Achondroplasia

The most common cause of dwarfism is a condition known as achondroplasia. It is an autosomal dominant condition caused by a mutation in Fibroblast Growth Factor Receptor 3 (FGFR3) and associated with advanced paternal age. Characteristics of achondroplasia include shortened limbs with normal axial skeleton size, delayed motor milestones, symptoms of spinal stenosis and possibility of developing hydrocephalus. These patients have normal fertility and life spans.

PLAY PICMONIC

Mechanism

Autosomal Dominant

Domino

When an inheritance pattern is autosomal dominant, only one gene needs to be affected to cause the condition. In achondroplasia, when two affected genes are inherited, the condition is fatal in-utero or shortly after birth, due to extremely underdeveloped bones.

Advanced Paternal Age

Elderly Father

An increased incidence of achondroplasia among newborns born to fathers aged 35 years old or older has been observed.

Most Common Cause of Dwarfism

#1 Foam-finger Dwarf

Other causes of dwarfism include syndromes, like Turner's or Noonan, hypothyroidism, osteogenesis imperfecta, and various enzymatic deficiencies. However, achondroplasia remains the most common cause of dwarfism by a large percentage of cases.

Mutation of FGFR3 (Fibroblast Growth Factor Receptor 3)

Mutant Frog-Firefighter in a (3) Tree

Found on chromosome 4, FGFR3 is a gene that encodes for a tyrosine-kinase receptor involved in cartilage production by chondroblasts. When this gene is mutated, endochondral ossification does not properly occur, and drastically short bones are formed. This mutation can be inherited, but may also be sporadic, and thus a child with achondroplasia can be born to two phenotypically normal parents.

Defective Endochondral Ossification

Defects In-condiment Bone-building

As opposed to intramembranous ossification, which does not involve a cartilage intermediate, endochondral ossification relies on cartilage from chondroblasts. These then form long bones, like the femur and humerus. This process occurs initially within the diaphysis of the bone and then later in the epiphyseal plate. When FGFR3 is mutated, this entire process is affected, resulting in achondroplasia, and shorter long bones.

Symptoms

Delayed Motor Milestones

Delayed-sign with Motor Milestone

Although intelligence is normal or near-normal in these patients, the physical abnormalities of achondroplasia limit a newborn from developing their motor skills at the same rate as an unaffected child.

Shortened Limbs with Normal Axial Skeleton Size

Short Limbs and Normal Axe Skeleton

In achondroplasia, long bone formation is the most severely affected. Shortened limbs are always present in this condition. The axial skeleton is not affected to the same degree and will appear near normal.

May Develop Hydrocephalus

Hydra-in-head

Hydrocephalus is the condition of having excess cerebrospinal fluid in the ventricles. In achondroplasia, the foramen magnum is narrowed, which may compress ventricular drainage and cause expansion of the ventricles due to accumulation of CSF.

Symptoms of Spinal Stenosis

Spine of Stone

Spinal stenosis results from a narrowed spinal canal and manifests with neurological symptoms such as radicular back pain and weakness in the lower extremities. Achondroplasia patients may have similar symptoms due to their bone abnormalities.

Normal Life Span and Fertility

Normal Life-line and Fertility-plant

Patients with achondroplasia are known to have nearly normal to normal intelligence and life spans. Fertility can be normal as well; fertility treatments like in-vitro fertilization may be needed, as well as close obstetrical monitoring throughout pregnancy due to possible complications involving the smaller anatomy of these patients.