

What is Macrocephaly-Capillary Malformation Syndrome (M-CM)?

M-CM is a rare syndrome that is highly variable and can cause a number of unusual characteristics including:

- Body overgrowth and asymmetry
- Distinctive facial features
- Vascular skin changes
- Poor muscle tone
- Abnormalities of the fingers and toes
- Connective tissue abnormalities affecting the joints and skin
- Developmental delay and significant neurological problems

The cause remains unknown, although it is suspected to be genetic. M-CM appears to affect boys and girls equally while occurring sporadically in families.

How is M-CM Diagnosed?

Because there is no specific blood test that can say for certain if someone has M-CM, the diagnosis is made solely based on a specific pattern of characteristics or problems seen in an individual. Just like anyone with or without an underlying condition, every child is different and no two children with M-CM are exactly alike. Approximately 130 cases have been reported, but there are likely many more affected individuals who have been misdiagnosed or have not been published in the medical literature.

How M-CM Affects the Brain

While there are a number of unusual features in individuals with M-CM, perhaps the most concerning are the neurological problems. The same overgrowth problem that is physically obvious in the body is also happening in the brain, leading to macrocephaly (an abnormally large head).

In M-CM, the head tends to grow faster than the rest of the body and can often be disproportionately larger. The main cause for a large head is megalencephaly (brain overgrowth), although an additional problem such as hydrocephalus (excessive collection of fluid within the brain) can make the head ever larger.

While there are number of characteristic brain findings, the greatest neurological concern involves overgrowth of a structure at the back of the brain called the cerebellum. The cerebellum tends to grow disproportionately faster in children with M-CM. The rate of brain growth is too fast for the skull to reshape and keep up. The oversized cerebellum can eventually protrude down into the spinal column (called cerebellar tonsillar herniation) leading to potentially life-threatening complications due to brainstem compression. Signs of brainstem compression include:

- difficulty breathing
- seizures
- numbness
- changes in vision
- hearing changes
- irritability
- neck pain
- balance problems
- dizziness
- vomiting
- headaches
- insomnia

Many children with M-CM require brain surgery (such as posterior fossa decompression, VP shunting or third ventriculostomy) at some point in their lives. Many are also affected with hypotonia (poor muscle tone). Hypotonia can be caused by problems within the brain or muscle and is not itself a specific medical disorder. Hypotonia in M-CM is thought to be due to problems within the brain and is a factor contributing to the developmental delays in affected children.

Learning Disabilities, Delays and Cognitive Impairment

In addition to structural brain abnormalities, functional problems are seen in nearly all individuals with M-CM. Developmental disabilities are common and can range from mild, moderate to occasionally severe.

- Motor delays are common and influenced by multiple factors including loose joints, limb asymmetry, and a large head and body size.
- Children learn to walk and talk at a later age than expected.
- Most children require special therapies including physical, occupational and speech.
- M-CM does not appear to be a condition associated with regression or decline in a person's mental functioning.

Skin, Hands and Feet

A child with M-CM has unique skin findings. These are described as capillary malformations (a purplish or reddish network of small blood vessels). This resembles what is called cutis marmorata (a type of marbling of the skin often seen in newborn babies that is worse in the cold) and contributed to M-CM's original name, macrocephaly cutis marmorata tenangiectatica congenita (M-CMTC). Babies born with M-CM have characteristic markings on their face, usually on their upper lip. These are also a kind of capillary malformation called a salmon patch. They may also have vascular patches on other parts of the body that may be called by other names such as port wine stains, nevus flammeus, stork bites or angel kisses. These tend to fade over time.

Children with M-CM often have very small, deep-set nails (particularly the toe nails), which are difficult to cut and care for. Many have broad puffy feet that are often large and asymmetric. Webbing or fusion of the skin between the toes is very common, particularly between the second and third toes. Occasionally, there are extra fingers or toes.

Connective Tissue and Growth

Children with M-CM often have connective tissue abnormalities affecting the skin and joints. Connective tissue is a scaffolding-type material that binds and supports different tissues in the body. There appears to be a connective tissue defect in M-CM causing a variety of features:

- The skin feels soft, doughy and may appear loose, as if it is too large for the body.
- Joints may be loose or lax and joint dislocations can occur.

Vascular, Lungs and Heart

The abnormal vascular malformations that manifest in the skin of individuals with M-CM can also be present deep within the body. There is an increased risk of strokes, although this appears to be in the minority cases, and the exact reason is currently unknown.

Because M-CM causes poor muscle tone, this can lead to respiratory problems and obstructive breathing issues. It is important to be aware of possible underlying respiratory problems prior to any surgical procedure to prevent potential complications during sedation.

A small percentage of children with M-CM are born with heart defects and there is also an increased risk of dysrhythmia (an irregular heartbeat) and possible sudden death. This risk seems greatest in younger children and appears to lessen as children mature.

M-CM and Cancer Risks

Many overgrowth conditions other than M-CM are generally associated with an increased risk of pediatric cancers, specifically a type of kidney cancer called Wilms tumor and a liver cancer called hepatoblastoma. For these conditions, the general recommendation is routine cancer screening by abdominal ultrasounds and blood tests throughout childhood.

While M-CM is also an overgrowth condition, it remains unclear if there is an increased risk of these cancers. There is no clear agreement in the medical community on whether routine cancer screening is recommended. Until more information is learned about M-CM and cancer risks, decisions regarding cancer surveillance are individual choices that should be made only after careful discussions with specialists taking into account a review of the medical literature, and an affected child's specific medical history.

M-CM Network's Goals

M-CM Network was founded in 2010 through a team effort between families and the medical genetics community. Our goals are to:

- Raise awareness among families and the medical community.
- Provide the most comprehensive and up-to-date medical information regarding M-CM through our website and other media resources.

Our ultimate fundraising goals are to start a registry and biobank. Our hopes are that such an endeavor will result in:

- A better understanding of the natural history of M-CM
- Provide more clear and comprehensive medical management guidelines and improve quality of life
- Possible discovery of the cause of M-CM

We can only accomplish our goals through the kindness, contributions and generosity of others. Please visit us at www.m-cm.net to learn more about how you can become involved in our organization.