In Brief: Achondroplasia
William B. Stratbucker
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In Brief

Achondroplasia

William B. Stratbucker, MD, MS
Helen DeVos Children’s Hospital
Michigan State University
Grand Rapids, Mich.

Achondroplasia is the most common of the skeletal dysplasias and the most common condition associated with disproportionate short stature. The incidence is 1 in 10,000 to 1 in 30,000 live births, with more than 250,000 people affected worldwide. The disorder is transmitted as an autosomal dominant trait with complete penetrance. However, in more than 75% of affected infants, achondroplasia results from a new mutation. The genetic defect in more than 95% of cases is an arginine-for-glycine substitution in amino acid 380 in the gene, mapped to band 4p16.3, that codes for fibroblast growth receptor 3 (FGFR3). This substitution results in a gain of function of the FGFR3 gene and decreased endochondral ossification and chondrocyte inhibition in growth plate cartilage. Advanced paternal age, especially older than 35 years, has been associated in sporadic cases. Homozygous mutation is fatal. A rare mutation leads to a condition known as severe achondroplasia with developmental delay and acanthosis nigricans (SADDAN). Hypochondroplasia is a milder form of achondroplasia.

Fetal diagnosis often is suspected when long-bone foreshortening is discovered during third-trimester ultrasound. However, families may be counseled inaccurately because other explanations for the ultrasonographic findings exist. Molecular diagnosis is available for confirmation. At birth, the condition can be confirmed radiologically with a skeletal survey that shows a contracted skull base, square-shaped long bones, trident hands, proximal femur radiolucency, and rhizomelic (proximal segment) long-bone shortening. Additional clinical features that aid in the diagnosis of newborns include macrocephaly and frontal bossing. The diagnosis has been delayed in up to 20% of patients when the condition is not suspected at birth. Additional characteristics noted during the first postnatal year include hypotonia and delay in motor development, although normal development usually is achieved eventually.

Life expectancy can reach close to the average, but newer evidence adds to the concern that age-specific mortality is increased at all ages. Abnormal linear bone growth leads to many predictable complications, some of which can be modified through anticipatory guidance and close monitoring.

Neurologic complications are the most concerning. Infants have large heads and can develop craniofacial junction narrowing. Spinal cord compression at the cervical medullary junction can lead to sudden death in infancy and, more commonly, causes hypotonia, which leads to developmental motor delays. Mechanical swings and carrier slings must be avoided to minimize movement of the infant’s head. Surgical suboccipital decompression is indicated for lower limb hyperreflexia, clonus, and central hypopnea on polysomnography. Head size measurements and, if indicated, head ultrasonography are recommended at birth and regularly during early childhood to monitor ventricular size due to the risk of hydrocephalus. Vertebral bodies have short pedicles and narrow interpedicular distance. The spinal canal size decreases in relation to the size of the spinal cord as patients age, which can lead to lumbar spinal stenosis. Indications for laminectomy include claudication and lower extremity hyperreflexia.

Among the orthopedic complications are thoracolumbar gibbus deformity (hump), which typically develops by 4 months of age. Bowing of the lower extremities is present early, and external rotation of the hips, typically seen at birth, resolves after the patient begins to bear weight. Persistent kyphosis worsens with age, exacerbating spinal stenosis.

Brainstem compression may lead to central apnea, and midface underdevelopment can lead to obstructive apnea. Tonsil and adenoid tissue can obstruct...
breathing by restricting space, and pa-
tients may benefit from tonsilload-
enoidectomy. Respiratory dysfunction
can result in abnormal gas exchange
and is associated with increased risk for
cognitive deficits. Patients who have
achondroplasia otherwise typically
would have near-normal intelligence.
Eustachian tubes are short, and recur-
rent otitis media is common. Some
degree of conductive hearing loss is
found in up to 40% of affected adults.
Speech delay and problems with artic-
ulation can result.

Obesity is common and particularly
troublesome for the patient who has
achondroplasia because it worsens
lumbar lordosis and contributes to a
higher rate of cardiac morbidity. Early
degenerative joint disease and upper
airway obstruction are exacerbated by
obesity. Weight-for-height-and-age
growth curves have been developed
specifically for patients who have
achondroplasia, and consultation with
a dietitian is recommended.

Growth hormone has been used in
clinical trials, but its long-term benefits
are questionable, and such therapy cur-
rently is not recommended. Limb-
lengthening surgical procedures are
somewhat effective yet arduous and,
therefore, controversial. Research into
FGFR3 tyrosine kinase inhibitors is un-
derway with animal models; success
has been limited thus far.

Comment: Dr. Stratbucker outlines
the anticipatory guidance and surveil-
lance that pediatricians must perform
to identify and prevent morbidity early.
Pediatricians also must be aware of the
psychosocial issues that children who
have achondroplasia may face, such as
the potential for low self-esteem and
mental health issues. Referral to family
support groups such as the Little People
of America Web site at www.lpaonline.
org, or introduction of families to oth-
ers who have children of short stature
may be helpful. Implementing home
and school adaptations can help a child
of shorter stature to function indepen-
dently, and occupational therapists can
be of assistance.

Janet R. Serwint, MD
Consulting Editor
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