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REVIEW ARTICLE

Charcot-Marie-Tooth syndrome: Orthopaedic considerations

P. Fernández de Retana, [a,*] **D. Poggio** [b]

[a] *Servicio de Cirugía Ortopédica, Hospital de San Rafael, Barcelona, Spain*
[b] *Servicio de Cirugía Ortopédica, Hospital Clínico, Universidad de Barcelona, Barcelona, Spain*

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Abstract Charcot-Marie-Tooth disease is a degenerative hereditary disease of the peripheral nervous system. The change is progressive and causes deformities in the feet and hands. The musculature of the leg and foot are most affected. The form of presentation is very diverse owing to the muscle involvement being different in each patient. The high-arched foot is the most common form of presentation. Conservative treatment consists of correction splints, in-soles and rehabilitation. Surgery may be indicated when conservative treatment fails. The deformity and pain are the main problems. In flexion deformities surgery is indicated to conserve the joints. Claw hammer toes should be treated with tendon transfers and arthroplasty. The claw deformity in the big toe is caused by the descent of the first metatarsal and hyperactivity of the hallucis longus extensor muscle. The Jones technique is performed as treatment for this deformity of the big toe. The descent of the first metatarsal requires a dorsiflexion osteotomy in the base of the first metatarsal. For the hind foot varus a calcaneal vagus osteotomy is used. The tightening of the plantar fascia, gastrocnemius and Achilles is treated with an extension of the muscle contractures. When the deformities are rigid, it will be necessary to perform an arthrodesis of the affected joints. The arthrodesis most used is the triple arthrodesis.

PALABRAS CLAVE
Enfermedad de Charcot-Marie-Tooth;
Ortopedia

Enfermedad de Charcot-Marie-Tooth: consideraciones ortopédicas

Resumen La enfermedad de Charcot-Marie-Tooth es una enfermedad heredodegenerativa del sistema nervioso periférico. La alteración es progresiva, y provoca deformidades en pies y manos. La musculatura de la pierna y el pie es la más afectada. La forma de presentación es muy diversa debido a que la afectación muscular es diferente en cada paciente. El pie cavo-varo es la forma de presentación habitual. El tratamiento conservador consiste en férulas correctoras, plantillas y rehabilitación. La indicación quirúrgica

* Corresponding author.
E-mail: pfernan@hsrafael.es (P. Fernandez de Retana).

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se plantea cuando fracasa el tratamiento conservador. La deformidad y el dolor son los problemas principales. En las deformidades flexibles se plantean cirugías para preservar las articulaciones. Los dedos en garra se tratarán con transferencias tendinosas o artroplastias. La deformidad en garra del dedo gordo se produce por el descenso del primer metatarsiano y la hiperactividad del músculo extensor hallucis longus. El tratamiento de esta deformidad del dedo gordo se realiza mediante la técnica de Jones. El descenso del primer metatarsiano necesitará una osteotomía dorsiflexora en la base del primer metatarsiano. Para el varo de retropié se utiliza la osteotomía valguizante de calcáneo. La retracción de la fascia plantar, gastrocnemio y Aquiles se trata con elongación de las estructuras retraídas. Cuando las deformidades son rígidas, será necesario realizar una artrodesis de las articulaciones afectadas. La artrodesis más utilizada es la triple artrodesis.

Introduction

Charcot-Marie-Tooth Syndrome (CMT) is a heterogeneous group of inherited diseases that alter the peripheral nerves. The problem is usually in the process of myelination, but the axon may also be affected. This syndrome is one of the most common neurological disorders. It affects 1 in 2,500 people in the United States. Patients can find information and help at www.charcot-marie-tooth.org. It was first discovered in 1886 by three doctors, Jean Marie Charcot and Pierre Marie from Paris, and Howard Henry Tooth from Cambridge, who gave name to the disease.[1,2] These authors found that the problem was neuropathic rather than myopathic. Other names for this disease are hereditary sensory and motor neuropathy, and peroneal muscular atrophy. The condition is a hereditary disorder that takes different forms, although most patients have type I or type II. A number of specific genetic defects have been identified.[3,4] Specific testing for the different phenotypes is available if the patient wishes to receive information on genetic counseling.[5]

