Pain Is Delayed

Fibrous Dysplasia *from page 1*

of papers on FD, a rare congenital disorder of bone metabolism in which normal bone and bone marrow are replaced with abnormal fibroosseous tissue.

Elizabeth Hart, of NIDCR, 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 ^{99m}Tc-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—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, 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 Brillante, R.N., came from 33 children aged 5-18 years and 43 adults aged 23-62 years.

Pain was reported by 65% overall, but the proportion among children was 45%, compared with 81% of adults. The lower extremities were the sites most likely to be painful (56% of children and 89% of adults).

The sites most commonly associated with FD were the head (94% of children and 86% of adults) and 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 pain morbidity.

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 fact, the parents' emotional state is the area most affected. "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."

The NIDCR program changed previous thinking about the clinical management of FD when 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 was that it was important to prophylactically decompress the nerve to avoid progressive vision loss. However, the NIDCR group found that 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).

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;87:5104-12).

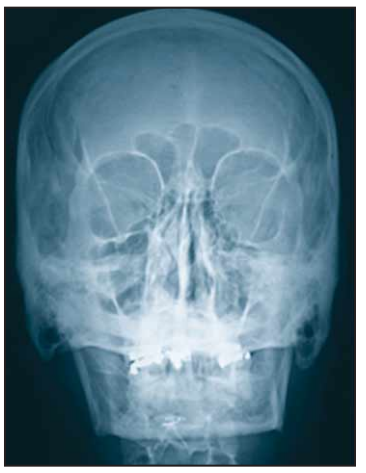
"This [finding] is significant because GH excess is often treatable, but unfortunately the diagnosis is often overlooked in children prior to complications," Dr. Collins said.

He added that it is still uncertain whether early diagnosis in children and treatment with GH will prevent morbidity.

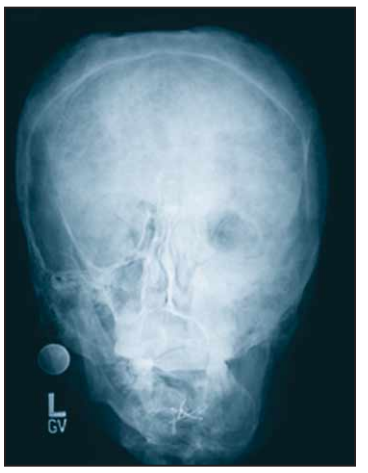
Scoliosis is another common and frequently unrecognized complication of FD. Whereas earlier literature had suggested that the spine was rarely involved in FD, a retrospective review of bone scans from 62 patients with polyostotic disease revealed spinal lesions in 63% and scoliosis in 40%. Scoliosis often occurred at FD sites (J. Bone Joint Surg. Am. 2004;86A:531-7).

"Importantly, we have also observed that in FD scoliosis responds well to surgical fixation," Dr. Collins noted.

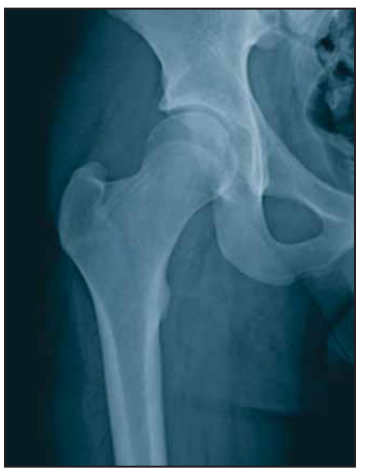
The fracture rate among FD patients diminishes with age—peaking at 6-10 years of age and declining thereafter—but some fracturing continues into adulthood. Among all potential predictors examined, only renal phosphate wasting was a significant predictor: Phosphaturia was associated with both an earlier age of first fracture (5.1 vs. 16.6 years) and a greater lifetime fracture rate, of 0.35 vs. 0.08 fractures/year (J. Bone Miner. Res. 2004;19:571-7). ■



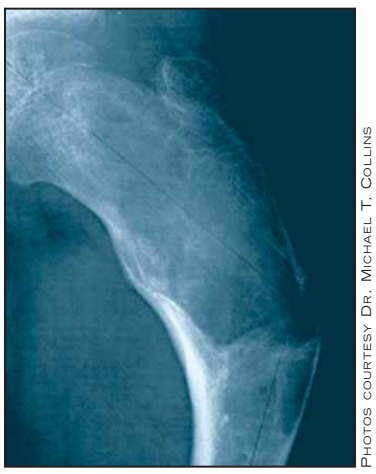
Radiograph shows fibrous dyplasia in craniofacial bone.



