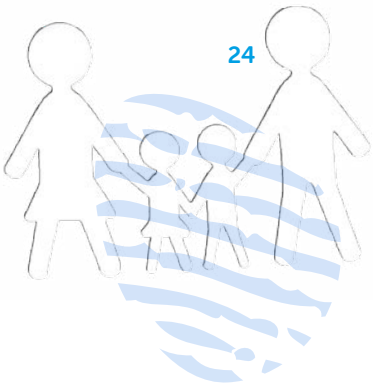
Information for the GP about

Cutis Marmorata Teleangiectatica Congenita (CMTC)

cmtCovm

www.cmtc.nl

Contents



Cutis marmorata teleangiectatica congenita (CMTC) is a rare, congenital vascular disorder in which dilated or malformed (extra) blood vessels are visible through the skin.

Key messages

- When injecting or administering an infusion, avoid the limb affected by CMTC because the blood vessels in the limb are laid-out differently.

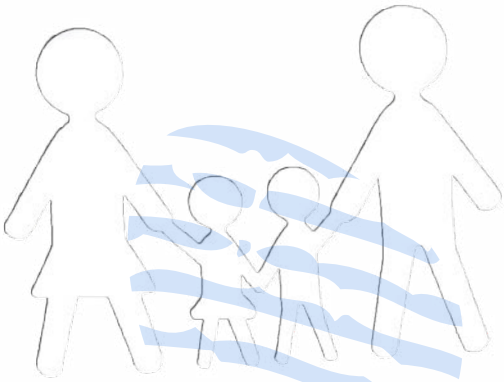
- Because the vessels of CMTC patients are laid-oud differently, they might have a higher risk of deep vein thrombosis. If someone has an increased risk of thrombosis, it is advised to use a preparation consisting of just progestogens when prescribing a hormonal birth control pill (see protocols on contraceptives by the College of General Practitioners). Consult a specialist at the vascular malformations centre if you are unsure if your patient has an increased risk of thrombosis.

- People with CMTC can suffer from delayed wound healing, because the vessels are positioned differently in the affected part of the body.

- Consult with the patient or refer them to a vascular malformations centre if the patient comes to a consultation with new symptoms that might be related to CMTC.

- If necessary, refer the patient and/or their parents to psychosocial counselling.

For a clarification of the key messages, see: Points of attention for the GP.



The skin conditions are most common on arms and legs. In addition to skin conditions, there may be other symptoms, such as asymmetric limbs.

Cutis marmorata teleangiectata congenita

Cutis marmorata teleangiectatica congenita (CMTC) is a rare, congenital vascular disorder in which dilated or malformed (extra) blood vessels are visible through the skin. This gives the skin a net-like or blotchy pattern and makes the skin resemble purple or blue marble. The skin conditions are most common on arms and legs. In addition to skin conditions, there may be other symptoms, such as asymmetric limbs.

Synonym

Dutch pediatrician Van Lohuizen first described this condition in 1922. Because of this, the condition was called 'Van Lohuizen syndrome' for a long time.

Aetiology

The cause of CMTC is still unknown. Genetic defects seem to play a role; mosaicism is probably involved. Mosaicism means that not all cells in the body have the same genetic material. A spontaneous mutation occurs in some cells of the embryo. After the mutated cells divide, all daughter cells will have the same mutation. For this reason, the mutation can only be found in the affected tissue

Heredity

As far as we know, CMTC is not hereditary.

Prevalence

CMTC is very rare. In 2009, only 300 cases were described in literature. CMTC is just as common in boys as it is in girls.

Progression and prognosis

The skin conditions are usually present at birth. In some cases, the signs start to appear when the child is somewhere between three and twelve months old. The prognosis is usually good if additional abnormalities are limited. The markings on the skin will usually become lighter in the first three years after birth. However, additional abnormalities will remain, such as asymmetry of limbs due to hypotrophy or hypertrophy.

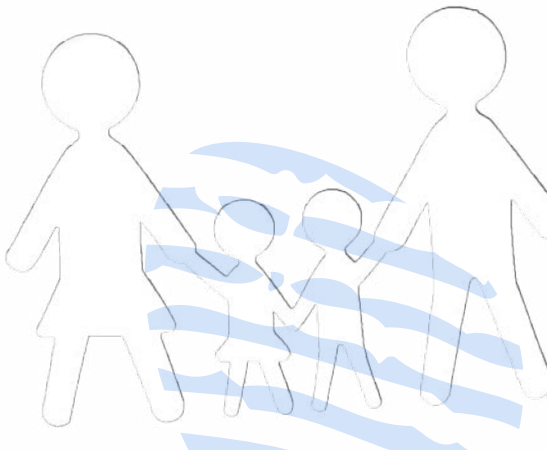
M-CMTC: a condition similar to CMTC

M-CMTC stands for macrocephaly-CMTC, of which macrocephaly and delayed mental development are the most important symptoms. For a long time, this was considered a variant of CMTC, but it is now considered a separate disorder.

