

Macrocephaly-capillary malformation syndrome is...

- ▶ **RARE**
There are under 300 known cases of M-CM worldwide.
- ▶ **POORLY UNDERSTOOD**
M-CM was first documented as a syndrome in 1997. At this time, the majority of known cases are in children. The full natural history of M-CM, particularly how it affects older children and adults, is unknown.
- ▶ **GENETIC AND NON-HEREDITARY**
M-CM is usually caused by a mutation that happens after cell division begins, resulting in only a percentage of the body's cells being affected. This is called somatic mosaicism. The affected gene is called PIK3CA.
- ▶ **VARIABLE**
Individuals can be affected in dramatically different degrees. Physical and cognitive disability can be anywhere from very mild to severe.
- ▶ **COMPLEX**
Specialists required for most patients include neurology, neurosurgery, orthopedics, and genetics. Many patients also require cardiology, ENT, ophthalmology, endocrinology, vascular anomaly specialists and general surgery. Recommended monitoring includes brain and spine MRI for brain overgrowth complications as well as abdominal ultrasounds in childhood for kidney tumors.

LEARN MORE

A detailed syndrome description, management guidelines, genetic testing information, and more can be found online at m-cm.net.

Diagnosed individuals are encouraged to register with the M-CM Network's contact registry. The purpose of the contact registry is to communicate significant research findings that may impact care decisions as well as opportunities to participate in research. You can register online at m-cm.net/contact-registry

A welcoming and knowledgeable peer-support group is on Facebook. This group is run by UK-based patient families. It can be found at facebook.com/groups/127511855574

INTERNATIONAL ORGANIZATIONS

AMCME (Spain) <http://amcme.es>
M-CM France <http://m-cmfrance.com>
M-CM UK <http://www.m-cm.org.uk>

The M-CM Network is a US 501(c)(3) non-profit founded in 2010 to accelerate research and expand understanding about M-CM. Donations are tax-deductible in the United States to the extent of the law.

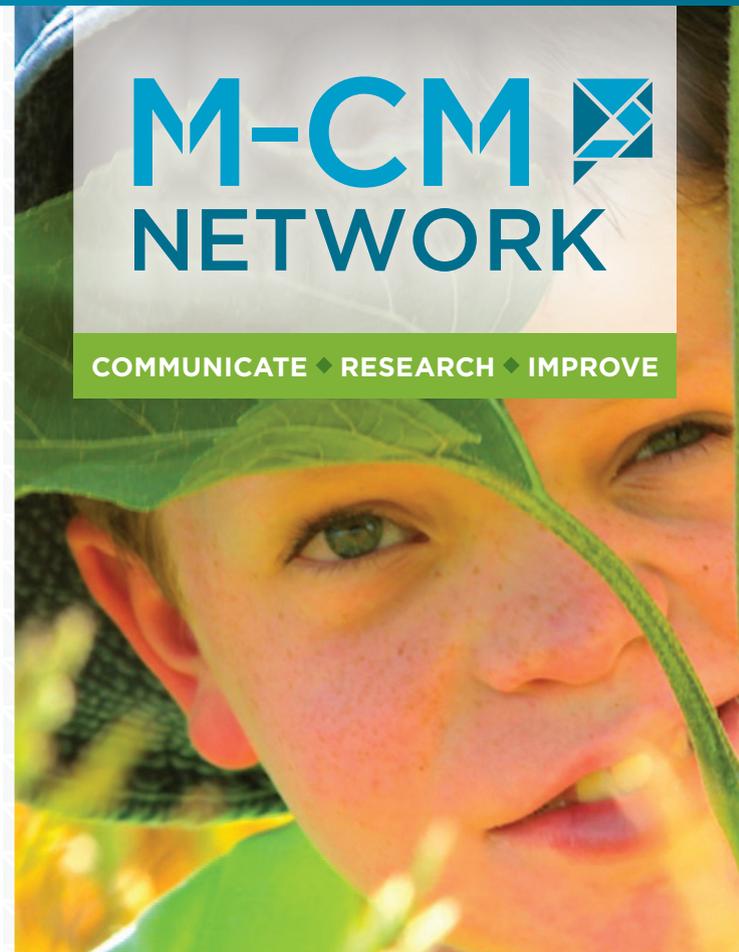
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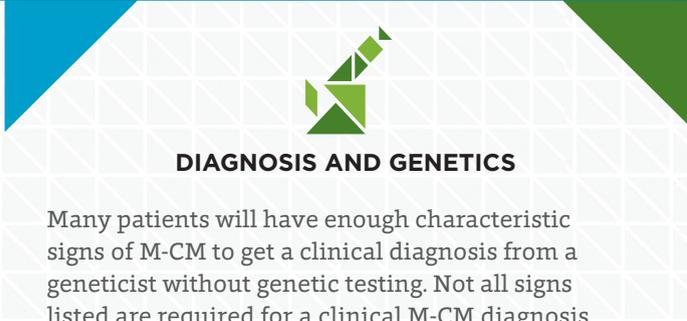
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*An Intro to Macrocephaly-Capillary Malformation
also known as M-CM, MCAP
and M-CMTC*





