

orphananesthesia

Anaesthesia recommendations for patients suffering from **Charcot-Marie-Tooth disease**

Disease name: Charcot-Marie-Tooth disease

ICD 10: G60.0

Synonyms: Hereditary motor and sensory neuropathy. Includes: Charcot-Marie-Tooth, Déjerine-Sottas, hereditary motor and sensory neuropathy (however this term includes several entities different from Charcot-Marie-Tooth with heterogeneous inheritance), hypertrophic neuropathy of infancy, peroneal muscular atrophy (axonal type) (hypertrophic type), Roussy-Lévy syndrome.

Charcot-Marie-Tooth (CMT) disease is the most prevalent peripheral inherited neuropathy (1/2500 to 10 000; 2.8/10 000 in Spain), and the mean age at onset is 16 years (range 2 to 50 years, but presentation in the early infancy and as late as the 80s has been reported). Patients present with motor and sensory polyneuropathic semiology (distal lower limb weakness and atrophy, gait abnormalities and frequent falls) and pes cavus. Apart from the motor nerve related deficits, most patients suffer slight sensory loss in hands and feet. The treatment of the disease is supportive. Life expectancy is not shortened - except in some forms of Déjerine-Sottas and severe forms of CMT-, but disabilities are the rule.

Medicine in progress



Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

Disease summary

The slow increase in physical disability in adulthood may well be explained by decreased reserves and compensatory mechanisms together with progression of skeletal deformations due to muscle weakness. However this classic concept is controversial, as can be related to CMT1A only: progression of axonal loss definitely occurs in most if not all CMT types and is a cause of progressive wasting and weakness in many patients.

Sometimes CMT disease is associated with moderate to severe chronic extremity pain, that is usually related to bone, joint and muscle involvement, and rarely neuropathic.

CMT is more frequently an autosomal dominant disease (but there is genetic heterogeneity, and more than 30 pathogenic genes have been implicated, X-linked and autosomal recessive forms, even mitochondrial DNA mutations showing a CMT-like phenotype have been reported). The most common syndrome is CMT1A, which accounts for 55% of all CMT cases and 66.8% of CMT1 cases, and which is usually caused by an allelic trisomy of a region spanning 1.5Mb in 17p11.2, containing the PM P22 gene (causing excessive gene dosage, and overproduction of PMP22 and its accumulation in Schwann cells that is a proposed mechanism resulting in programmed cell death, the ultimate mechanism of CMT development remaining unknown), but the percentages can vary according to different series reported and geographic origin. The 1970s classification from Dyck is valid, but molecular genetics has changed the nosology (see Berciano J, et al. for complete information): **a)** type I (CMT1, demyelinating or hypertrophic) with AD or AR inheritance; **b)** type II (CMT2, neuronal or axonal) with AD or AR inheritance; **c)** type III (CMT3, usually with de novo heterozygous gene mutations, AR uncommon) reserved for Déjérine-Sottas disease or patients with severe forms of hypomyelinating CMT; **d)** X-linked forms, and **e)** complex forms (e.g. associated with pyramidal involvement, optic atrophy, deafness -occurring in several CMT types; pigmentary degeneration of the retina suggest mitochondrial disease). The disease shows the more prevalent phenotypes caused by mutations in the gene encoding peripheral myelinprotein-22 (duplication), dynamin-2 being very rare.

Diagnostic: lineage of affected ancestors, and/or (in the case of negative family survey), onset during childhood; prolonged and slowly progressive clinical course; presence of pes cavus, and - unlike in acquired neuropathies - absence of positive sensory symptoms (paraesthesias or dysaesthesias) despite a clear semiology of sensory deficit. An electrophysiologic examination should follow (CMT1 and CMT2 classification depends on the cutoff value 38m/s by convention, for the upper limb motor nerves conduction velocity, both median and ulnar nerves), and, in selected cases, neuropathologic criteria (nerve biopsy). Finally genetic testing specifically targeted (molecular diagnosis).

Typical surgery

Orthopaedic procedures are common:

Soft tissue, osteotomies and arthrodesis (both isolated or combined), i.e. multiple tendinous transposition in foot deformities, and scoliosis. Nerve biopsy. A case of diaphragmatic plication has been reported.

Type of anaesthesia

Case reports or case series are the source of information.

General anaesthesia is usually selected: Balanced (halogenated agents) and total intravenous (propofol based) anaesthesia have been safely used, with or without muscle relaxation.

Neuraxial blocks have been successfully performed (epidural, spinal and combined spinal-epidural anaesthesia).

