Achondroplasia

Overview

Achondroplasia is a form of disproportionate dwarfism that affects on in 25,000 people and is characterized by shortened limbs (particularly in the upper arms and legs), enlarged head with frontal bossing, midface hypoplasia and bowed legs. Achondroplasia is the result of a mutation in the \textit{FGFR3} gene and may be detected using radiological techniques, physical exams and genetic testing. Treatment of symptoms may include monitoring and surgery by doctors who specialize in skeletal dysplasia.

Heredity and genetics

The \textit{FGFR3} gene encodes the fibroblast growth factor receptor 3 on chromosome 4. Typically, FGFR3 is a membrane-spanning receptor that is active in slowing the production and development of cartilage. In achondroplasia, a single point mutation in \textit{FGFR3} results in a virtually identical amino acid change of glycine to arginine, G380R. This modification causes fibroblast growth factor receptor 3 to be overexpressed, decreasing bone growth and causing disproportionate small stature. The mutant gene’s increased ability to slow bone growth is called a “gain-of-function” mutation.

Achondroplasia is inherited in an autosomal dominant pattern, meaning only one mutant copy of the gene must be present to have the disorder. As a result, affected individuals have a 50 percent chance of passing the abnormal gene to their offspring. However, achondroplasia can also appear in individuals with no prior family history of the disease. In these situations, a spontaneous mutation was introduced. The risk of having another child with a spontaneous mutation resulting in achondroplasia is near zero. Achondroplasia gene abnormalities are fully penetrant, so any person with achondroplasia will show physical characteristics and symptoms of the disease.

Diagnosis and testing

A diagnosis can be obtained during fetal development after 22 weeks gestation. Routine ultrasound can detect the presence of short limbs, but an achondroplasia diagnosis is confirmed by testing the fetal DNA using amniocentesis. For families with a history of achondroplasia, amniocentesis or chorionic villus sampling (CVS) may be used to diagnose achondroplasia. However, not all individuals are diagnosed at birth, in which case clinical and radiologic evaluation by an experienced physician may be used to confirm achondroplasia.

Clinical features:

- Short stature
  - Mean adult height for men: 4-foot-3
Mean adult height for women: 4-1

- Large head with frontal bossing
- Depressed nasal bridge
- Midface retrusion
- Short fingers, may have a trident-like appearance
- Joint contractures
- Genu varum
- Lordosis
- Kyphosis (particularly during infancy)

Radiographic features:

- Decrease interpediculate distance of the lumbar spine
- Shortened tubular bones
- Flat, rounded iliac bones and horizontal acetabula
- Small sacrosiatic notches
- Radiolucent proximal femur and humerus
- Mild metapyleseal abnormalities
- Disproportionate humeral shortening

If an achondroplasia diagnosis is still in doubt after clinic and radiographic evaluations, genetic testing may be necessary.

**Orthopaedic problems and treatment**

**Growth monitoring**

Growth should be monitored using achondroplastic growth, weight, weight-by-height and **BMI charts**.

Limb-lengthening can be used to increase stature but should only be performed by surgeons trained in skeletal dysplasias. We feel that the patient should be old enough to make an informed decision regarding lengthening and weigh the benefits versus the risks involved.

**Kyphosis**

Many infants develop outward curvature of the spine known as kyphosis due to weak muscle tone. As the infant grows and the core muscles become stronger, kyphosis usually disappears without requiring treatment. In these cases, the curve is flexible and tends to resolve when the child is laying face downward.

Persistent kyphotic curves occur in approximately 10-15 percent of children with achondroplasia, in which case a clinical follow-up with spine X-rays is recommended. Treatment varies depending on the degree of kyphosis present, measured using a Cobb angle.
Kyphosis may be prevented by providing stable, supported seating of a child with achondroplasia. When the child is in a sitting position, angle the back at around 45 degrees to decrease the amount of weight pressing on the spine. Tummy time can also help spine stability.

**Hypotonia**

Mild to moderate hypotonia, or weak muscle tone, is common during infancy and will improve as the patient ages. Hypotonia and macrocephaly may make it hard for children to support their head. Delayed developmental milestones such as walking (18-24 months), crawling, standing, etc., may occur as a result of weakened muscle tone.

**Genu varum**

Bowing of the legs affects an estimated 60-80 percent of all children with achondroplasia and can arise from hypotonia, internal tibia torsion or twisting, and/or knee instability. A physical exam should be used to monitor genu varum, searching specifically for a lateral thrust — the appearance that the knee suddenly jumps out to the side while walking. A series of X-rays called an extremity alignment series is also necessary to monitor the mechanical axis of the femoral head, knees and ankles. Surgical intervention is typically not necessary but may be needed if the patient experiences extremity pain or if a lateral thrust is observed. Surgery should be performed by an orthopaedic doctor that specializes in skeletal dysplasia and may include derotational osteotomy or 8-plate.

**Lordosis**

Perhaps all children develop hyperlordosis and a prominent sacrum that tends to be parallel with the ground. In severe cases, it may result in chronic pain and may require physical therapy to stretch the hip flexors and strengthen the core muscles. Bracing and surgical intervention are not necessary. In adults with lordosis, surgical intervention may be necessary should the individual develop spinal stenosis with associated neurological symptoms.

**Elbow contractures**

Limitation in fully extending the elbows is common and usually ranges between 20 and 60 degrees shy of extension. As a result, adaptive devices may be necessary to aid in personal hygiene.