M-CMTC is also know as: M-CAP and M-CM

Diagnostics

Patients are usually diagnosed based on clinical characteristics. CMTC is usually diagnosed on sight. An MRI is the gold standard to confirm the diagnosis, but for practical reasons, an ultrasound is often made. Histopathological examination of a skin biopsy may show an increase in the number and size of capillaries and veins, but normally this isn't needed to diagnose a patient. It is especially important in order to exclude other conditions.



Physiological cutis marmorata in healthy infants disappears after the body warms up, unlike CMTC skin disorders.

Differential diagnosis

A number of syndromes resemble CMTC, such as:

Physiological cutis marmorata

Differential diagnosis
A number of syndromes resemble CMTC, such as:

Physiological cutis marmorata

This is caused by physiologic dilatation of capillaries and veins, especially if the healthy infant's temperature is low. This skin disorder disappears after the body warms up, unlike CMTC skin disorders.

Adams-Oliver syndrome

This condition is often associated with:

- a congenital disorder of the skin or scalp (aplasia cutis congenita);
- fusion of toes and/or fingers (syndactyly);
- cardiac abnormalities.

Macrocephaly-CMTC (MCAP)

This condition is characterised by:

- development delays;
- structural brain abnormalities;
- neonatal hypotonia;
- syndactyly;
- asymmetry;
- connective tissue disorders.

Skin disorders are more permanent with this condition and the prognosis is worse.

Bockenheimer's syndrome

This is a condition with congenital vascular malformations in the arms or legs, which increase progressively during life.

Sturge-Weber syndrome

This condition is characterised by a port-wine stain in combination with neurological disorders and glaucoma.

Klippel-Trenaunay syndrome

The three symptoms associated with this condition are:

- varicose veins;
- port-wine stain;
- abnormal growth of soft tissue and bones.

CMTC as part of another condition

CMTC can be part of other conditions, but these conditions can often be recognised by other typical characteristics, such as Down's syndrome (see Information for the GP for more information about Down's syndrome) and Cornelia de Lange syndrome (see Information for the GP for more information about Cornelia de Lange syndrome).

Symptoms

In most cases, skin disorders that characterise CMTC will be noticed shortly after birth. CMTC manifests itself as:

Cutis marmorata
This represents a blue/purple marbled/reticulated vascular network in the skin, which may be accompanied by atrophy and ulceration.

Localisation:
- the extremities are affected in two thirds of CMTC cases, especially in the legs;
- unilateral skin disorders (in 65% of the cases);
- the face and the torso are affected less often;
- palms of the hands, soles of the feet and the mucous membranes are usually not affected

Possible results of the abnormalities and vascular malformations in CMTC

- Limb infections
- Pain in the affected area
- Reduced blood flow, which causes:
  - fatigue in the affected extremity;
  - delayed wound healing in the affected area;
  - an increased risk of thrombosis in the affected extremity.

Table of associated conditions

Associated cutaneous or extracutaneous conditions occur in 27-80% of people with CMTC. There is a large individual variation in severity of symptoms and risk of complications. This depends on the location of the associated abnormalities, which are usually at the level of the CMTC abnormalities.

CONDITION	INFORMATION
Asymmetrical body	- Caused by hypotrophy or hypertrophy - Limb length discrepancy (in 50% of the cases)
Vascular diseases	- Telangiectasia - Port-wine - Haemangioma
Glaucoma or congenital glaucoma	when the face is affected Aplasia cutis congenita
Aplasia cutis congenita	This is a skin condition that is present from birth: a round or oval shaped delimited sun ken area, usually on the head or at the back of the head.
Schisis	n/a
Internal organ abnormalities	- Cysts - Asymmetric kidneys
Neurological disorders	- Epilepsy - Hypotonia
Skeletal disorders	- Syndactyly - Hip dysplasia - Club foot
Brain abnormalities	- Hydrocephalus - Cerebral haemorrhage
Dental abnormalities	- Caused by hypoplasia or hyperplasia of the underlying tissue
Hyperkeratosis	n/a

The diagnosis is best made by a dermatologist at a vascular malformation centre.

Policy

Synonym

There is no curative treatment for CMTC. The policy objective is to reduce symptoms and to monitor associated conditions.

Care coordination

In most cases, the dermatologist makes the diagnosis shortly after birth or in the first year of life. In principle, after diagnosis, a patient will always be seen by a dermatologist in a centre for vascular malformations. Depending on the severity and the comprehensiveness of the conditions, the dermatologist (or paediatric dermatologist) or the involved specialist will provide treatment for the patient himself or transfer care to the dermatologist close to home or the GP. In case of extracutaneous disorders, the patient is preferably overseen by a specialist centre for vascular malformations.