In a few cases, ultrasound-guided nerve blocks for postoperative analgesia have been used, without long lasting neurologic complications. Muscle response to neurostimulation can be abnormal (low).

Necessary additional diagnostic procedures (preoperative)

Patients need to be closely evaluated in a few cases, restrictive pulmonary impairment has been described in association with phrenic nerve dysfunction, diaphragm dysfunction, or thoracic cage abnormalities. Central sleep apnoea may be associated with diaphragm dysfunction and hypercapnia, whereas obstructive sleep apnoea has been reported as possibly due to a pharyngeal neuropathy. Restless legs and periodic limb movement during sleep are found in some patients with CMT2. Vocal cord dysfunction, possibly due to laryngeal nerve involvement, is found in association with some CMT types, and there are some risks of progression to bilateral paralysis and aspiration.

Patients should be assessed for the presence of autonomic denervation as this is common.

Assessment for other co-morbidities should be undertaken as the presence of diabetes mellitus can lead to further deterioration in neuropathy.

Particular preparation for airway management

Not reported.

Particular preparation for transfusion or administration of blood products

Not reported.

Particular preparation for anticoagulation

Not reported.

Particular precautions for positioning, transport or mobilisation

Cautious positioning and protection of pressure points is recommended because nerve compression may aggravate the neuropathy.

Probable interaction between anaesthetic agents and patient's long term medication

Drugs for neuropathy (restless legs syndrome) or chronic pain.

Some patients can be under psychoactive drug therapy due to psychiatric symptoms (i.e. depression, anxiety).

In a few cases, spinal cord stimulation has been used to treat chronic limb pain.

Anaesthesiologic procedure

In a case series, thiopental dose required for induction in CMT was less than in control patients, and was related with the severity of the neuropathy.

Theoretically nitrous oxide use could cause neurotoxicity through its inhibition of methionine synthase in patients with CMT, and it is quoted as 'moderate to significant' risk of potential toxicity and worsening neuropathy in people with CMT by the CMT Association (USA), CMT Association of Australia, CMT International (Canada) and CMT United Kingdom. Nevertheless a systematic review (11 studies, 41 exposures) observed no neurologic worsening, with the authors quoting the drug as safe in adults and children.

Avoiding succinylcholine is recommended.

Response to non-depolarizing neuromuscular blocking agents can be unpredictable.

Safe sugammadex neuromuscular block reversal has been reported.

Patients severely affected (as the kyphoscoliotic ones) can develop respiratory insufficiency after neuraxial anaesthesia (higher than expected sensory and motor block level).

Particular or additional monitoring

Neuromuscular block monitoring is recommended. Monitoring at the ulnar nerve-adductor pollicis brevis is recommended as lower limbs are often severely denervated. However sometimes monitoring can be difficult especially if upper limbs are affected, too.

Possible complications

Probably this disease is not especially associated with hyperkalemic response after succinylcholine, but it has been recommended to avoid it.

Response to non-depolarizing neuromuscular blocking agents can be quite variable, prolonged and attenuated responses have both been described.

Lung aspiration due to vocal cord paresis has been described.

If associated pulmonary diseases present: postoperative ventilatory assistance (i.e. BiPAP or CPAP) should be considered. This includes patients under spinal anaesthesia.

Postoperative care

Care should be taken regarding possible disautonomy and lower urinary tract dysfunction (male and female).

See before for ventilatory support.

Information about emergency-like situations / Differential diagnostics

caused by the illness to give a tool to distinguish between a side effect of the anaesthetic procedure and a manifestation of the disease

Respiratory insufficiency can develop after surgery. The cause may be multifactorial. Patients whose respiratory system is affected (thoracic muscles and diaphragm) can be at risk of this complication, and this should be taken into account to minimize other factors (drugs, type of surgery, surgical approaches).

Ambulatory anaesthesia

In this setting, avoiding neuromuscular blocking agents might be recommended.

Obstetrical anaesthesia

In a study (Medical Birth Registry of Norway, n=108), women with CMT had a higher occurrence of presentation anomalies and bleeding post partum; the rate of operative delivery was twice that of the reference group), and forceps was used three times as often in the CMT group. The majority of CMT caesarean sections were emergency sections.

Epidural or combined spinal-epidural anaesthesia for labour and caesarean delivery can be chosen. Most published cases showed no symptoms or functional status worsening.

Spinal anaesthesia has been used for caesarean section (both scheduled and emergency), as has been epidural anaesthesia.

Literature and internet links

Anaesthesia related:

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