Nerve alteration in CMT

Nerve dysfunction in CMT disease is progressive and inexorable, although the rate of progression varies greatly. Berciano defined a symmetric reduction of the reflexes in the lower extremities as a constant finding even before the onset of symptoms.[4] Orthopaedic surgeons should keep in mind that they are treating a progressive problem when suggesting surgical treatment.

The intrinsic muscles of the hand and foot are affected during the initial stages of the disease. The development of claw toes tends to be an initial manifestation of the disease. One of the characteristics of CMT disease is that different muscle groups are affected to varying degrees. Mann and Missirian noted that the lateral leg compartment was more seriously affected than other compartments.[6] The muscle least affected in the lateral compartment is the peroneus longus (PL). In MRI studies, less muscle atrophy in the peroneus longus muscle has been observed.[7] This observation justifies the transfer of the peroneus longus to the peroneus brevis (PB) to improve averting power in these patients. The posterior leg compartment is not usually affected until the final stages of the disease. Muscle involvement in CMT generally progresses from distal to proximal. However, the involvement of the extensor hallucis longus (EHL) muscle is paradoxical, given that the tibialis anterior (TA) muscle is generally involved whereas the EHL is not. There is no clear explanation for this fact. The role of neural compression in the neurological alteration has been postulated.[8] The greater involvement of the anterior and lateral compartments is due to the increased vulnerability of the peroneal nerve branches in the neck of the fibula. The nerve branches innervating the peroneus longus muscle originate proximal to the neck of the fibula, which would explain the minimal involvement of this muscle.

The involvement of the TA muscle with preserved posterior muscles causes foot drop due to the weakening of the ankle extensor muscles, which causes stoppage gait. The dropping of the first metatarsal (1MTT) contributes to the loss of ankle dorsiflexion. Muscular alteration and reduced ankle dorsiflexion explain the retraction of the posterior compartment leg muscles.

Clinical symptoms

The most common reason for an initial consultation is a gradually progressive deformity of the foot, which appears in the second decade of life, although it sometimes manifests itself in adulthood. Cavovarus foot is the most common manifestation of the disease. Whenever we see a cavovarus foot, we should consider a neurological cause. There are many neurological causes that can result in a cavovarus foot: polio, degenerative neurological diseases, cerebral palsy and changes in neurological structures (tumour, syringomyelia, etc.). Hyperreflexia will make us think of a central lesion. A disease of the peripheral nervous system, CMT does not cause spasticity.[8] It is essential to ask the patient about the family history in order to exclude a hereditary degenerative disease. It is common to find episodes of ankle instability in the clinical history of the patient.

One of the first symptoms is fatigue at the end of the day. Sensory nerves are also affected, but patients rarely

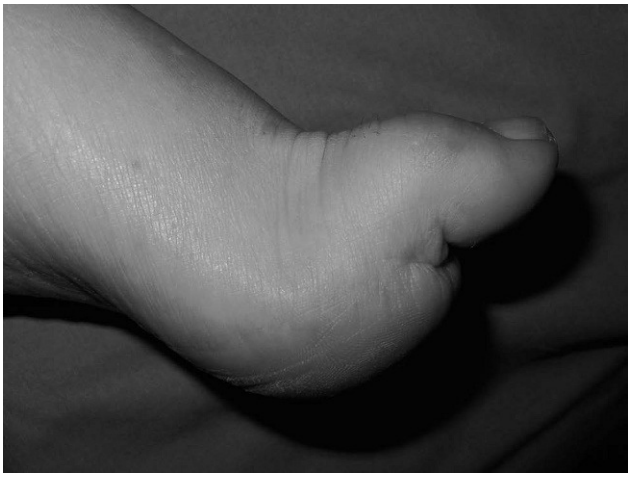

Figure 1 Claw deformity in the big toe. The MTP joint is hyperextended and the IP is in hyperflexion.