Policy on skin disorders

Laser treatment

Laser treatment is an option in case of cosmetic objections, but the results of this treatment vary.
At a young age, laser treatment for CMTC stains is not recommended. Stains caused by skin disorders often get lighter or disappear spontaneously in the first years of life. Laser treatment is painful, so on a young child it is preferable to perform this procedure under anaesthesia. The physical and mental impact of the anaesthesia must be

carefully balanced against the expected outcome of the treatment.

Anaesthetic

The general advice for elective treatments is to wait until a child is at least three years old before putting them under anaesthetics. It is also recommended to only perform laser treatment when the child really wants it, preferably from puberty onwards. Anaesthesia is then usually no longer necessary.

Possible complications of laser treatment

Laser treatment can cause complications instantly, but also over time, such as:

Early complications:
- infections;
- bleedings;
- incrustation.

Late complications:
- changes in pigment: a pigment increase or decrease because of infections;
- scarring.

Policy on asymmetric limbs

The advice is to treat people with asymmetric limbs in one of the specialised treatment centres for vascular malformations.

Treatment of leg length discrepancy

A leg length discrepancy of less than 2 centimetres rarely prompts complaints and requires no treatment. Referral to an orthopaedist is indicated in case of a difference of 2 centimetres or more, or in case of discomfort. There are several therapeutic possibilities, such as orthopaedic aids (soles), physiotherapy and surgical correction. The orthopaedist judges which treatment is suitable.

Policy on other symptoms

There are huge differences in nature and severity of complaints between CMTC patients. The policy for CMTC related symptoms will be adjusted individually and preferably in consultation with a specialised centre for vascular malformations. If you suspect that new symptoms are related to CMTC, please refer the patient to a specialised centre for vascular malformations for diagnostics and, if necessary, make sure they receive treatment.

Besides medical counselling, psychosocial counselling is important as well.

Psychosocial counselling

Parents

The first months can be very stressful for parents with a child who has CMTC. They experience a lot: they may feel sad or angry, worry about their child's health and have questions about the best way to deal with the situation.

Children

In general, children with skin problems and or physical problems, such as CMTC, have a low self-esteem. Very often, they are dissatisfied about their own appearance. Children with visible skin disorders m be afraid of being bullied.

Psychosocial counselling may be desirable at different times, for both parents and patients. The chief practitioner or the GP may refer the patient and/or their parents to counselling.

Information about heredity and pregnancy

Heredity

As far as we know, CMTC is not hereditary.

Recurrence risk

The risk of CMTC in a subsequent pregnancy is as high as for other couples without a child with CMTC.

Antenatal diagnostics

At this moment, it is not possible to determine whether CMTC is present using antenatal diagnostics.

Fertility

As far as we know, CMTC does not affect fertility.

Pregnancy

Whether CMTC may complicate a pregnancy depends on associated conditions and the severity thereof. If there are any complicating factors, the gynaecologist will make agreements with the patient about policy and counselling during pregnancy.


“Peer support is important for the whole family,, including the patient’s siblings.

Focus points for the GP

Increased risk of thrombosis

The risk of thrombosis in the affected area may increase because the vessels are positioned differently. For that reason it's important to avoid the extremity affected by CMTC if an infusion is injected or administered.

Hormonal contraception

Keep in mind that if you prescribe hormonal contraception, there may be an increased risk of thrombosis, because the vessels are positioned differently. If there is an increased risk of thrombosis, a preparation containing only progestogens is preferred (see NHG Standard Contraception). Consult a specialist at the vascular malformations centre if you are unsure whether your patient has an increased risk of thrombosis.

Delayed wound healing

People with CMTC can suffer from delayed wound healing, because the vessels are positioned differently in the affected part of the body.

No increased risk of sunburn

The affected skin is not more sensitive to sunburn than normal skin.

Psychosocial counselling

If necessary, refer the patients or parents to psychosocial counselling. The CMTC-OVM organisation has a medical psychologist in the team.

The GP's role

The GP is involved in monitoring the patients' follow-up. If the patient comes to you with new symptoms, you may associate this with CMTC. Consult with the vascular malformations centre where the patient is being treated.

Peer support

Via the patient organisation CMTC-OVM, patients are able to contact fellow peers.

The attachment contains additional general focus points for GPs, that are important for the care of people with a rare condition.

Each year, the CMTC-OVM organisation organises a worldwide congress for patients and families in the Netherlands.

