KCNK9 Imprinting Syndrome

Subjects: Genetics & Heredity

Contributor: Camila Xu

KCNK9 imprinting syndrome is a rare condition characterized by weak muscle tone (hypotonia) from birth.

genetic conditions

1. Introduction

As a result, affected infants have a lack of energy (lethargy), a weak cry, and they move less than normal. Facial weakness and a poor ability to suck cause feeding difficulties, which can lead to an inability to grow and gain weight (failure to thrive). Difficulty swallowing (dysphagia) often lasts into adolescence. While muscle tone may improve over time, affected individuals usually have some weakness into adulthood. The weakness can lead to permanently bent joints (contractures) and abnormal curvature of the spine (scoliosis).

KCNK9 imprinting syndrome is also characterized by intellectual disability and delayed development of speech and motor skills, such as sitting and walking. Many affected individuals have limited speech throughout life.

This condition is associated with unusual facial features, including an elongated face that narrows at the temples; an upper lip that points outward (called a tented lip); a short, broad space between the lip and the nose (philtrum); a small lower jaw (micrognathia); and abnormally shaped eyebrows. Some affected individuals have an opening in the roof of the mouth (cleft palate). In addition to unusual facial features, some people with *KCNK9* imprinting syndrome have a long neck, a narrow chest, and tapered fingers.

2. Frequency

KCNK9 imprinting syndrome is a rare condition. At least 19 affected individuals have been described in the medical literature.

3. Causes

Mutations in the *KCNK9* gene cause *KCNK9* imprinting syndrome. This gene provides instructions for making a protein called TASK3, which functions as a potassium channel. Potassium channels transport positively charged atoms (ions) of potassium into and out of cells.

TASK3 channels are especially abundant in nerve cells (neurons) in the brain, particularly the region of the brain that coordinates movement (cerebellum). The flow of ions through potassium channels in neurons is involved in activating (exciting) the neurons and sending electrical signals in the brain. TASK3 channels, in particular, maintain the neuron's ability to generate electrical signals and regulate the neuron's activity (excitability).

The genetic changes that cause *KCNK9* imprinting syndrome alter the TASK3 channels. This alteration reduces the flow of ions through the channels, which disrupts normal neuron development and excitability. Impairment of neuron function likely underlies the hypotonia, intellectual disability, and developmental problems characteristic of *KCNK9* imprinting syndrome.

3.1. The gene associated with KCNK9 imprinting syndrome

- KCNK9

4. Inheritance

KCNK9 imprinting syndrome follows an autosomal dominant pattern of inheritance, which means one copy of the altered gene in each cell is sufficient to cause the disorder. People inherit two copies of their genes, one from their mother and one from their father. Usually both copies of each gene are active, or "turned on," in cells. However, for some genes, including *KCNK9*, only one of the two copies is normally turned on, which is a phenomenon known as genomic imprinting. The *KCNK9* gene is a maternally expressed imprinted gene, which means that only the copy of the gene that comes from the mother is active. The copy of the gene that comes from the father is turned off (silenced).

In most cases of *KCNK9* imprinting syndrome, an affected person inherits the mutation from his or her mother. Because the copy of the gene from the father is silenced, fathers cannot pass the condition to their kids. About 20 percent of cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

5. Other Names for This Condition

- Birk-Barel mental retardation dysmorphism syndrome
- Birk-Barel syndrome
- intellectual disability, Birk-Barel type
- intellectual disability-hypotonia-facial dysmorphism syndrome

- mental retardation with hypotonia and facial dysmorphism

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