experience sensory involvement. The disease usually manifests itself with asymmetrical deformities in the hands and feet. Hands are less affected than the feet. There may be a hypotrophy of the thenar and hypothenar muscles. Burns et al. compared the hand dynamometry of CMT patients with that of the healthy population, observing a weakening in patients with CMT.[9] These objective data can be used to assess disease progression. The disease can manifest itself in a number of different ways which means it does not have a characteristic clinical presentation. If CMT is suspected, we should order an electromyographic study and advise the patient to visit a neurologist who can study the genetic aspects of the disease.

The classic clinical presentation is a cavovarus foot with weakness of the intrinsic muscles of the hands and feet, peroneal muscle hypotrophy and muscle weakness. Claw toes are a result of intrinsic muscle atrophy. The big toe usually presents a characteristic claw deformity due to the weakness of the intrinsic muscles and hyperactivity of the

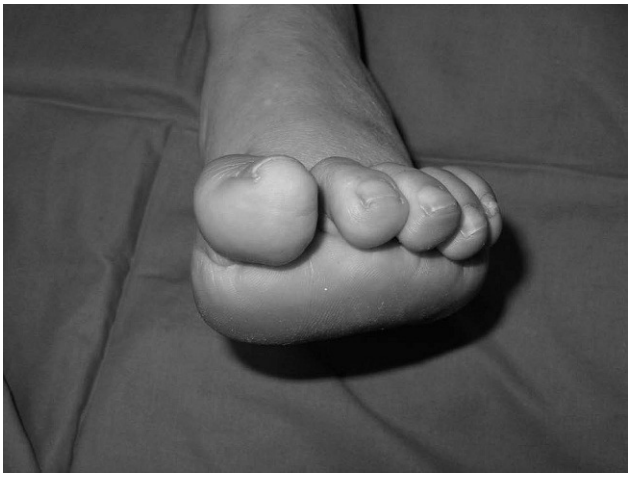

Figure 2 Anteroposterior view of the lifted foot. The first metatarsal is lowered.

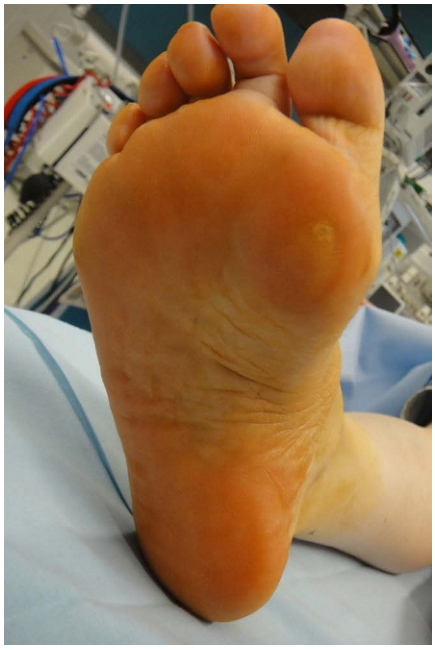

Figure 3 Plantar callosity on the head of the first metatarsal.

EHL muscle (fig. 1). Hyperflexion of the interphalangeal joint (IP) of the big toe causes discomfort at the back of the IP because it rubs against the shoe. Hind foot cavus is due to a structural alteration and the alteration of muscular balance. The structural change begins with the drop of the first metatarsal, which is produced by hyperactivity of the peroneus longus muscle and weakness of the tibialis anterior muscle. This drop of the first metatarsal causes forefoot pronation, which is detected when the foot is examined in a non-weight-bearing posture (fig. 2). When patients put their weight on the pronated forefoot, the forefoot deformity is corrected by the load, but the hindfoot goes into varus. In addition to structural deformity, the patient experiences muscular alteration. The tibialis posterior muscle is more powerful than its antagonist -the peroneus brevis muscle- and contributes to varus deformity.