**Joint hypermobility**

Hypermobility, or loose joints, causes joint instability in the wrists and knees. When severe hypermobility is present, one might experience difficulty in fine motor activities such as knitting, writing, drawing, etc., and may find the hypermobile joints to fatigue more easily. Joint hypermobility is often noted at a young age then monitored as the child gets older. If symptoms
interfere with everyday activities, consider modifying the environment with ergonomic keyboards, modified eating and writing utensils, etc.

Other common problems and treatment

Weight management

Weight management is important for everyone, regardless of his or her stature. Going above a healthy weight increases the amount of pressure on the joints and can increase the risk of complications during surgeries or other medical procedures in addition to cardiovascular symptoms. When extra weight becomes distributed over a smaller surface area like that seen in any skeletal dysplasia, these observations may be more dramatic or more noticeable. However, there may be less incidence of obesity-related type 2 diabetes. Because Body Mass Index (BMI) takes height and weight into account, dwarfs tend to have a naturally higher BMI but can still be considered healthy for their size. Use achondroplasia-specific BMI charts to monitor appropriate height and weight ratios. When exercising or engaging in physical activity, avoid high-impact sports such as football, wrestling, etc., unless the activity has been modified for achondroplasia (such as DAAA activities). Low-impact and individualized sports and activities such as tennis, swimming, walking, etc., tend to put less pressure on the joints and are typically more comfortable forms of exercise.

Risk for hydrocephalus

Large head size is characteristic of those with achondroplasia. In children, this is accompanied with excess fluid in the brain, which may or may not need treatment. Symptomatic hydrocephalus presents in around 5 percent of children with achondroplasia. Ventricle size and extra-axial fluid volume should be assessed in infancy using neuroimaging to establish a baseline. For the first year of life, head circumferences should be measured every one to two months and compared to an achondroplasia head circumference chart. After age 1, head circumference should be monitored with each regular check-up. Parents should be aware and check for signs of increased intracranial pressure. Symptoms include, but are not limited to, the following:

- Rapid increase of head circumference
- Seizures
- Irritability
- Vomiting
- Headaches
- Blurred or double vision
- Poor coordination

Risk for craniosynostosis
Although it is uncommon, children with achondroplasia may be more likely to experience premature closing of the skull sutures. This should be monitored by a pediatrician and referred to neurosurgery or a craniofacial surgeon if craniosynostosis is present.

**Foramen magnum stenosis**

The opening at the base of the skull is smaller and more constricted in all infants and children with achondroplasia, though risk of death from this complication is almost exclusively during the first year of life. As a result of foramen magnum stenosis, the respiratory system and upper cervical cord may become damaged. Respiratory system deficits can cause central sleep apnea. Infants should be assessed thoroughly to assess any neurological symptoms. If symptoms are present, neuroimaging should be completed and the foramen magnum size compared to achondroplasia-specific charts. If treatment is required, a suboccipital decompression is necessary to relieve the compression of the respiratory centers and nerves. Parents should ensure their child has proper neck support when being held, as well as use a solid-back stroller and solid sleeping surface. Try to avoid umbrella strollers, baby swings/jumper swings, front or back carriers, and/or any other equipment that may cause neck instability.

**Central sleep apnea**

Central sleep apnea can be life-threatening and may occur because of foramen magnum stenosis or constriction. Unlike obstructive sleep apnea, the airway passages are open and functioning. However, the body is not receiving the signal from the breathing centers of the brain to inhale. People with central sleep apnea experience periodic episodes where breathing ceases altogether or breathing is shallow and not effective for appropriate respiratory activity. A polysomnography can be used to determine if the breathing problems result from airway obstruction or irregular respiratory signals from the brain. Daytime continuous or spot oximetry may also be necessary. Treatment can include oxygen supplementation (used in a small percentage of patients) or a cervical decompression to treat foramen magnum compression.

**Obstructive sleep apnea**

Obstructive sleep apnea is common in children with achondroplasia between ages 2 and 10 and is a result of the inability to effectively breathe during sleep because of airway collapse. However, it is a lifelong issue in people with achondroplasia. It may be more likely because of small airways, redundant pharyngeal soft tissue and enlarged tonsils and adenoids. Obesity can also be a contributing factor. When left untreated, obstructive sleep apnea can cause chronic low levels of oxygen in the blood, high blood pressure and heart problems. Snoring does not always signal significant airway obstruction. For this reason, monitoring additional symptoms of obstruction is appropriate. Symptoms may include:

- Self-arousals
- Loud snoring
- Nighttime vomiting
- Daytime irritability (or other signs of poor sleep)
- Bed-wetting
- Waking up gasping or choking

If serious obstructive sleep apnea is suspected, then polysomnography should be obtained for further information. There are several options for treatment, depending on the severity of the apnea:

- Adenoidectomy and/or tonsillectomy
- CPAP machine use
- BIPAP machine use

Ears and hearing

Middle ear dysfunction and/or conductive hearing loss is common in individuals with achondroplasia. If not treated from an early age, language and speech developmental delays may occur. Middle ear dysfunction is often unable to be managed. Hearing tests (behavioral audiometric and tympanometric) should be completed around 9-12 months of age and then repeated approximately annually. Myringotomy and pressure equalizing tubes should be used aggressively. Ventilating tubes, should the child need them, should be used until ages 6-8. After this age, the Eustachian tubes should be functioning well and ventilation tubes are usually no longer necessary.

Resources for families

Achondroplasia General Information

Growth Charts
http://www.lpaonline.org/assets/documents/Age-appropriate%20body%20mass%20index%20in%20children%20with%20achondroplasia.pdf

https://lpamrs.memberclicks.net/index.php?option=com_content&view=article&id=66

Little People of America
http://www.lpaonline.org/

Adaptive Products
http://www.lpaonline.org/adaptive-products-