670-6).

Other previous data suggest that growth hormone (GH) excess is common in patients with both FD and the related disorder, McCune-Albright syndrome, and when present is associated with more severe craniofacial abnormalities (J. Clin. Endocrinol. Metab. 2002;87:3104-12). “This finding is significant because GH excess is often treatable, but unfortunately the diagnosis is often overlooked in children prior to complications,” Dr. Collins said, adding that it is still uncertain whether early diagnosis in children and treatment with GH will prevent morbidity.

More information is available at www.fibrousdysplasia.com.

Early RA Medical Therapy May Prevent Need for Surgery

By Nancy Walsh
New York Bureau

SAN DIEGO — Patients in the Utrecht Rheumatoid Arthritis Cohort who began treatment early in the course of disease were less likely to need joint surgery later on, Dr. Suzan M.M. Verstappen said at the annual meeting of the American College of Rheumatology.

In the ongoing Utrecht cohort study, begun in 1990, patients initially were randomized to early treatment with methotrexate, intramuscular gold, or hydroxychloroquine—or to a “pyridium” treatment approach, which was at that time the traditional paradigm. In the pyridium strategy patients first take aspirin and other NSAIDs, delaying treatment with the disease-modifying antirheumatic drugs (DMARDs), until in the course of disease.

At the time of the first analysis, in 1994, it was apparent that patients in the early DMARD group were faring better, and half, all patients were randomized to one of the three drugs, she said.

“In the present study we investigated the prevalence of joint surgery and located at which clinical, radiographic, and demographic variables in the first 2 years of treatment—when we all know a lot of disease activity occurs—predict delayed joint surgery,” said Dr. Verstappen of University Medical Center Utrecht (the Netherlands).

The cohort included 482 patients, whose mean age was 56 years and mean disease duration was 7.4 years. A total of 32% were major surgeries such as total joint replacement, 50% were intermediate procedures such as arthrodesis, and 18% were minor interventions such as arthroscopy.

By the end of the fifth year, about 18% of patients had required at least one type of surgical intervention, according to Kaplan-Meier survival analysis. Overall mean survival time until surgery was 10 years, and for the major surgical interventions, the mean survival time was 12 years.

With regard to the need for surgical intervention among patients who responded to drug therapy, compared with those who were nonresponders, at the end of the first year no significant difference was seen between the two groups, but by the end of the second year, patients who responded to drug therapy had fewer surgical interventions, she said.

Furthermore, surgical interventions were significantly more common in those whose disability was worse at baseline and those who initially were randomized to NSAID therapy.

Multivariate Cox regression analyses of the 1-year data found that female gender, delayed start with DMARDs, and radiographic progression were predictive of later surgery. Hazard ratios for these variables were 1.55, 1.68, and 1.016, respectively, Dr. Verstappen said.

At the end of the second year, only a delayed start of DMARD therapy and radiographic progression were predictors, with hazard ratios of 1.73 and 1.029, respectively. The multivariate analysis, she said.

The need for joint surgery can be considered an outcome measure reflecting an unfavorable course of rheumatoid arthritis, and a significant number of patients still require some type of surgical intervention, Dr. Verstappen said.

“This is the first study to demonstrate that early treatment prevents later surgical intervention, and we hope that with even more aggressive treatment the percentage of patients requiring surgery later on will decrease further,” she said.