Tubular Bone Alterations in Familial Short Stature: Two Reports

Familial short stature (FSS) accounts for about 50% of the children who are seen by pediatric endocrinologists for assessment of growth. These children usually are in good health, have no obvious dysmorphology, and grow at a consistently normal rate. Growth usually proceeds parallel to the 5th percentile, and the predicted adult height is within range for the child's family. Essentially, these patients are short because their parents and families are short. Since such children are considered "normal," their skeletal anthropometric characteristics are presumed to be similar to those in the rest of the "normal" population.

In these two reports, however, a high prevalence of skeletal alterations in individuals with FSS was noted. The occurrence of these characteristics has not been reported previously in this patient group.

A detailed anthropometric study was performed in 40 white children with FSS. Measurements were compared with those from 40 children of normal stature who were matched for age, race, and sex, and from 958 adolescent boys and girls with normal stature. Anthropometric measurements were also obtained from 30 short parents of FSS children and compared with those from 26 normal-statured parents with FSS children and from 33 unrelated normal-statured adults.

Shortening of the fifth metacarpal bone was more prevalent in the 40 FSS children (78%) than in the children with normal stature (28%) and the healthy adolescents (39%, $P < 0.001$). Rhizomelia was also more prevalent in all FSS children (42%) than in the children with normal stature (15%, $P < 0.01$) and the healthy adolescents (17%, $P < 0.001$). Likewise, shortening of the fifth metacarpal bone was more prevalent in the short parents of the FSS children (73%) than in the unrelated adults with normal stature (27%, $P < 0.001$). Also, the prevalence of rhizomelia was higher in the short parents of the FSS children (33%) than in the unrelated adults with normal stature (12%, $P < 0.05$).

Disproportionate shortening of the lower limbs was more prevalent in the FSS children (32%) than in the healthy adolescents (11%, $P < 0.001$). Disproportionate shortening of the arms was more prevalent in the FSS children (35%) than in children with normal stature (10%, $P < 0.01$) and healthy adolescents (8%, $P < 0.001$).

The presence of more than one form of tubular bone alteration occurred more frequently in the children and adults with FSS than in the groups with normal height. Most children and adults with FSS had one to four types of tubular bone alteration, while the majority of individuals with normal stature had either no tubular bone defect or only one type of this defect.

In view of the high prevalence of brachymetacarpia V in FSS patients, the authors also performed detailed radiologic anthropometry of the hand in 28 FSS children. Lengths of each of the hand bones were measured and compared with the normal standards developed by Garn and Poznanski. Moreover, the fifth metacarpal was compared with the other metacarpal bones by obtaining ratios and comparing these ratios with the normal standards set by Garn.

The results of this latter study revealed that most patients with clinical brachymetacarpia V had radiologic evidence of fifth metacarpal bone shortening. The metacarpal pattern profiles of the patients with and without brachymetacarpia V differed. The shortest metacarpal bones in children with clinical brachymetacarpia V were the first and fifth, while in the children without clinical brachymetacarpia V, the shortest metacarpal bone was the fourth, followed by the third and fifth. The phalangeal pattern profiles of these two groups were similar.

The ratios between the fifth metacarpal and the other metacarpal bones in the children with brachymetacarpia V showed that the fifth metacarpal bone was short in relation to the third and fourth metacarpal bones, while the opposite was true in the group without clinical brachymetacarpia V. Moreover, it was also observed that there is a significant positive correlation between height reduction and metacarpal and proximal phalangeal bone shortening in the group with clinical brachymetacarpia V. There was no correlation between height reduction and the length of the distal and middle phalanges.

Cervantes C, Lifshitz F. *Human Biology* 1988;60:151-165. Cervantes C, Lifshitz F, Levenbrown J. *Pediatr Radiol* 1988;18:248-253.

Editor's comment—*The results of these two studies indicate a very high prevalence of tubular bone alterations, mainly disproportionate shortening of the limbs, rhizomelia, brachymetacarpia V, and possible brachymetacarpia I, in children and adults with FSS. Since these characteristics are frequently seen in various syndromes characterized by skeletal dysplasia, it seems reasonable to speculate that children who fall in the lower end of the normal growth standards are short statured because of an inherited abnormality in endochondral growth, the major process responsible for increase in stature. The possibility of mild hypochondroplasia in FSS patients cannot be entirely ruled out, since this condition can present with no stigmata other than short limbed FSS and brachydactyly. There are isolated reports of families with dominantly inherited brachymetacarpia and short stature but no other associated abnormalities. The presence of brachymetacarpia V in the parents of*

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affected FSS children suggests an autosomal dominant mode of inheritance of this characteristic. This trait is also fairly common even in the normal population. Therefore its association with FSS may be coincidental. However, since these tubular bone alterations were significantly more prevalent in the FSS children and their parents and siblings than in the normal population, an inherited trait is most likely responsible for these pleiomorphic manifestations. Segregation analysis may help determine the mode of inheritance of these skeletal alterations.

The findings in these two studies illustrate the major role that endochondral ossification plays in determining stature by expressing itself not only in overall height but also in disproportionate shortening of tubular bones in those with FSS.

The presence of tubular bone alterations in an otherwise healthy patient with FSS should be carefully evaluated before instituting therapy with growth hormone (GH). This is especially important since GH is now available in unlimited supply and pressure to treat the short child with the drug is again high. It may be reasonable to expect that children with FSS who also have skeletal abnormalities would respond less favorably to GH or require a higher dose of GH than would those with FSS and no bone abnormalities.

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