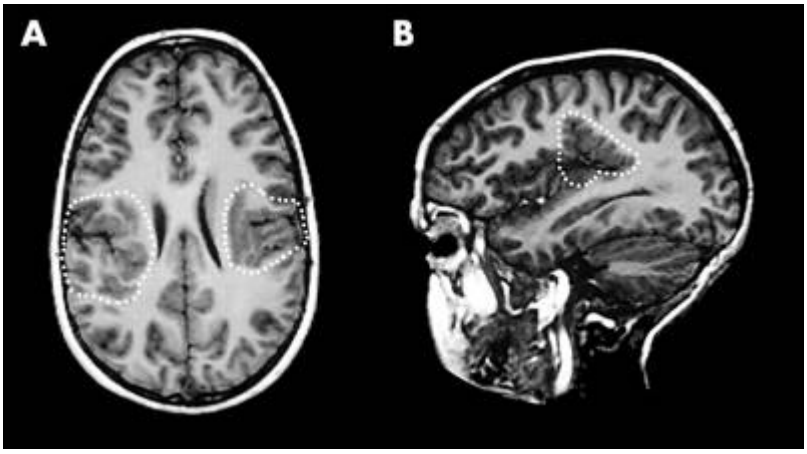
Polymicrogyria



Small gyri with shallow sulci.

Epidemiology

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.

Classification

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.

Etiology

Gene abnormalities e.g. WDR62 and PIK3R2

Intrauterine cerebral injury, after approximately 20 weeks gestation, e.g. infection such as CMV, or hypoxia-ischemia

Metabolic etiology e.g. peroxisomal disorders.

Isolated polymicrogyria can have different inheritance patterns. Several forms of the condition, including bilateral frontoparietal polymicrogyria (which is associated with mutations in the 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.

Proteins anchored to the cell surface via glycosylphosphatidylinositol (GPI) play various key roles in the human body, particularly in development and neurogenesis. As such, many developmental disorders are caused by mutations in genes involved in the GPI biosynthesis and remodeling pathway.

Murakami et al. described ten unrelated families with biallelic mutations in PIGB, a gene that encodes phosphatidylinositol glycan class B, which transfers the third mannose to the GPI. Ten different PIGB variants were found in these individuals. Flow cytometric analysis of blood cells and fibroblasts from the affected individuals showed decreased cell surface presence of GPI-anchored proteins. Most of the affected individuals have global developmental and/or intellectual delay, all had seizures, two had polymicrogyria, and four had peripheral neuropathy. Eight children passed away before four years old. Two of them had a clinical diagnosis of DOORS syndrome (deafness, onychodystrophy, osteodystrophy, mental retardation, and seizures), a condition that includes sensorineural deafness, shortened terminal phalanges with small finger and toenails, intellectual disability, and seizures; this condition overlaps with the severe phenotypes associated with inherited GPI deficiency. Most individuals tested showed elevated alkaline phosphatase, which is a characteristic of the inherited GPI deficiency but not DOORS syndrome. It is notable that two severely affected individuals showed 2-oxoglutaric aciduria, which can be seen in DOORS syndrome, suggesting that severe cases of inherited GPI deficiency and DOORS syndrome might share some molecular pathway disruptions [1)].

Associations

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, Zellweger syndrome.

Megalencephaly-capillary malformation syndrome (MCAP).

Schizencephaly.

Diagnosis

May be difficult to diagnose by CT/MRI, and may be confused with pachygyria.

Treatment

Polymicrogyria (PMG), although the most common brain malformation, represents a low percentage among patients operated on for epilepsy. In cases of hemispheric PMG, electrical status epilepticus during slow sleep (ESESS) may occur leading to an aggravation of the neurological condition and risk of drug resistance. In such cases, surgical treatment can be offered.

Case series

From a population of 230 children who underwent hemispherotomy for epilepsy in the Rothschild Foundation Hospital Fohlen et al. retrospectively reviewed the patients with unilateral PMG and drug-resistant electrical status epilepticus during slow sleep (ESESS) focusing on clinical charts, electrophysiological data, and post-surgical outcome.

Eighteen patients were operated on at a mean age of 7.2 years. The average age was 2 years at seizure onset and 4.4 years at diagnosis of ESESS. All the patients preoperatively had some degree of developmental delay associated with hemiparesis. During ESESS all of them evidenced a cognitive decline and eight experienced a worsening of the hemiparesis; ESESS was resistant to at least three antiepileptic drugs. The outcome of epilepsy, with a mean follow-up of 12.8 years showed that ESESS disappeared in all patients while 16 of 18 became seizure-free. Improvement of behavior and cognitive condition was observed in all.

Hemispherotomy can be helpful in patients with drug-resistant ESESS and hemispheric PMG while keeping in mind that more often an accurate medical treatment can be sufficient. The main benefit of surgery is to definitively stop the seizures and to withdraw the medical treatment while keeping in mind the risk of motor aggravation [2].

References

[1]
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