The skull of an affected patient has a "sclerotic" appearance.



Radiograph shows fibrous dysplasia in long bones.



The appearance is "lytic," compared with normal bone.

Photos courtesy Dr. Michael T. Collins

Supplements, Range of Motion Exercise Work Well in Osteopenia of Prematurity

BY PATRICIA L. KIRK
Contributing Writer

DALLAS — Early recognition of high-risk infants and excellent nutrition are the best treatments for osteopenia of prematurity, Dr. Charles P. McKay said at a conference sponsored by the American Society for Parenteral and Enteral Nutrition.

Premature infants are at risk for osteopenia of prematurity, or neonatal rickets, due to insufficient calcium and phosphorus accrual before birth, said Dr. McKay, director of the bone and mineral program at Alfred I. duPont Hospital for Children, Wilmington, Del.

Left untreated, children can have fractures, rachitic changes, and shorter stature later in life, he said. Infants born prior to 28 weeks' gestation are at highest risk for osteopenia, which is usually diagnosed at age 2-4 months. The skeleton of at-term infants contains, on average, 25 g of calcium and 13 mg of phosphorus. Total bone calcium at 26 weeks' gestation, however, is just 5 g and accrues exponentially until term.

Premature infants, therefore, should receive formula or breast milk fortified with calcium (200-230 mg/kg) per day, phosphorus (110-123 mg/kg per day), and vitamin D (400 mg/day) to encourage normal bone growth. Fortified milk should be started when the infant tolerates 20-30 mL/kg per day of unfortified milk or breast milk. Preterm infant formulas or fortified human milk should be continued until the infant is aged 6 months or the infant's growth rate is within the normal range, said Dr. McKay.

Length and weight should be followed carefully, he noted. Calcium, phosphorus, and alkaline phosphatase should be measured every 1-4 weeks, depending on growth. "Be careful of ratios," he warned. "The infant can develop hypercalcemia, or if [minerals are] out of balance, they won't be absorbed. If you see hypercalcemia in an infant, the first thing you should suspect is low phosphorus."

Daily passive range of motion exercises increase bone mineral density Dr. McKay noted, adding that he recommends extension, flexion, and range of motion exercises of upper and lower extremities, taking care to avoid movements that could cause fracture or stress.

Osteopenia of prematurity is usually diagnosed using lab results and radiologic tools. Low phosphate or high alkaline phosphatase is an indication of osteopenia. A radiologic diagnosis involves right forearm and chest x-rays to check for incidental fractures, or lucency of cortical bone, or bone density measurement with dual-energy x-ray absorptiometry or ultrasound.

Follow-up studies show low bone density persists until age 8-12 years; however, incidental fracture rates are no higher than for the rest of the population. ■

Cathepsin K at 3 Months Predicts Response in Paget's

FORT LAUDERDALE, FLA. — Serum cathepsin K levels could be used to measure treatment response in patients with Paget's disease of bone, Dr. Daniela Merlotti said at a meeting sponsored by the Paget Foundation for Paget's Disease of Bone and Related Disorders.

Cathepsin K, a cysteine protease enzyme, is the most abundantly synthesized protein of the resorbing osteoclast and plays a role in the degradation of organic matrix in the bone, noted Dr. Merlotti of the University of Siena, Italy.

At baseline, serum cathepsin K levels were significantly higher in 60 Paget's disease patients, compared with 50 age-matched controls, and were higher in patients with polyostotic disease than in those with monostotic disease. Baseline cathepsin K correlated positively with cross-linked telopeptide of type I collagen (sCTX) and urinary calcium, but not with total or bone-specific alkaline phosphatase (ALP).

Overall, intravenous bisphosphonate treatment reduced cathepsin K levels by 28% at 3 days, 34% at 30 days, 45% at 3 months, 29% at 6 months, and 32% at 1 year. For the group as a whole, serum ALP dropped by 33% at 30 days and 24% at 90 days, then increased slightly thereafter up to 1 year.

Cathepsin K levels at 3 months predicted treatment response: Patients whose cathepsin K was decreasing at 3 months had an 18% reduction in total serum ALP levels at 6 months. Those whose cathepsin K was rising at 3 months showed a 5% increase in total serum ALP at 6 months.

—Miriam E. Tucker