Osteoglophonic dysplasia

Description

Osteoglophonic dysplasia is a condition characterized by abnormal bone growth that leads to severe head and face (craniofacial) abnormalities, short stature, and other features. The term osteoglophonic refers to the bones (osteo-) having distinctive hollowed-out (-glophonic) areas that appear as lesions or holes on x-ray images. These lesions typically affect the long bones of the arms and legs.

In people with osteoglophonic dysplasia, bones in the skull often fuse together too early (craniosynostosis). The craniosynostosis seen in people with this disorder may give the head a flat appearance or a "cloverleaf" shape, depending on which bones fuse first. Characteristic facial features in people with osteoglophonic dysplasia include a prominent forehead, widely spaced eyes (hypertelorism) that are prominent (proptosis), low-set ears, a flattening of the bridge of the nose and the middle of the face (midface hypoplasia), a protruding jaw (prognathism), a high arch in the roof of the mouth (a high-arched palate), and a short neck. People with this condition usually have no visible teeth because the teeth never emerge from the jaw (clinical anodontia). In addition, the gums are often overgrown (hypertrophic gingiva).

Most people with osteoglophonic dysplasia have hollowed lesions in the long bones. These lesions are likely non-ossifying fibromas, which are benign (noncancerous) bone tumors made up of fibrous tissue that does not harden into bone. The lesions appear early in life and gradually increase in size and number during childhood. Later in life, the lesions may get smaller or go away once the bones have stopped growing. Individuals with osteoglophonic dysplasia can also have short, bowed legs and arms. They also have flat feet; overlapping toes; and short, broad hands and fingers.

Infants with osteoglophonic dysplasia often experience failure to thrive, which means they do not gain weight and grow at the expected rate. Affected individuals can experience episodes of increased body temperature and excessive sweating.

Some people with osteoglophonic dysplasia develop pyloric stenosis, which is a narrowing of the opening from the stomach into the small intestines. Others can develop inguinal hernia, in which the contents of the abdomen causes a soft out-pouching through the lower abdominal wall.

The life expectancy of people with osteoglophonic dysplasia depends on the extent of the craniofacial abnormalities. People with abnormalities that obstruct the air passages

and affect the mouth and teeth may have respiratory problems and difficulty eating and drinking. Despite the skull abnormalities, intelligence is generally not affected in people with this disorder, but speech delays can occur.

Frequency

Osteoglophonic dysplasia is a rare disorder, though its exact prevalence is unknown. Only about 24 cases are currently known or have been reported in the medical literature.

Causes

Osteoglophonic dysplasia is caused by certain variants (also called mutations) in the *FGFR1* gene, which provides instructions for making a protein called fibroblast growth factor receptor 1 (FGFR1). This protein is one of four fibroblast growth factor receptors, which are a family of proteins that attach (bind) to other proteins called fibroblast growth factors (FGFs). The growth factors and their receptors are involved in processes such as cell division, regulation of cell growth and maturation, formation of blood vessels, wound healing, and embryonic development. In particular, they play a major role in skeletal development.

The FGFR1 protein spans the cell membrane, so that one end of the protein is inside the cell and the other end sticks out from the outer surface of the cell. When a fibroblast growth factor binds to the part of the FGFR1 protein outside the cell, it starts a series of chemical reactions inside the cell that instruct the cell to undergo certain changes or to learn new functions. The FGFR1 protein is thought to play an important role in the development of the nervous system. This protein also helps regulate the growth of the skull and the long bones in the arms and legs.

The *FGFR1* gene variants that cause osteoglophonic dysplasia change a single building block (amino acid) in the FGFR1 protein sequence. These variants are described as " gain-of-function" variants because they appear to enhance the activity of the FGFR1 protein.The altered FGFR1 protein promotes premature fusion of bones in the skull and disrupts the regulation of bone growth in the arms and legs. This overactive FGFR1 protein can also increase the release (secretion) of a bone hormone called FGF23, resulting in abnormally high amounts of phosphate in the urine and low levels of phosphate in the blood. This further impairs bone health and growth in individuals with osteoglophonic dysplasia.

Learn more about the gene associated with Osteoglophonic dysplasia

- FGFR1

Inheritance

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. Most cases result from

new (de novo) variants in the gene that occur during the formation of reproductive cells (eggs or sperm) in an affected individual's parent or in early embryonic development. These affected individuals have no history of the disorder in their family. However, some individuals with the condition inherit the variant from one parent who also has the condition.

Other Names for This Condition

- Fairbank-Keats syndrome
- FGFR1-related osteoglophonic dysplasia
- OGD
- Osteoglophonic dwarfism

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Osteoglophonic dysplasia (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0432283/)

Genetic and Rare Diseases Information Center

- Osteoglosphonic dysplasia (https://rarediseases.info.nih.gov/diseases/4142/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- OSTEOGLOPHONIC DYSPLASIA; OGD (https://omim.org/entry/166250)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28osteoglophonic+dysplasia%5BTIAB%5D%29+OR+%28osteoglophonic+dwarfism%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

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