EpiCARE

Mild Malformation of Cortical Development with Oligodendroglial Hyperplasia in Epilepsy (MOGHE)

Also known as: MOGHE

What is MOGHE?

Mild Malformation of Cortical Development with Oligodendroglial Hyperplasia in Epilepsy (MOGHE) is a structural abnormality in the cerebral cortex that develops before birth, while the foetal brain is forming. It is an increasingly recognised cause of **focal epilepsy**, meaning that seizures usually start in one area of the brain. In many patients, seizures are difficult to control with **anti-seizure medications (ASM)**. When medicines do not control the seizures, epilepsy surgery may be a treatment option.

MOGHE has only recently been recognised as a separate type of brain malformation histopathologically distinguishable from focal cortical dysplasia. As doctors have learned more about it and brain imaging techniques have improved, more people are now being diagnosed.

The brain changes caused by MOGHE can be difficult to see on routine MRI scans, which can make the diagnosis challenging. High-resolution MRI images within specialized epilepsy protocols—such as those used in epilepsy centers—and radiological expertise significantly increase the likelihood that this condition will be detected. The diagnosis can only be confirmed after epilepsy surgery, when the removed brain tissue is examined under a microscope.

Studies show that genetic changes that occur during brain development in the affected area of the brain (called **somatic mutations**) are linked to MOGHE in the vast majority of cases. These somatic mutations occur spontaneously and are not inherited from the parents and arise either in the SLC35A2 gene or with a gain of the Y chromosome. SLC35A2 mutations lead to altered transport proteins for specific sugars (galactose), which are essential for normal brain development. More research is needed to understand fully how these mutations lead to the MOGHE phenotype.

When do symptoms usually begin?

Seizures can begin at different ages, from infancy to adulthood. However, in most patients, the seizures begin very early, often as early as the first year of life. Because epilepsy in MOGHE begins so early, up to 80% of patients develop epileptic infantile spasms at the onset of epilepsy. Early-onset epilepsy associated with MOGHE is linked to severe developmental impairments, which can often lead to intellectual disability, sometimes in combination with severe autism spectrum disorder.

Patients whose epilepsy begins late in life (after age 10) often have an IQ that is only slightly below average, bordering on a learning disability.

Most patients with MOGHE have frequent, often daily seizures. Most have **focal seizures**, meaning that the seizures start in one area of the brain. The first symptoms of a focal seizure depend upon the region of the brain initially involved, before the spreading of the epileptic discharge. Infantile spasms, tonic, myoclonic and hyperkinetic seizures, as well as focal-to-bilateral tonic-clonic seizures are common.

Early referral, without waiting confirmation of drug-resistance, to centres specialized in paediatric epileptology is essential.

How is MOGHE diagnosed?

Diagnosing MOGHE radiologically can be difficult because the brain changes are often subtle and may not be easy to see on MRI scans although they are often very extensive and can affect several lobes of the brain. **Early MRI images** (taken before the age of 3) often show very characteristic changes that appear as laminar or band-like signal hyperintensities at the boundary between the cerebral cortex and the underlying nerve fibers (white matter). If only MRI scans from later childhood, adolescence or adulthood are available, MOGHE may be confused with focal cortical dysplasia type 1 or type 2 or a complex cortical malformation. Having the scan reviewed by specialists with expertise in epilepsy imaging and MOGHE may help identify these changes.

Long term video-EEG is part of the basic workup and provides information about interictal epileptic discharges during the day and at night, as well as about the seizure onset zone of the recorded seizures. To date, no clear pathognomonic EEG pattern for MOGHE has been described in surface EEG recordings.

In rare cases a **stereo-electroencephalography (SEEG)** could be necessary. This invasive recording, is part of the pre-surgical evaluation, using very thin electrodes placed in the brain to help doctors find exactly where the seizures start.

Other investigations, such as a Positron Emission Tomography (PET) or Magnetoencephalography (MEG) may be indicated.

A PET scan can indicate underlying interictal functional abnormalities in epileptogenic brain regions, an **ictal SPECT** may refer to the area where the seizure originated. **A MEG** may reveal the pathways along which epileptic activity spreads in the brain.

The reference epilepsy centre will recommend the investigations that are most appropriate for you or your affected child.

What treatments are available?

Anti-seizure medications (ASM) are usually the first treatment for MOGHE. However, in many patients, seizures remain difficult to control with medication.

If seizures continue despite medication, epilepsy surgery may be considered. Before surgery, specialized medical teams carry out a detailed assessment (see above) to find where the seizures start and to decide whether surgery is possible and likely to help.

Suspecting MOGHE as early as possible is important because it allows patients to be referred as early to a specialist epilepsy centre, where experts can do the tests needed to confirm the diagnosis and decide whether epilepsy surgery may be a treatment option, without waiting for a proof of drug-resistance.

Can epilepsy surgery help?

As epilepsy in the vast majority of MOGHE patients becomes refractory to treatment, epilepsy surgery, when possible, represents a very important and successful treatment option. Recent studies have shown that post-operative seizure freedom following epilepsy surgery was achieved in 50–76 % of MOGHE patients.

Before surgery, doctors will do several tests to find out where the seizures start and how much of the affected brain can be safely removed. Sometimes the area of the brain causing the seizures is larger than the changes seen on the MRI scan.

This is one reason why extra tests, such as Stereo-EEG, may be needed before surgery.

Different types of surgery may be recommended depending on where the seizures start and how much of the affected brain can be safely removed.

If only a small part of the brain is affected, a lesionectomy may be performed; however, this procedure is rarely carried out in cases of MOGHE due to the extensive nature of the pathology. In most cases, patients require the removal of either one lobe of the brain (lobectomy) or several lobes (multilobectomy). A hemispherotomy – the separating of an entire hemisphere of the brain – is also a commonly performed surgical procedure for MOGHE with hemispheric extent.

Your epilepsy surgery team will explain which operation is **best for you or your child** and why it has been recommended.

What could I ask my doctor or epilepsy specialist about?

- Can you explain what my MRI scan and video-EEG results mean?
- Am I a suitable candidate for epilepsy surgery?
- Do I need any more tests, such as SEEG?
- What type of surgery do you recommend, and why?
- What are the chances that I (or my child) will stop having seizures after surgery?
- If the surgery is successful, will anti-seizure medicines still be needed?
- What are the chances that seizures could continue or come back after surgery?
- What complications might happen after surgery?
- Will I need rehabilitation or any extra support after surgery?
- What follow-up care will I need after surgery?

Find an ERN EpiCARE centre in your country

https://epi-care.eu/ern-epicare-centres/

Patient groups contact:

ariadneslight@gmail.com

EpiCARE
The European Reference Network for Rare and Complex Epilepsies

Contact ERN EpiCARE:

https://epi-care.eu/contact-us/

Authors: Prs. HARTLIEB T[1], BLÜMCKE I[2], at the initiative and contribution from Mrs. Loukia CHRISTODOULOU, patient advocate from Cyprus
[1]Center for Pediatric Neurology, Neurorehabilitation, and Epileptology, Schoen Clinic, Vogtareuth, Germany & Research Institute for Rehabilitation, Transition, and Palliation, Paracelsus Medical University, Salzburg, Austria;
[2]Department of Neuropathology, University Hospital Erlangen, Erlangen, Germany
*Members of the ERN EpiCARE (https://epi-care.eu/members-of-epicare/)

The European Commission, support for the production of this publication, does not constitute endorsement of the contents which reflects the views only of the authors, and the Commission cannot be held responsible for any use which may be made of the information contained therein.