DIAGNOSIS AND GENETICS

Many patients will have enough characteristic signs of M-CM to get a clinical diagnosis from a geneticist without genetic testing. Not all signs listed are required for a clinical M-CM diagnosis, the determination depends on the judgement of the clinician.

In 2012, activating mutations in the gene PIK3CA were identified as the genetic cause of M-CM. In most cases, these mutations happen after conception, resulting in mosaicism -- only a portion of the body's cells are affected. Many different mutations in PIK3CA have been identified in M-CM patients. The percentage of cells affected varies from person to person. Genetic testing is available through clinical tests that can be ordered by a doctor as well as through research studies.



PIK3CA, OVERGROWTH AND CANCER

Several other rare conditions have been found to also be caused by mosaic activating mutations in PIK3CA, all cause abnormal growth. These conditions collectively have been named PIK3CA Related Overgrowth Spectrum (PROS). A genetic test result that shows a PIK3CA mutation does not differentiate between these conditions, they are differentiated by characteristics in an individual patient. Some patients with PIK3CA overgrowth may not fit squarely in the diagnostic definition of a currently named syndrome.

PIK3CA mutations are known to play a role in cancer. A screening protocol for Wilms' tumor, a childhood kidney cancer, is recommended for children with M-CM under 8 years. There is not currently enough research data to know if there is an elevated lifetime cancer risk for those with PIK3CA overgrowth conditions.



THERAPY AND SCHOOL

Babies and young children with an M-CM diagnosis should be evaluated for early childhood intervention, most will qualify for physical therapy, speech therapy, and occupational therapy services. The early use of augmentative and alternative communication systems can benefit all patients, and will be particularly important for some that do not develop spoken language. Some children with M-CM are eventually diagnosed with autism spectrum disorder and then may qualify for autism-related therapies and services. Schooling accommodations will vary according to the needs of each student, but almost all M-CM patients will need educational supports.



NOMENCLATURE

Several different names and abbreviations have been used since the first syndrome description in 1997. They include: macrocephaly-capillary malformation, M-CM, megalencephaly-capillary malformation, MCAP, macrocephaly-cutis marmorata telangiectasia congenita, and M-CMTC. All of these names refer to the same condition.

Macrocephaly-capillary malformation is a complex, non-inherited genetic syndrome characterized by overgrowth, vascular anomalies, and brain abnormalities.



CHARACTERISTICS OF M-CM

A key sign of M-CM is progressive brain overgrowth, resulting in macrocephaly (larger than normal head). Macrocephaly is not always apparent at birth. Complications can include hydrocephalus and brain stem compression. Many patients are diagnosed with Chiari malformation.

Aside from overgrowth, a variety of other brain abnormalities are sometimes seen in M-CM patients. Some patients develop seizures. Most patients have some degree of developmental delay and/or disability.

Other common characteristics of M-CM include hypotonia, body asymmetry (hemihypertrophy or hemihyperplasia), vascular birthmarks that cover a significant portion of the body at birth (capillary malformation), doughy skin, hypermobile joints, finger and/or toe polydactyly (extra digits) or syndactyly (fused digits), wide feet, and distinctive facial features. Many children have a red birthmark on their upper lip at birth. The vascular birthmarks in most individuals will fade over time.