The dropping of the first metatarsal explains the excess weight bearing on the head of the first metatarsal, which manifests itself in the anterior plantar callus over the first metatarsal (fig. 3). The lack of eversion of the forefoot together with the cavus foot deformity changes the plantar support area, which in turn causes excess weight bearing on the outer edge of the foot. The external plantar callus will give us an idea of the change in the weight bearing. Patients complain of pain in areas of excess weight bearing: head of the first metatarsal and outer edge of the foot. When the disease progresses slowly, we can observe a reducible deformity. If it progresses rapidly, the deformities may become fixed. Coleman's block test will help us with the examination to determine if the varus deformity is flexible or rigid.[10] For the test, the lateral border of the patient's foot is placed on a wooden block, so a dropped first metatarsal will not alter the position of the heel. In a

Figure 4 Coleman Test. A: Varus heel. B: Flexible deformity because there is correction of the varus when placing a block in the external edge of the foot.

flexible deformity, the Coleman block test will show that the heel varus deformity is secondary to the drop of the first metatarsal as the heel varus is corrected by this test (fig. 4). If the varus deformity persists with this test, then the deformity is rigid. The treatment to follow will depend on the rigidity of the deformity. When we treat a flexible deformity, we must respect the joints and correct the muscle alterations with different transfers. Due to CMT progression, the outcome of joint preservation surgery can worsen over time and the patient may require another operation. Rigid deformity requires correction by arthrodesis. Hyperactivity of the toe extensors causes two changes: increase of the plantar arch and retraction of the plantar fascia. To assess gait, patients should be asked to tiptoe and to walk with their heels on the ground.

Patients with CMT present symptoms of external ankle instability. The reasons for this instability are: heel varus, lack of averting force, impaired proprioception and repeated sprains that cause tears in the lateral collateral ligament. An ankle varus stability test and an anterior drawer test will be conducted during the examination.

The initial radiological study consists of anteroposterior radiographs and lateral weight-bearing foot x-rays, which show the deformities observed in the clinical examination. In the anteroposterior radiograph, the claw toes give the impression of subluxation. There is often an abduction of the forefoot in weight-bearing positions. Heel varus can often be observed using Meary's angle. In the lateral weight-bearing foot x-ray, we can see how the varus alters the position of the calcaneus with respect to the talus. The tarsal sinus is wider than usual due to the fact that the superposition of the talus and calcaneus diminishes. The angle between the talus and the first metatarsal is usually zero in the lateral radiograph. With cavus foot, this angle is altered and a superior apex is formed. The tilt angle of the first metatarsal increases due to the drop of the first metatarsal. In the heel we measure the calcaneal inclination angle, which is the angle between the inferior cortex of the calcaneus and the weight-bearing surface. This angle increases in the pes cavus foot (normal calcaneal inclination angle: 25° ± 5°). To assess ankle instability, a stress x-ray in varus and anterior drawer test have to be conducted to reveal a lateral collateral ligament rupture. In longstanding deformities, degenerative joint signs are found. Although an MRI can reveal the fatty degeneration of the muscle groups that have been affected, it is not very useful from a clinical point of view.[7]

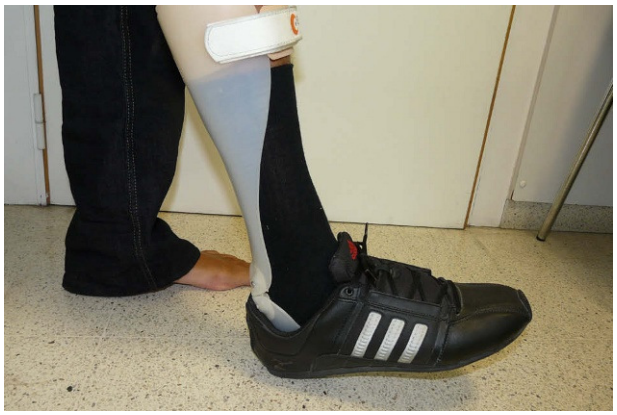

Figure 5 Tamarack splint.

