PACS1 Syndrome

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PACS1 syndrome is a condition in which all affected individuals have intellectual disability, speech and language problems, and a distinct facial appearance. Many affected individuals have additional neurological, behavioral, and health problems.

genetic conditions

1. Introduction

In *PACS1* syndrome, intellectual disability typically ranges from mild to moderate. Individuals with this condition also have problems with producing speech (expressive language). Speech development ranges from limited language to few words or no speech.

Individuals with *PACS1* syndrome have a distinct facial appearance. Facial features include thick and highly arched eyebrows, long eyelashes, widely set eyes (hypertelorism), outside corners of the eyes that point downward (downslanting palpebral fissures), droopy eyelids (ptosis), a rounded nasal tip, a wide mouth with corners that point downward, a thin upper lip, a smooth area between the nose and upper lip (philtrum), widely spaced teeth, and ears that are low-set with fewer folds and grooves than normal (described as "simple"). Abnormalities of other body systems can also occur, such as malformations of the heart, brain, eyes, or other organs. Males may have undescended testes (cryptorchidism).

Children with *PACS1* syndrome often have problems learning to eat solid food and prefer soft foods. When given solid foods, affected children often swallow without chewing. These food issues tend to persist throughout life. Some affected individuals experience a backflow of stomach acids into the esophagus (gastroesophageal reflux).

Additional neurological problems can occur in *PACS1* syndrome. Some affected individuals have features of autism spectrum disorder, which is characterized by impaired communication and social interaction. Attention-deficit/hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), self-injury, or frustration leading to tantrums can also occur. Most individuals with *PACS1* syndrome have seizures that vary in type and age of onset. Some people with *PACS1* syndrome have weak muscle tone (hypotonia). Individuals with this condition are often delayed in walking, with some developing an unsteady walking style (gait). Rarely, affected individuals have frequent falls and gradually lose their ability to walk in late childhood, requiring wheelchair assistance.

2. Frequency

The prevalence of *PACS1* syndrome is unknown; more than 30 affected individuals have been described in the scientific literature.

3. Causes

PACS1 syndrome is caused by mutations in a gene called *PACS1*. This gene provides instructions for making a protein that helps transport molecules and other proteins to cells and tissues where they are needed. The PACS1 protein is found in a complex network of membranes known as the trans-Golgi network, which sorts proteins and other molecules and sends them to their intended destinations inside or outside the cell. The PACS1 protein is most active during development before birth.

Almost all cases of *PACS1* syndrome are caused by the same mutation. This and other *PACS1* gene mutations are thought to impair the protein's ability to aid in the transport of certain molecules and proteins. Such an impairment likely results in the accumulation or misplacement of molecules or proteins within cells; however, the effects of these accumulated substances is unclear. Research suggests that impaired PACS1 protein function disrupts normal development of structures in the face, leading to a distinct facial appearance. It is likely that the development of other body systems are similarly affected by impaired PACS1 protein function, leading to other signs and symptoms of *PACS1* syndrome, but more research is needed to understand the mechanisms.

The Gene Associated with PACS1 Syndrome

- PACS1

4. Inheritance

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Most cases of this condition result from new (de novo) mutations in the gene that occur during the formation of reproductive cells (eggs or sperm) in an affected individual’s parent or in early embryonic development. These cases occur in people with no history of the disorder in their family.

5. Other Names for This Condition

- autosomal dominant intellectual disability-17
- intellectual disability-craniofacial dysmorphism-cryptorchidism syndrome
- PACS1-related syndrome
- Schuurs-Hoeijmakers syndrome
- SHMS

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