Shprintzen-Goldberg Syndrome

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Shprintzen-Goldberg syndrome is a disorder that affects many parts of the body.

Keywords: genetic conditions

1. Introduction

Affected individuals have a combination of distinctive facial features and skeletal and neurological abnormalities.

A common feature in people with Shprintzen-Goldberg syndrome is craniosynostosis, which is the premature fusion of certain skull bones. This early fusion prevents the skull from growing normally. Affected individuals can also have distinctive facial features, including a long, narrow head; widely spaced eyes (hypertelorism); protruding eyes (exophthalmos); outside corners of the eyes that point downward (downslanting palpebral fissures); a high, narrow palate; a small lower jaw (micrognathia); and low-set ears that are rotated backward.

People with Shprintzen-Goldberg syndrome are often said to have a marfanoid habitus, because their bodies resemble those of people with a genetic condition called Marfan syndrome. For example, they may have long, slender fingers (arachnodactyly), unusually long limbs, a sunken chest (pectus excavatum) or protruding chest (pectus carinatum), and an abnormal side-to-side curvature of the spine (scoliosis). People with Shprintzen-Goldberg syndrome can have other skeletal abnormalities, such as one or more fingers that are permanently bent (camptodactyly) and an unusually large range of joint movement (hypermobility).

People with Shprintzen-Goldberg syndrome often have delayed development and mild to moderate intellectual disability.

Other common features of Shprintzen-Goldberg syndrome include heart or brain abnormalities, weak muscle tone (hypotonia) in infancy, and a soft out-pouching around the belly-button (umbilical hernia) or lower abdomen (inguinal hernia).

Shprintzen-Goldberg syndrome has signs and symptoms similar to those of Marfan syndrome and another genetic condition called Loeys-Dietz syndrome. However, intellectual disability is more likely to occur in Shprintzen-Goldberg syndrome than in the other two conditions. In addition, heart abnormalities are more common and usually more severe in Marfan syndrome and Loeys-Dietz syndrome.

2. Frequency

Shprintzen-Goldberg syndrome is a rare condition, although its prevalence is unknown. It is difficult to identify the number of affected individuals, because some cases diagnosed as Shprintzen-Goldberg syndrome may instead be Marfan syndrome or Loeys-Dietz syndrome, which have overlapping signs and symptoms.

3. Causes

Shprintzen-Goldberg syndrome is often caused by mutations in the *SKI* gene. This gene provides instructions for making a protein that regulates the transforming growth factor beta (TGF-β) signaling pathway. The TGF-β pathway regulates many processes, including cell growth and division (proliferation), the process by which cells mature to carry out special functions (differentiation), cell movement (motility), and the self-destruction of cells (apoptosis). By attaching to certain proteins in the pathway, the SKI protein blocks TGF-β signaling. The SKI protein is found in many cell types throughout the body and appears to play a role in the development of many tissues, including the skull, other bones, skin, and brain.

SKI gene mutations involved in Shprintzen-Goldberg syndrome alter the SKI protein. The altered protein is no longer able to attach to proteins in the TGF-β pathway and block signaling. As a result, the pathway is abnormally active. Excess TGF-β signaling changes the regulation of gene activity and likely disrupts development of many body systems, including the bones and brain, resulting in the wide range of signs and symptoms of Shprintzen-Goldberg syndrome.

Not all cases of Shprintzen-Goldberg syndrome are caused by mutations in the *SKI* gene. Other genes may be involved in this condition, and in some cases, the genetic cause is unknown.

3.1. The Genes Associated with Shprintzen-Goldberg Syndrome

- FBN1
- SKI

4. Inheritance

Shprintzen-Goldberg syndrome is described as autosomal dominant, which means one copy of the altered gene in each cell is sufficient to cause the disorder. The condition almost always results from new (de novo) gene mutations and occurs in people with no history of the disorder in their family. Very rarely, people with Shprintzen-Goldberg syndrome have inherited the altered gene from an unaffected parent who has a gene mutation only in their sperm or egg cells. When a mutation is present only in reproductive cells, it is known as germline mosaicism.

5. Other Names for This Condition

- Marfanoid-craniosynostosis syndrome
- Shprintzen-Goldberg craniosynostosis syndrome

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