Conservative treatment

Conservative treatment of CMT disease by orthosis continues to have little support in literature. Refshauge et al demonstrated the lack of patient response to night splinting.[11] Conservative treatment should be reserved for cases of mild or moderate deformities with flexible feet. The Coleman block test makes it possible to assess the flexibility and reducibility of heel varus. If the test corrects the heel, it will guide both our orthotic and surgical treatment of the first radius. If an orthosis is used in conservative treatment, it should position the subtalar joint in neutral or valgus position. To do this, the first metatarsal should be allowed to drop into a specially-designed cavity.

The most common cause of pure anterior pes cavus is CMT disease. The key factor in heel cavus is that the forefoot deformity causes the heel varus deformity, which is

secondary. This occurs in CMT because the role of the PL is preserved whereas the function of the AT is lost.

Sometimes muscle involvement is atypical, and dorsiflexion deficit prevails. This leads to a weak club foot that can benefit from an articulated splint with withdrawal (Tamarack splint)[12] (fig. 5).

Surgical treatment

The first thing to consider with surgical treatment of foot involvement in CMT is that there is no standard surgery. This disease is a typical progressive disease with progressive and changing deformities; this has to be taken into account when considering therapeutic treatment. When surgical treatment is considered, it is important to convey to the patient that, especially when the disease occurs in childhood or adolescence, the deformities invariably progress and worsen due to muscle imbalance.

Thanks to current knowledge of CMT disease, we know that there are many genetically-defined variants. As a result of this variability, the process of the disease is also very heterogeneous; this makes treatment of the foot in CMT a challenge. Its success will depend not only on correct diagnosis and effective surgery, but also on the knowledge of progression risks and the deformity patterns of the different mutation forms. However, we cannot presently predict the progression of a deformity based on the genetic subtype, which means that our actions are accompanied by a certain evolutionary uncertainty caused by the heterogeneous progression of these patients.

Due to the evolving nature and heterogeneous manifestations of CMT, the best possible course of action, in our opinion, is to perform tailor-made surgery, based on the currently available knowledge of the asymmetric involvement of the muscles of these patients.

We must consider that, within this extreme variability, a characteristic phenotypic pattern with varying degrees of severity can be pinpointed. It is vital to be able to understand the individual characteristics of each patient within this common phenotype.

Current cumulative experience, together with the fact that the patients are generally young, makes us lean towards joint preservation surgery. It seems that deformities can be adequately corrected with well-designed multilevel osteotomies and tendon transpositions. The final treatment for a patient should be the right combination of surgeries designed to correct the different abnormalities.

Balancing deforming forces

This involves correcting or improving muscle imbalance and minimising the deforming forces. To do so, there are several mechanisms: structural correction by osteotomies that alter the torques and/or tendon transfers and the release of soft tissue. We wanted to address all these actions in the same section given that in practice they are almost always connected.

Joint actions of this kind make it possible to achieve many goals:

- To correct deformities (e.g., claw toe: Jones procedure).
- To correct biomechanical disadvantages that cause instability (e.g., varus heel, short Achilles).
- To retain as much mobility as possible and prevent joint degeneration secondary to the deformity.

Before beginning any reconstructive treatment, it should be known whether the deformity is flexible and whether the muscles maintain sufficient minimal function. If they don't, the best option is probably an arthrodesis.

