Miller-Dieker syndrome

Description

Miller-Dieker syndrome is a condition characterized by a pattern of abnormal brain development known as lissencephaly. Normally the exterior of the brain (cerebral cortex) is multi-layered with folds and grooves. People with lissencephaly have an abnormally smooth brain with fewer folds and grooves. These brain malformations cause severe intellectual disability, developmental delay, seizures, abnormal muscle stiffness (spasticity), weak muscle tone (hypotonia), and feeding difficulties. Seizures usually begin before six months of age, and some occur from birth. Typically, the smoother the surface of the brain is, the more severe the associated symptoms are.

In addition to lissencephaly, people with Miller-Dieker syndrome tend to have distinctive facial features that include a prominent forehead; a sunken appearance in the middle of the face (midface hypoplasia); a small, upturned nose; low-set and abnormally shaped ears; a small jaw; and a thick upper lip. Some individuals with this condition also grow more slowly than other children. Rarely, affected individuals will have heart or kidney malformations or an opening in the wall of the abdomen (an omphalocele) that allows the abdominal organs to protrude through the navel. People with Miller-Dieker syndrome may also have life-threatening breathing problems. Most individuals with this condition do not survive beyond childhood.

Frequency

Miller-Dieker syndrome appears to be a rare disorder, although its prevalence is unknown.

Causes

Miller-Dieker syndrome is caused by a deletion of genetic material near the end of the short (p) arm of chromosome 17. The signs and symptoms of Miller-Dieker syndrome are probably related to the loss of multiple genes in this region. The size of the deletion varies among affected individuals.

Researchers are working to identify all of the genes that contribute to the features of Miller-Dieker syndrome. They have determined that the loss of a particular gene on chromosome 17, *PAFAH1B1*, is responsible for the syndrome's characteristic sign of lissencephaly. The loss of another gene, *YWHAE*, in the same region of chromosome

17 increases the severity of the lissencephaly in people with Miller-Dieker syndrome. Additional genes in the deleted region probably contribute to the varied features of Miller-Dieker syndrome.

Learn more about the genes and chromosome associated with Miller-Dieker syndrome

- PAFAH1B1
- YWHAE
- chromosome 17

Inheritance

Most cases of Miller-Dieker syndrome are not inherited. The deletion occurs most often as a random event during the formation of reproductive cells (eggs or sperm) or in early fetal development. Affected people typically have no history of the disorder in their family.

When Miller-Dieker syndrome is inherited, its inheritance pattern is considered autosomal dominant because a deletion in one copy of chromosome 17 in each cell is sufficient to cause the condition. About 12 percent of people with Miller-Dieker syndrome inherit a chromosome abnormality from an unaffected parent. In these cases, the parent carries a chromosomal rearrangement called a balanced translocation, in which no genetic material is gained or lost. Balanced translocations usually do not cause any health problems; however, they can become unbalanced as they are passed to the next generation. Children who inherit an unbalanced translocation can have a chromosomal rearrangement with extra or missing genetic material. Individuals with Miller-Dieker syndrome who inherit an unbalanced translocation are missing genetic material from the short arm of chromosome 17, which results in the health problems characteristic of this disorder.

Other Names for This Condition

- Classical lissencephaly syndrome
- MDS
- Miller-Dieker lissencephaly syndrome

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Miller Dieker syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0265219/)

Genetic and Rare Diseases Information Center

- Miller-Dieker syndrome (https://rarediseases.info.nih.gov/diseases/3669/index)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- MILLER-DIEKER LISSENCEPHALY SYNDROME; MDLS (https://omim.org/entry/247200)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28miller-dieker+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

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