Malignant migrating partial seizures of infancy

Description

Malignant migrating partial seizures of infancy (MMPSI) is a severe form of epilepsy that begins very early in life. Recurrent seizures begin before the age of 6 months but commonly start within a few weeks of birth. The seizures do not respond well to treatment. Although affected individuals may develop normally at first, progression stalls and skills decline when seizures begin; as a result, affected individuals have profound developmental delay.

The seizures in MMPSI are described as partial (or focal) because the seizure activity occurs in regions of the brain rather than affecting the entire brain. Seizure activity can appear in multiple locations in the brain or move (migrate) from one region to another during an episode. Depending on the region affected, seizures can involve sudden redness and warmth (flushing) of the face; drooling; short pauses in breathing (apnea); movement of the head or eyes to one side; twitches in the eyelids or tongue; chewing motions; or jerking of an arm, leg, or both on one side of the body. If seizure activity spreads to affect the entire brain, it causes a loss of consciousness, muscle stiffening, and rhythmic jerking (tonic-clonic seizure). Episodes that begin as partial seizures and spread throughout the brain are known as secondarily generalized seizures.

Initially, the seizures associated with MMPSI are relatively infrequent, occurring every few weeks. Within a few months of the seizures starting, though, the frequency increases. Affected individuals can have clusters of five to 30 seizures several times a day. Each seizure typically lasts seconds to a couple of minutes, but they can be prolonged (classified as status epilepticus). In some cases, the seizure activity may be almost continuous for several days. After a year or more of persistent seizures, the episodes become less frequent.

Seizures can affect growth of the brain and lead to a small head size (microcephaly). The problems with brain development can also cause profound developmental delay and intellectual impairment. Affected babies often lose the mental and motor skills they developed after birth, such as the ability to make eye contact and control their head movement. Many have weak muscle tone (hypotonia) and become "floppy." If seizures can be controlled for a short period, development may improve. Some affected children learn to reach for objects or walk. However, most children with this condition do not develop language skills.

Because of the serious health problems caused by MMPSI, many affected individuals

do not survive past infancy or early childhood.

Frequency

MMPSI is a rare condition. Although its prevalence is unknown, approximately 100 cases have been described in the medical literature.

Causes

The genetic cause of MMPSI is not fully known. Mutations in the *KCNT1* gene have been found in several individuals with this condition and are the most common known cause of MMPSI. Mutations in other genes are also thought to be involved in the condition.

The *KCNT1* gene provides instructions for making a protein that forms potassium channels. Potassium channels, which transport positively charged atoms (ions) of potassium into and out of cells, play a key role in a cell's ability to generate and transmit electrical signals. Channels made with the KCNT1 protein are active in nerve cells (neurons) in the brain, where they transport potassium ions out of cells. This flow of ions is involved in generating currents to activate (excite) neurons and send signals in the brain.

KCNT1 gene mutations alter the KCNT1 protein. Electrical currents generated by potassium channels made with the altered KCNT1 protein are abnormally increased, which allows unregulated excitation of neurons in the brain. Seizures develop when neurons in the brain are abnormally excited. It is unclear why seizure activity can migrate in MMPSI. Repeated seizures in affected individuals contribute to the developmental delay that is characteristic of this condition.

Learn more about the genes associated with Malignant migrating partial seizures of infancy

- KCNT1
- SCN1A
- TBC1D24

Inheritance

MMPSI is not inherited from a parent and does not run in families. This condition is caused by a new mutation that occurs very early in embryonic development (called a de novo mutation).

Other Names for This Condition

- Early infantile epileptic encephalopathy 14
- EIEE14

- Malignant migrating partial epilepsy of infancy
- Migrating partial epilepsy of infancy
- Migrating partial seizures in infancy
- Migrating partial seizures of infancy
- MMPSI

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Developmental and epileptic encephalopathy, 14 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C3554195/)

Genetic and Rare Diseases Information Center

- Malignant migrating focal seizures of infancy (https://rarediseases.info.nih.gov/diseases/12919/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Malignant migrating partial seizures of infancy%22)

Catalog of Genes and Diseases from OMIM

- DEVELOPMENTAL AND EPILEPTIC ENCEPHALOPATHY 14; DEE14 (https://omim.org/entry/614959)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28malignant+migrating+partial+seizures+of+infancy%29+OR+%28early+infantile+epileptic+encephalopathy+14%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+2520+days%22%5Bdp%5D)

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