Consultation and reference

Centres specialised in vascular malformations

- Erasmus MC: work group vascular malformations Rotterdam (WGVMR)
- Radboudumc Nijmegen: Heco-van work group
- Amsterdam UMC (location AMC)
- UMCU, Utrecht

CMTC-OVM organisation

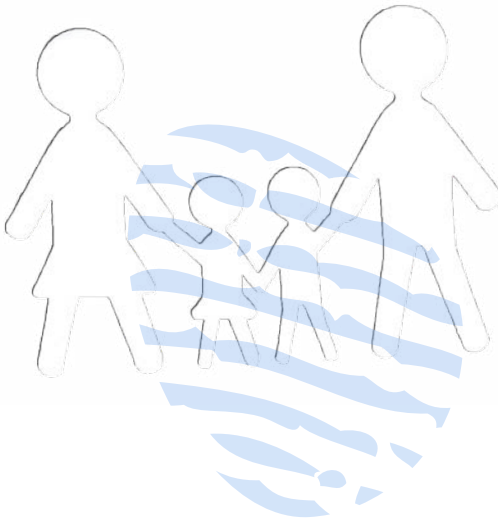
This is a global non-profit patient organisation based in the Netherlands. Activities are aimed at the well-being of people with vascular malformations such as CMTC, and at promoting scientific research about these disorders.

CMTC-OVM organises annual meetings for members. At these meetings, there are doctors with expertise in the field of CMTC who can be asked for advice, including doctors from the WGVAR team in Rotterdam. The CMTC-OVM organisation also advises people with CMTC to regularly take photos to track changes.

Background information

Relevant websites:

- Patients organisation CMTC-OVM www.cmtc.nl/nl
- Huidhuis. This is an online platform for children and teenagers with skin disorders, but also for their parents, caretakers and engaged professionals. www.huidhuis.nl
- Website that contain information about rare conditions. www.zichtopzeldzaam.nl/aandoeningen/cutis-marmorata-telangiectatica-congenita-23/



For the most up to date information, please visit the website: www.cmtc.nl.

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Attachment 1

General focus points

A survey conducted by GPs about people with rare muscular diseases revealed focus points that also apply to GP care for people with a rare condition such as CMTC.3.4

After diagnosing

- Approach the patient as soon as you know what the diagnosis is.
- Ask how the patient experienced your approach in the pre-diagnosis phase. Then find out how that approach or attitude has influenced the relationship between doctor and patient.
- Ask to what extent the patient and relatives have processed and accepted the diagnosis. Repeat this question later on in the process in order to know how the patient managed to cope with changes, especially in case of deterioration.

Care coordination

- Ask what agreements have been made with the patient about a division of tasks between the practitioners and care coordination.
- Discuss the patient's expectations in respect of you as GP.

How will you communicate and what can you offer the patient? If necessary, adjust expectations.

- Ask the patient who the chief practitioner in the hospital is.
- In case the main treatment provider is transferred, adjust the contact details. Ask for any changes in the agreements on the division of tasks.
- Ask if an executive doctor has been appointed. In case of some rare conditions, the patient has an executive doctor who coordinates, has a general overview and acts proactively. For adults, it can be one of the various specialists. Sometimes, the chief practitioner is the executive doctor as well, but not always.
- Discuss the policy (and continue coordinating it) with the chief practitioner or executive doctor and other attending physicians. Preferably use the HASP guideline.
- Declare that you are the first point of contact for the patient, unless agreed otherwise with the chief practitioner or executive doctor.
- Make sure that the general practitioners on duty (e.g. the general practitioner's office) can inform themselves about the patient via the available file, especially about the specific characteristics (see Specific focus points).

Treatment of symptoms

- Treat and guide the patient in case of medical symptoms without specific disease related risks, unless agreed otherwise with the chief practitioner or executive doctor. If the relationship between symptoms and the condition is unclear, please contact the chief practitioner or executive doctor.
- Make sure that you are familiar with the effects of the condition on other symptoms or treatments (see Specific focus points). If in doubt, discuss with the attending physicians.
- Pay attention to the additional disease related risks and draw the patient's attention to these as well (see Specific focus points).
- Refer the patient to the right counsellor in case of complications, preferably after consultation with the chief practitioner or executive doctor.

COLOPHON

This information is produced by a collaboration between the CMTC-OVM organization, the Dutch Genetic Alliance (VSOP: Vereniging. Samenwerkende Ouder- en Patiëntenorganisaties) and the Dutch College of General Practitioners (NHG: Nederlands Huisartsen Genootschap)

This information is part of a chain of information for general practitioners that can be downloaded from www.nhg.org/thema/zeldzame-ziekten, the VSOP websites: www.vsop.nl and www.zichtopzeldzaam.nl/documenten. The text has been carefully compiled on the basis of actual information from medical scientific literature and expert opinion.
If in doubt and/or in case of patient related questions: please contact the chief practitioner or executive doctor.

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