Partington syndrome

Description

Partington syndrome is a neurological disorder that causes intellectual disability along with a condition called focal dystonia that particularly affects movement of the hands. Partington syndrome usually occurs in males; when it occurs in females, the signs and symptoms are often less severe.

The intellectual disability associated with Partington syndrome usually ranges from mild to moderate. Some affected individuals have characteristics of autism spectrum disorders that affect communication and social interaction. Recurrent seizures (epilepsy) may also occur in Partington syndrome.

Focal dystonia of the hands is a feature that distinguishes Partington syndrome from other intellectual disability syndromes. Dystonias are a group of movement problems characterized by involuntary, sustained muscle contractions; tremors; and other uncontrolled movements. The term "focal" refers to a type of dystonia that affects a single part of the body, in this case the hands. In Partington syndrome, focal dystonia of the hands, which is called the Partington sign, begins in early childhood and gradually gets worse. This condition typically causes difficulty with grasping movements or using a pen or pencil.

People with Partington syndrome may also have dystonia affecting other parts of the body; dystonia affecting the muscles in the face and those involved in speech may cause impaired speech (dysarthria). People with this disorder may also have an awkward way of walking (gait). Signs and symptoms can vary widely, even within the same family.

Frequency

The prevalence of Partington syndrome is unknown. At least 20 cases have been described in the medical literature.

Causes

Partington syndrome is caused by mutations in the *ARX* gene. This gene provides instructions for producing a protein that regulates the activity of other genes. Within the developing brain, the ARX protein is involved with movement (migration) and communication of nerve cells (neurons). In particular, this protein regulates genes that

play a role in the migration of specialized neurons (interneurons) to their proper location. Interneurons relay signals between other neurons.

The normal ARX protein contains four regions where a protein building block (amino acid) called alanine is repeated multiple times. These stretches of alanines are known as polyalanine tracts. The most common mutation that causes Partington syndrome, a duplication of genetic material written as c.428_451dup, adds extra alanines to the second polyalanine tract in the ARX protein. This type of mutation is called a polyalanine repeat expansion. The expansion likely impairs ARX protein function and may disrupt normal interneuron migration in the developing brain, leading to the intellectual disability and dystonia characteristic of Partington syndrome.

Learn more about the gene associated with Partington syndrome

- ARX

Inheritance

This condition is inherited in an X-linked recessive pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), a mutation would have to occur in both copies of the gene to cause the disorder. Because it is unlikely that females will have two altered copies of this gene, males are affected by X-linked recessive disorders much more frequently than females. Females with one altered copy of the gene may have some signs and symptoms related to the condition. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Rarely, the genetic change that causes Partington syndrome is not inherited but occurs at some point during embryonic development. As cells continue to grow and divide, some of these cells will have the genetic change, and others will not (a situation known as mosaicism). The mosaic nature of these genetic changes lead to relatively mild features of Partington syndrome.

Other Names for This Condition

- MRX36
- Partington X-linked mental retardation syndrome
- Partington-Mulley syndrome
- PRTS
- X-linked intellectual deficit-dystonia-dysarthria
- X-linked mental retardation with dystonic movements, ataxia, and seizures

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Partington syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0796250/)

Genetic and Rare Diseases Information Center

- Partington syndrome (https://rarediseases.info.nih.gov/diseases/4235/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- PARTINGTON SYNDROME; PRTS (https://omim.org/entry/309510)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28partington+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

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