IMAGe Anomaly

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The combination of intrauterine growth restriction, metaphyseal dysplasia, adrenal hypoplasia congenita, and genital anomalies is commonly known by the acronym IMAGe. This rare syndrome has signs and symptoms that affect many parts of the body.

genetic conditions

1. Introduction

Most affected individuals grow slowly before birth (intrauterine growth restriction) and are small in infancy. They have skeletal abnormalities that often become apparent in early childhood, although these abnormalities are usually mild and can be difficult to recognize on x-rays. The most common bone changes are metaphyseal dysplasia and epiphyseal dysplasia; these are malformations of the ends of long bones in the arms and legs. Some affected individuals also have an abnormal side-to-side curvature of the spine (scoliosis) or thinning of the bones (osteoporosis).

Adrenal hypoplasia congenita is the most severe feature of IMAGe syndrome. The adrenal glands are a pair of small glands on top of each kidney. They produce a variety of hormones that regulate many essential functions in the body. Underdevelopment (hypoplasia) of these glands prevents them from producing enough hormones, a condition known as adrenal insufficiency. The signs of adrenal insufficiency begin shortly after birth and include vomiting, difficulty with feeding, dehydration, extremely low blood sugar (hypoglycemia), and shock. If untreated, these complications can be life-threatening.

The genital abnormalities associated with IMAGe syndrome occur only in affected males. They include an unusually small penis (micropenis), undescended testes (cryptorchidism), and the opening of the urethra on the underside of the penis (hypospadias).

Several additional signs and symptoms have been reported in people with IMAGe syndrome. Some affected individuals have distinctive facial features, such as a prominent forehead, low-set ears, and a short nose with a flat nasal bridge. Less commonly, people with this condition have premature fusion of certain bones of the skull (craniosynostosis), a split in the soft flap of tissue that hangs from the back of the mouth (cleft or bifid uvula), a high-arched roof of the mouth (palate), and a small chin (micrognathia). Other possible features of IMAGe syndrome include high levels of calcium in the blood (hypercalcemia) or urine (hypercalcuria) and a shortage of growth hormone in childhood that results in short stature.

2. Frequency

IMAGe syndrome is very rare, with only about 20 cases reported in the medical literature. The condition has been diagnosed more often in males than in females, probably because females do not have associated genital abnormalities.

3. Causes

IMAGe syndrome is caused by mutations in the *CDKN1C* gene. This gene provides instructions for making a protein that helps control growth before birth. The mutations that cause IMAGe syndrome alter the structure and function of the CDKN1C protein, which inhibits normal growth starting in the early stages of development before birth. Researchers are working to determine how these genetic changes underlie the bone abnormalities, adrenal gland underdevelopment, and other signs and symptoms of this condition.

People inherit one copy of most genes from their mother and one copy from their father. For most genes, both copies are fully turned on (active) in cells. The *CDKN1C* gene, however, is most active when it is inherited from a person's mother. The copy of *CDKN1C* inherited from a person's father is active at much lower levels in most tissues. This sort of parent-specific difference in gene activation is caused by a phenomenon called genomic imprinting. When genomic imprinting reduces the activity of the copy of a gene inherited from the father, that gene is said to be paternally imprinted.

3.1. The gene associated with Intrauterine growth restriction, metaphyseal dysplasia, adrenal hypoplasia congenita, and genital anomalies

- CDKN1C

4. Inheritance

The inheritance of IMAGe syndrome is complex. The condition is described as having an autosomal dominant inheritance pattern because one copy of the altered *CDKN1C* gene in each cell is sufficient to cause the disorder. However, because this gene is paternally imprinted, IMAGe syndrome results only when the mutation is present on the maternally inherited copy of the gene. When a mutation affects the paternally inherited copy of the *CDKN1C* gene, it does not cause health problems. Therefore, IMAGe syndrome is passed only from mothers to their children.

5. Other Names for This Condition

- IMAGe association
- IMAGe syndrome

- Intrauterine growth restriction, metaphyseal dysplasia, adrenal hypoplasia congenita, and genital anomalies

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