

Trichorhinophalangeal Syndrome Type II

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Trichorhinophalangeal syndrome type II (TRPS II) is a condition that causes bone and joint malformations; distinctive facial features; intellectual disability; and abnormalities of the skin, hair, teeth, sweat glands, and nails. The name of the condition describes some of the areas of the body that are commonly affected: hair (tricho-), nose (rhino-), and fingers and toes (phalangeal).

Keywords: genetic conditions

1. Introduction

People with this condition have multiple noncancerous (benign) bone tumors called osteochondromas. Affected individuals may develop a few to several hundred osteochondromas. These bone growths typically begin in infancy to early childhood and stop forming around adolescence. Depending on the location of the osteochondromas, they can cause pain, limited range of joint movement, or damage to blood vessels or the spinal cord. Individuals with TRPS II may have reduced bone mineral density (osteopenia). Affected individuals often have slow growth before and after birth resulting in short stature. In TRPS II, the ends (epiphyses) of one or more bones in the fingers or toes are abnormally cone-shaped. Additionally, the fingernails and toenails are typically thin and abnormally formed.

Children with TRPS II often have an unusually large range of joint movement (hypermobility). However, as osteochondromas begin to develop, typically starting between infancy and mid-childhood, the joints begin to stiffen, leading to decreased mobility. Individuals with TRPS II may also have a misalignment of the hip joints (hip dysplasia), which often develops in early adulthood but can occur in infancy or childhood.

The characteristic appearance of individuals with TRPS II involves thick eyebrows; a broad nose with a rounded tip; a long, smooth area between the nose and the upper lip (philtrum); a thin upper lip; and small teeth that are either decreased (oligodontia) or increased (supernumerary) in number. Almost all affected individuals have sparse scalp hair. Males are particularly affected by hair loss, with many being nearly or completely bald soon after puberty. Some children with this condition have loose skin, but the skin becomes tighter over time. Individuals with TRPS II may experience excessive sweating (hyperhidrosis).

Most individuals with TRPS II have mild intellectual disability.

2. Frequency

TRPS II is a rare condition; its prevalence is unknown.

3. Causes

TRPS II is caused by the deletion of genetic material on the long arm (q) of chromosome 8. The size of the deletion varies among affected individuals; studies suggest that larger deletions tend to result in a greater number of features than do smaller deletions.

The signs and symptoms of TRPS II are related to the loss of multiple genes on chromosome 8. The *TRPS1*, *EXT1*, and *RAD21* genes are missing in people with TRPS II. These genes play significant roles in regulating gene activity, protein function, and cell division.

Researchers have determined that the loss of the *EXT1* gene is responsible for the multiple osteochondromas seen in people with TRPS II. Loss of the *TRPS1* gene is thought to cause the other bone and facial abnormalities. Deletion of the *RAD21* gene may contribute to intellectual disability. The loss of other genes from this region of chromosome 8 likely contributes to the additional features of this condition.

TRPS II is often described as a contiguous gene deletion syndrome because it results from the loss of several neighboring genes.

A condition similar to TRPS II is caused by gene changes that affect only the *TRPS1* gene. This condition, called trichorhinophalangeal syndrome type I (TRPS I), features similar bone, joint, skin, and facial characteristics as TRPS II. Individuals with TRPS I do not have osteochondromas or intellectual disability, which are not associated with the *TRPS1* gene.

3.1 The genes and chromosome associated with Trichorhinophalangeal syndrome type II

- *EXT1*
- *RAD21*
- *TRPS1*
- chromosome 8

4. Inheritance

Most cases of TRPS II are not inherited, but occur as random events during the formation of reproductive cells (eggs or sperm) in a parent of an affected individual. These cases occur in people with no history of the disorder in their family. In a very small number of cases, people with TRPS II have inherited the chromosomal deletion from a parent with the condition.

TRPS II is considered an autosomal dominant condition because one copy of the altered chromosome 8 in each cell is sufficient to cause the disorder.

5. Other Names for This Condition

- chromosome 8q24.1 deletion syndrome
- Giedion-Langer syndrome
- Langer-Giedion syndrome
- LGS
- tricho-rhino-phalangeal syndrome type II
- trichorhinophalangeal syndrome with exostosis
- TRPS II
- TRPS2

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