Megalencephaly-polymicrogyria-polydactyly-hydrocephalus syndrome

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Megalencephaly-polymicrogyria-polydactyly-hydrocephalus syndrome

Description

Megalencephaly-polymicrogyria-polydactyly-hydrocephalus (MPPH) syndrome is a rare disorder that primarily affects the development of the brain. Affected individuals are born with an unusually large brain and head size (megalencephaly). The head and brain continue to grow rapidly during the first 2 years of life. MPPH syndrome is also associated with a brain abnormality called bilateral perisylvian polymicrogyria (BPP). The surface of the brain normally has many ridges or folds, called gyri. In people with BPP, an area of the brain called the perisylvian region develops too many gyri, and the folds are irregular and unusually small. Other brain abnormalities, including a buildup of fluid in the brain (hydrocephalus), have also been reported in people with MPPH syndrome.The problems with brain development cause a variety of neurological signs and symptoms. People with MPPH syndrome have delayed development and intellectual disability that ranges from mild to severe. About half of affected individuals develop recurrent seizures (epilepsy) beginning early in childhood. People with MPPH syndrome also have difficulty coordinating movements of the mouth and tongue

(known as oromotor dysfunction), which leads to drooling, difficulty swallowing (dysphagia), and a delay in the production of speech (expressive language).About half of people with MPPH syndrome have an extra finger or toe on one or more of their hands or feet (polydactyly). The polydactyly is described as postaxial because it occurs on the same side of the hand or foot as the pinky finger or little toe.The brain abnormalities characteristic of MPPH syndrome are also found in a closely related condition called megalencephaly-capillary malformation syndrome (MCAP). However, MCAP includes abnormalities of small blood vessels in the skin (capillary malformations) and several other features that are not usually part of MPPH syndrome.

Frequency

MPPH syndrome appears to be a rare disease. About 60 affected individuals have been described in the medical literature.

Causes

MPPH syndrome can be caused by mutations in the AKT3, CCND2, or PIK3R2 gene. The proteins produced from all three genes are involved in a chemical signaling pathway called the PI3K-AKT-mTOR pathway. This signaling influences many critical cell functions, including the creation (synthesis) of new proteins, cell growth and division (proliferation), and the survival of cells. The PI3K-AKT-mTOR pathway is essential for the normal development of many parts of the body, including the brain.Mutations in the AKT3, CCND2, or PIK3R2 gene increase the activity of their respective proteins or prevent the proteins from being broken down when they should. As a result, chemical signaling through the PI3K-AKT-mTOR pathway is enhanced, which increases cell growth

and division. In the brain, the increased number of cells leads to rapid and abnormal brain growth starting before birth. The rapid growth disrupts the structure and function of the developing brain. It is less clear how increased PI3K-AKT-mTOR signaling contributes to polydactyly, although the extra digits are probably related to abnormal cell proliferation in the developing hands and feet. CCND2 and PIK3R2 gene mutations are more likely to cause polydactyly than are AKT3 gene mutations.

Learn more about the genes associated with Megalencephaly-polymicrogyria-polydactyly-hydrocephalus syndrome

AKT3

CCND2

PIK3R2

Inheritance

This condition is considered autosomal dominant, which means one copy of the altered gene in each cell is sufficient to cause the disorder.Almost all cases of this condition result from new (de novo) gene mutations that occur during the formation of reproductive cells (eggs or sperm) or in early embryonic development. These cases occur in people with no history of the disorder in their family.In a small number of cases, people with MPPH syndrome have inherited the altered gene from an unaffected parent who has a mutation only in their sperm or egg cells. This phenomenon is

called germline mosaicism.Rarely, the condition can also result from somatic mosaicism, in which some of an affected person's cells have a gene mutation and others do not. The genetic changes, which are called somatic mutations, arise randomly in one cell during embryonic development. As cells continue to divide, only cells arising from the first abnormal cell will have the mutation.

Other Names for This Condition

MEG-PMG-POLY-HYD Megalencephaly-postaxial polydactyly-polymicrogyria-hydrocephalus syndrome MPPH MPPH syndrome

Additional Information & Resources

Genetic Testing Information

Genetic Testing Registry: Megalencephaly-polymicrogyria-polydactyly-hydrocephalus syndrome 1

Genetic Testing Registry: Megalencephaly-polymicrogyria-polydactyly-hydrocephalus syndrome 2

Genetic Testing Registry: Megalencephaly-polymicrogyria-polydactyly-hydrocephalus syndrome 3

Genetic and Rare Diseases Information Center

Megalencephaly-Polymicrogyria-Polydactyly-Hydrocephalus syndrome

Patient Support and Advocacy Resources

National Organization for Rare Disorders (NORD)

Catalog of Genes and Diseases from OMIM

MEGALENCEPHALY-POLYMICROGYRIA-POLYDACTYLY-HYDROCEPHALUS SYNDROME 1; MPPH1

MEGALENCEPHALY-POLYMICROGYRIA-POLYDACTYLY-HYDROCEPHALUS SYNDROME 2; MPPH2

MEGALENCEPHALY-POLYMICROGYRIA-POLYDACTYLY-HYDROCEPHALUS SYNDROME 3;

MPPH3

Scientific Articles on PubMed

PubMed

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