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Achondroplasia

Cause: gene change of *FGFR3*

Clinical complications:

- Mild to moderate hypotonia
- Obesity, with increased risk of lumbar stenosis, joint problems, and cardiovascular complications
- Risk of having compression in the head and neck regions, which may affect breathing during sleep
- Bowing of the lower leg
- Risk of having spinal kyphosis and/or spinal stenosis (compressed spinal gap)
- Potential middle ear dysfunction

Occurrence rate:

Achondroplasia is the most common form of inherited short stature disease with disproportionate limbs and trunk. Prevalence is best estimated to be 1 in 26,000 to 28,000.
This disorder is inherited in autosomal dominant manner. 80% of patients with this condition have a new gene change, with no affected parents. An individual with achondroplasia whose partner is unaffected has a 50% chance of conceiving a child with achondroplasia in each pregnancy. When both parents have achondropasia, in each pregnancy, the child has a 25% chance of having normal stature, 50% of having achondroplasia and 25% chance of having a lethal condition (i.e. having both copies of the abnormal *FGFR3* gene).

Possible treatments/ therapies:

Management would depend on the clinical manifestations of the patient with achondroplasia.
Surveillance would include the following:

- CT/MRI of the brain, skull and neck region in infancy
- Growth and head circumference documentation
- Neurological exam for signs of spinal cord being damaged
- Auditory evaluation (if there is sign of middle ear problems or hearing loss)
- Physical assessment for bowing of the legs
- Sleep study (if sleep apnea is affecting sleep quality)

If necessary, the following are the potential management for affected individuals:
An option of extended limb lengthening using various techniques (with the affected individuals' understanding of risks involved)

- Ventriculoperitoneal shunt will be considered for increased intracranial pressure
- Treatment to improve sleep apnea Spinal surgery for severe spinal problem
- Weight management

Routine management for middle-ear infections/ persistent middle-ear fluid If speech is affected due to hearing problem, speech evaluation would be carried out

Diastrophic dysplasia

Cause: gene change of a gene *SLC26A2*

Clinical complications:

- Spinal deformities
- Early-onset osteoarthritis
- Clubfoot in some individuals may affect movement(or mobility)

Occurrence rate:

(Prevalence) no reliable data regarding to the prevalence but it is generally believed to be approximately 1 in 100,000. This condition is inherited in an autosomal recessive manner. An affected individual would have 2 copies of changed *SLC26A2* genes. If couples who are carriers (carrying only 1 copy of changed gene), the chance of having next child affected with the same condition in each pregnancy would be 25%.

Possible treatments/ therapies:

The treatments depend on the extent of disease and needs of the patient. The evaluations will include

- Cervical films
- Complete skeletal survey
- Orthopedic assessment

Treatment:

- Physiotherapy and casting to maintain joint positioning and mobility as much as possible
- Surgical correction of clubfoot if it causes problems of mobility
- Surgical correction of scoliosis in individuals at risk for rapid increase of curvature
- Total arthroplasty of hips and knees in relatively young adults to reduce pain and iimprove mobility

Pseudoachondroplasia

Cause: gene change in *COMP* gene

Clinical complications:

- Joint pain during childhood is common
- Degenerative joint disease is progressive
- about 50% of affected individuals undergo hip replacement surgery

Occurrence rate:
(Prevalence): 1 in 30,000
This condition is inherited in an autosomal dominant manner. Some individuals diagnosed with pseudoachondroplasia have one affected parent. Proportion of patients with this condition has a new gene change, with no affected parents. A person with pseudoachondroplasia has 50% chance of passing the changed gene to each of his/her children.

Possible treatments/ therapies:
The treatments depend on the extent of disease and needs of the patient. Evaluation includes:

- Measurement of height and plotting on growth chart
- Evaluation by history and physical examination for skeletal manifestation
- Physical examination of hips, knees, hands and spine
- Evaluation of cervical vertebrae
- Assessment of ligamentous laxity and its clinical implication

Treatment of manifestations:
Surgical treatment of cervical spine instability or cord compression (if the patient has neurological symptoms and radiographic evidence)

- Surgical treatment of scoliosis for severely affected individuals

Spondyloepiphyseal dysplasia congenital

Cause: gene change in *COL2A1*

Clinical complications:

- Skeletal abnormalities, including abnormal curvature of spine
- Respiratory problems may occur
- Chance of having arthritis
- Severe nearsightedness and other vision problems
- Clubfoot may affect movement
- Joint mobility may be diminished

Occurrence rate:

The prevalence is unknown.

This condition is inherited in autosomal dominant manner. Some individuals diagnosed with pseudoachondroplasia have one affected parent. Proportion of patients with this condition has a new gene change, with no affected parents. A person with the dominant form of OI has 50% chance of passing the changed gene to each of his/her children.

Possible treatments/therapies:

The treatments depend on the extent of disease and needs of the patient.

- Evaluation of cervical vertebrae

Treatment of manifestations:

- Surgical treatment of cervical spine instability or cord compression (if the patient has neurological symptoms and radiographic evidence)
- Surgical treatment of scoliosis for severely affected individuals
- Surgical correction of clubfoot if it causes problems regarding mobility

Osteogenesis imperfecta (OI)

Cause: gene change in *COL1A1* or *COL1A2* gene

Clinical complications:
There are 8 subtypes of OI. The features and severities vary, even to individuals with the same subtype of OI. The complications depend on the manifestation of the affected individual:

- Fractures with minimal or no trauma without other factors (e.g. abuse or other disorders of bone)
- Bone deformity
- Brittle teeth
- Hearing loss
- Respiratory problems (for individuals with OI Type II, the most severe form), often result in death at or shortly after birth
- Tinted sclera (scelera is the white area of the eye)

Occurrence rate:
(Prevalence) Considering all types, OI has a prevalence of approximately 6-7 in 100,000 liveborns. Most cases of OI (85-90%) are inherited in an autosomal dominant manner. The affected individual has only one copy of changed gene. Patients with the dominant form of OI have either inherited from an affected parent, or got a new gene change when neither of the parents has OI. A person with the dominant form of OI has 50% chance of passing the changed gene to each of his/her children. Approximately 10-15% of OI cases are inherited in an autosomal recessive manner. Affected patient has two copies of the changed gene. In such situation, parents do not have OI but each has one copy of changed gene. In each pregnancy, there is 25% chance of having a child with recessive form of OI. Healthy siblings of a person with recessive form of OI have a 50% chance of being a carrier.

Possible treatments/therapies:
Exercise (e.g. swimming and water therapy) as much as possible to promote muscle and bone strength, which can help prevent fractures

- Surgical intervention for strengthening long bones and prevent and/or correct deformities
- Nutritional advice for patients with OI, especially on avoiding excessive alcohol and caffeine consumption for protecting bones from being more fragile
- Medications, including growth hormone treatment and oral drugs called bisphosphonates, are potential treatments for OI