Polymicrogyria

Polymicrogyria is a condition characterized by abnormal development of the brain before birth. The surface of the brain normally has many ridges or folds, called gyri. In people with polymicrogyria, the brain develops too many folds, and the folds are unusually small. The name of this condition literally means too many (poly-) small (micro-) folds (-gyria) in the surface of the brain.

Polymicrogyria can affect part of the brain or the whole brain. When the condition affects one side of the brain, researchers describe it as unilateral. When it affects both sides of the brain, it is described as bilateral. The signs and symptoms associated with polymicrogyria depend on how much of the brain, and which particular brain regions, are affected.

Researchers have identified multiple forms of polymicrogyria. The mildest form is known as unilateral focal polymicrogyria. This form of the condition affects a relatively small area on one side of the brain. It may cause minor neurological problems, such as mild seizures that can be easily controlled with medication. Some people with unilateral focal polymicrogyria do not have any problems associated with the condition.

Bilateral forms of polymicrogyria tend to cause more severe neurological problems. Signs and symptoms of these conditions can include recurrent seizures (epilepsy), delayed development, crossed eyes, problems with speech and swallowing, and muscle weakness or paralysis. The most severe form of the disorder, bilateral generalized polymicrogyria, affects the entire brain. This condition causes severe intellectual disability, problems with movement, and seizures that are difficult or impossible to control with medication.

Polymicrogyria most often occurs as an isolated feature, although it can occur with other brain abnormalities. It is also a feature of several genetic syndromes characterized by intellectual disability and multiple birth defects. These include 22q11.2 deletion syndrome, Adams-Oliver syndrome, Aicardi syndrome, Galloway-Mowat syndrome, Joubert syndrome, and Zellweger spectrum disorder.

Frequency

The prevalence of isolated polymicrogyria is unknown. Researchers believe that it may be relatively common overall, although the individual forms of the disorder (such as bilateral generalized polymicrogyria) are probably rare.

Causes

In most people with polymicrogyria, the cause of the condition is unknown. However, researchers have identified several environmental and genetic factors that can be
responsible for the disorder. Environmental causes of polymicrogyria include certain infections during pregnancy and a lack of oxygen to the fetus (intrauterine ischemia).

Researchers are investigating the genetic causes of polymicrogyria. The condition can result from deletions or rearrangements of genetic material from several different chromosomes. Additionally, mutations in one gene, \textit{ADGRG1}, have been found to cause a severe form of the condition called bilateral frontoparietal polymicrogyria (BFPP). The \textit{ADGRG1} gene appears to be critical for the normal development of the outer layer of the brain. Researchers believe that many other genes are probably involved in the different forms of polymicrogyria.

\textbf{Inheritance Pattern}

Isolated polymicrogyria can have different inheritance patterns. Several forms of the condition, including bilateral frontoparietal polymicrogyria (which is associated with mutations in the \textit{ADGRG1} gene), have an autosomal recessive pattern of inheritance. In autosomal recessive inheritance, both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Polymicrogyria can also have an autosomal dominant inheritance pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. Other forms of polymicrogyria appear to have an X-linked pattern of inheritance. Genes associated with X-linked conditions are located on the X chromosome, which is one of the two sex chromosomes. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Some people with polymicrogyria have relatives with the disorder, while other affected individuals have no family history of the condition. When an individual is the only affected person in his or her family, it can be difficult to determine the cause and possible inheritance pattern of the disorder.

\textbf{Other Names for This Condition}

- \textit{PMG}

\textbf{Diagnosis & Management}

\textbf{Genetic Testing Information}

- What is genetic testing? /primer/testing/genetictesting
• Genetic Testing Registry: Polymicrogyria, bilateral frontoparietal

• Genetic Testing Registry: Polymicrogyria, bilateral temporooccipital

Research Studies from ClinicalTrials.gov
• ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22polymicrogyria%22

Other Diagnosis and Management Resources
• GeneReview: Polymicrogyria Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1329

Additional Information & Resources

Health Information from MedlinePlus
• Health Topic: Brain Malformations
  https://medlineplus.gov/brainmalformations.html

Genetic and Rare Diseases Information Center
• Bilateral frontoparietal polymicrogyria
  https://rarediseases.info.nih.gov/diseases/10784/bilateral-frontoparietal-polymicrogyria

• Bilateral perisylvian polymicrogyria
  https://rarediseases.info.nih.gov/diseases/6011/bilateral-perisylvian-polymicrogyria

• Megalencephaly-Polymicrogyria-Polydactyly-Hydrocephalus syndrome

• Polymicrogyria
  https://rarediseases.info.nih.gov/diseases/12271/polymicrogyria

Educational Resources
• Christopher A. Walsh Laboratory, Harvard University
  http://www.walshlab.org/

• MalaCards: polymicrogyria
  https://www.malacards.org/card/polymicrogyria

• Orphanet: Polymicrogyria
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=35981
Patient Support and Advocacy Resources

- American Epilepsy Society
  https://www.aesnet.org/
- PMG Awareness Organization
  https://pmgawareness.org/
- Resource list from the University of Kansas Medical Center: Lissencephaly and related brain malformations
  http://www.kumc.edu/gec/support/lissence.html

Clinical Information from GeneReviews

- Polymicrogyria Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1329

Scientific Articles on PubMed

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

Catalog of Genes and Diseases from OMIM

- CORTICAL DYSPLASIA, COMPLEX, WITH OTHER BRAIN MALFORMATIONS 7
  http://omim.org/entry/610031
- POLYMICROGYRIA, BILATERAL FRONTAL-PARIETAL
  http://omim.org/entry/606854
- POLYMICROGYRIA, BILATERAL PERISYLVIAN, X-LINKED
  http://omim.org/entry/300388
- POLYMICROGYRIA, BILATERAL TEMPOROOCIPITAL
  http://omim.org/entry/612691

Sources for This Summary

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