Tendinous transpositions and other procedures on soft parts

When performing a tendon transfer, it is important to adhere to some basic guidelines:

a) A sufficiently strong muscle should be used, since it is known that the transferred muscle will lose one degree of strength. For this reason, osteotomies that put the transferred muscle in the most biomechanically advantageous position to generate a moment of force should also be considered.
b) Wherever possible, it is preferable to transpose agonist muscles.

Although we do not know why, we do know that some muscles are affected earlier on, whereas others are less affected by the disease

The peroneus longus tendon is not strongly affected by the disease,[6] which is why the transfer of PL to PB may be

Table 1 Most common tendon transfers in CMT disease

Donor	Receptor	Indication	Associated procedures
Extensor *halllucis longus*	Dorsal 1MTT	First toe in claw + deficit of dorsiflexion	Arthrodesis IP *hallux*
Extensor *hallucis longus*	Lateral wedges	Deficit of dorsiflexion with excessive inversion	Arthrodesis IP *hallux*
Extensor *digitorum longus*	Dorsal MTT or mid-foot	Toes in claw + deficit of dorsiflexion	Arthrodesis IP minor toes
Long peroneus	Short peroneus	Deficit of eversion	Calcaneal osteotomy
Posterior tibial	Anterior tibial	Deficit of dorsiflexion	Elongation of Achilles

1MTT: first metatarsal; IP: interphalangeal.

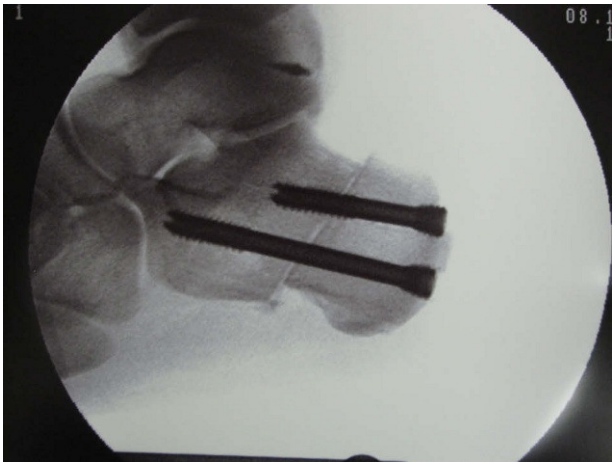

Figure 6 Calcaneal osteotomy with elevation of the greater tuberosity.

indicated in the case of excessively inverted feet from the preponderance of the tibialis posterior muscle (TP) and an anterior pes cavus with a dropped first metatarsal. This would benefit both the forefoot pes cavus and the heel varus.

Another tendon whose function is preserved for longer is the extensor hallucis longus, which causes the claw deformity of the big toe, known as claw toe. This also implies a drop of the first metatarsal, which worsens the anterior pes cavus. It is also accompanied by a weakening of the TA and the extensor digitorum, which stop assisting ankle dorsiflexion. For this reason, transposing the extensor hallucis longus to the metatarsal neck would be ideal, associated (as Jones describes it) to arthrodesis of the hallux interphalangeal joint. We thus correct the claw deformity and preserve the function of the ankle dorsiflexion with the EHL muscle.

The most common transposition of antagonistic muscles is TP to TA. It should not be forgotten that in CMT, the TA is one the first muscles to be affected.

The transposition of TP to TA is used in cases where the lack of dorsiflexion predominates (fig. 5). The lengthening of the Achilles tendon is also frequently associated. Bear in mind that non-phasic muscle transpositions should be reserved for young patients with lower motor neuron diseases or muscle injuries.

Numerous tendon transfers have been described, which are summarised in table 1.

Osteotomies

Osteotomies correct deformities and affect the ability of muscles to generate torque. Consequently, osteotomies should put those muscle groups still functioning, albeit deficiently due to CMT disease, in a better biomechanical situation. In turn, tendon transpositions should help the osteotomy to maintain this correction and balance.

