Schinzel-Giedion Syndrome

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Schinzel-Giedion syndrome is a severe condition that is apparent at birth and affects many body systems.

genetic conditions

1. Introduction

Signs and symptoms of this condition include distinctive facial features, neurological problems, and organ and bone abnormalities. Because of their serious health problems, most affected individuals do not survive past childhood.

Children with Schinzel-Giedion syndrome can have a variety of distinctive features. In most affected individuals, the middle of the face looks as though it has been drawn inward (midface retraction). Other facial features include a large or bulging forehead; wide-set eyes (ocular hypertelorism); a short, upturned nose; and a wide mouth with a large tongue (macroglossia). Affected individuals can have other distinctive features, including larger than normal gaps between the bones of the skull in infants (fontanelles), a short neck, low-set ears, and an inability to secrete tears (alacrima). Babies with Schinzel-Giedion syndrome often have excessive hairiness (hypertrichosis) that usually disappears in infancy.

Children with Schinzel-Giedion syndrome have severe developmental delay. Other neurological problems can include severe feeding problems, seizures, or visual or hearing impairment. They may also experience short pauses in breathing during sleep (sleep apnea).

Affected individuals can also have abnormalities of organs such as the heart, kidneys, or genitals. Heart defects include problems with the heart valves, which control blood flow in the heart; the chambers of the heart that pump blood to the body (ventricles); or the dividing wall between the sides of the heart (the septum). Most children with Schinzel-Giedion syndrome have an accumulation of urine in the kidneys (hydronephrosis), which can occur in one or both kidneys. Affected individuals can have genital abnormalities such as underdevelopment (hypoplasia) of the genitals. Affected boys may have the opening of the urethra on the underside of the penis (hypospadias).

Bone abnormalities are common in people with Schinzel-Giedion syndrome. The bones at the base of the skull are often abnormally hard or thick (sclerotic), or the joint between the bones at the base of the skull (occipital synchondrosis) can be abnormally wide. In addition, affected individuals may have broad ribs, abnormal

collarbones (clavicles), inward- and upward-turning feet (clubfeet), or shortened bones in the arms or legs or at the ends of the fingers (hypoplastic distal phalanges).

Children with Schinzel-Giedion syndrome who survive past infancy have a higher than normal risk of developing certain types of brain tumors called neuroepithelial tumors.

2. Frequency

Schinzel-Giedion syndrome is very rare, although the exact prevalence is unknown. At least 50 cases of the condition have been reported in the scientific literature.

3. Causes

Schinzel-Giedion syndrome is caused by mutations in the *SETBP1* gene. This gene provides instructions for making a protein that attaches (binds) to certain regions of DNA to increase gene activity (expression). The SETBP1 protein is found throughout the body, but protein levels are highest during brain development before birth. During this time, nerve cells grow and divide (proliferate) and move (migrate) to their proper location in the brain. The SETBP1 protein is thought to control the activity of genes involved in these developmental processes.

The *SETBP1* gene mutations that have been identified in Schinzel-Giedion syndrome are described as "gain-of-function" mutations because they increase the activity of the SETBP1 protein. Increased SETBP1 activity likely alters the expression of other genes, particularly genes involved in development before birth. Researchers are working to understand how mutations in the *SETBP1* gene cause the signs and symptoms of Schinzel-Giedion syndrome.

3.1.The Gene Associated with Schinzel-Giedion Syndrome

- SETBP1

4. Inheritance

Schinzel-Giedion syndrome results from new mutations in the *SETBP1* gene and occurs in people with no history of the disorder in their family. One copy of the altered gene in each cell is sufficient to cause the disorder.

5. Other Names for This Condition

- Schinzel Giedion syndrome
- Schinzel-Giedion midface retraction syndrome

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