Osteotomies act directly on the deformity and biomechanics, but also indirectly on the soft tissues. It is therefore sometimes necessary to treat the Achilles-calcaneal-plantar by elongating the plantar fascia or the gastrocnemius. However, doing this on its own is unfounded; it should generally be combined with osteotomies. It is sometimes essential to elongate the triceps surae, for example to correct structured clubfoot. However, in many cases the Achilles is treated indirectly by valgus or lifting calcaneal osteotomies (fig. 6). This indirectly "elongates" the Achilles and, above all, shortens the distance between the point of heel contact and the axis of the leg, resulting in a better biomechanical position and reducing the moment of Achilles tendon eversion.[13] A frequently associated anomaly in CMT is ankle instability, which will have to be continually monitored and treated if necessary. The instability is determined by the combination of heel varus with peroneal weakness and short Achilles tendon. As explained earlier, calcaneal valgus osteotomies improve ankle instability secondary to mechanical disadvantage of inverters in CMT.

If the heel corrects with the Coleman block test, both our orthotic and surgical treatment will focus on the first radius. In these cases of a dropped radius, which causes a secondary heel varus, a metatarsal elevation osteotomy would be indicated. This could be combined with the transposition of PL to PC to remove a deforming force in flexion of the first metatarsal.

In lesser toes, claw deformity is common and metatarsalgia almost constant. Sometimes this is the initial reason why the patient consults a surgeon. The first thing to consider with the deformity of the lesser toes and metatarsalgia in the cavovarus feet of patients with CMT is that the pathogenesis is in the muscle imbalance caused by the disease and its worsening is due to an extensor substitution mechanism. Weil-type distal osteotomies of the metatarsals would be formally contraindicated in these cases because it is known that they always fail. If osteotomies are conducted, they should be proximal elevation ones (e.g., BRT or Golfard).

The most frequently recommended treatment is IP arthrodesis of the toes, together with the transposition of the EDL to the back of the foot or of the metatarsals, leaving MTP flexion to the flexor digitorum longus, since the IPs are fused.

It is important to emphasise that indication to treat the lesser toes on their own is rare; treatment is more commonly recommended in conjunction with midfoot or heel bone osteotomies or soft tissue releases (e.g., plantar fascia).

Correction of structured deformities

All authors agree that joint mobility must be preserved as much as possible. However in cases of gross deformities or if the deformity is fixed or degenerative involvement is severe, joint fusion is recommended. The patient must understand that, although part of the foot and ankle function will be lost, this does not necessarily interfere with the final goal of a foot that is painless and plantigrade.

A triple arthrodesis remains the treatment of choice for severe, non-reducible deformities. Limited heel fusions are usually not recommended in these patients due to the progressive nature of the deformity. Although it is not

common, ankle arthrodesis should occasionally be considered. In the case of severe ankle involvement and severe heel deformity, panarthrodesis may be the only alternative.

Arthrodesis should be considered with caution in adolescents, and it should be kept in mind that the deformity may recur around the arthrodesis. If a fusion is decided upon, it is advisable to assess the possibility of including tendon transfers to balance the foot and reduce recurrences.

In general, it can be said that we should avoid arthrodesis whenever possible and use tendon transfers even when an arthrodesis is going to be performed.

Conclusions

- CMT is a very heterogeneous disease from a genetic point of view.
- CMT manifests itself in a large number of ways, and its progression affects the foot and ankle in many different forms.
- The most common clinical presentation is cavovarus foot, claw toes and claw deformity of the first metatarsal. These are due to an asymmetric muscle involvement that leads to common but varying muscle imbalances.
- Surgery should be tailor-made and respond to the muscle imbalances of each particular case.
- Flexible deformities should be treated with joint preservation methods, working generally on both soft tissue and bone. Osteotomies should be combined with tendon transfers and soft tissue procedures.
- Arthrodesis combined with transpositions is reserved for severe rigid deformities.

Level of evidence

Level of evidence V.

Conflict of interest

The authors declare no conflict of interest.

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