Charcot Marie Tooth

OVERVIEW

Charcot-Marie-Tooth (CMT), also called hereditary motor and sensory neuropathy (HMSN) or peroneal muscular atrophy (PMA), is a common hereditary peripheral neuropathy. The disease affects an estimated 1 in 2,500 individuals and has profound manifestations in the foot and ankle.

ANATOMY

The foot is a delicate balance of stability and motion and is driven by coupled motor forces across the foot and ankle to allow form and function. The tibialis anterior is force coupled with the peroneus longus, and the posterior tibialis is coupled with the peroneus brevis. Uneven loss of motor strength in these paired muscle groups disrupts the balance of forces in the forefoot and ankle, resulting in progressive deformity.

BIOMECHANICS

Denervation of the tibialis anterior and peroneus brevis results in an imbalance of forces across the foot. The weaker tibialis anterior is overpowered by a stronger peroneus longus. The result is plantarflexion of the first ray and eversion of the foot, disrupting the normal tripod for the foot. As the deformity progresses, a stronger posterior tibialis overpowers a weaker peroneus brevis and the hindfoot is driven into varus. The deformity is initially flexible but will eventually become fixed if left untreated. Claw deformity results from intrinsic muscle weakness and recruitment of lesser toe extensors to compensate for weak ankle dorsiflexors.

PATHOGENESIS

CMT is a heterogenous group of neuropathies of varying forms (CMT1, CMT2, CMT3, CMT4 and CMTX). The condition can be divided into two types, Type I (demylemating) and Type II (non-demyelinating) that cause nerve axon degeneration. The condition can be inherited as autosomal dominant, autosomal recessive, x-linked or sporadic.

CMT1 is the most common and has 2 forms. The first, CMT1A, results from duplication of a region on the short arm of chromosome 17 that codes for peripheral myelin protein 22 (PMP 22) and is inherited as autosomal dominant. This gene codes for a dysfunctional myelin sheath protein that accumulates, causing loss of myelin sheath function. CMT1B is autosomal dominant and the result of a loss of myelin protein zero (P0). Presentation is similar to that of CMT1A.

Other forms of the disease are less common. CMT2 affects neuronal axons. CMT3 is a more severe form of disease, presenting in infancy. CMT4 has numerous mutations and presents in infancy with severe disability by adolescence. CMTX is unique in that it is x-linked, caused by a point mutation in connexin affecting Schwann cells.

CLINICAL PRESENTATION

Presentation typically occurs in adolescence with complaints of symmetric weakness and atrophy of the lower legs and hands. Patient or family members may complain of difficulty running, clumsiness with frequent trips or falls or numerous ankle sprains. The foot and ankle may have a varied extent of involvement, with potential deformities that include foot drop, lesser toes deformity and cavus arch. Involvement of the hands often occurs later in the disease course, and includes complaints of weakness or loss of fine motor control. Muscle cramps or neuropathic pain are rare presenting symptoms. Additionally, patients may report a family history of diagnosed disease or similar complaints.

EXAM

Patients will show significant signs of muscle atrophy in the distal legs, causing them to take on a storklike or inverted champagne-bottle shaped appearance. Foot deformities may include hammer toes, claw toes, pes cavus and varus hindfoot. Gait abnormality can often be appreciated with sensory ataxia or a steppage gait in the setting of foot drop. Additionally, the planar surface of the foot may develop areas of callus or ulceration. Shoes may have abnormal wear patterns. Sensation to the distal extremities may be diminished and reflexes may be diminished or absent.

Deformity may be flexible or fixed. Coleman block testing is essential for deformity assessment and serves as a guide for potential surgical interventions. Additionally, scoliosis

and hip dysplasia are other potential orthopeadic manifestations for which evaluation is warranted.

STAGES

CMT is not defined by stages but rather a continuum of a progressive weakness and sensory deficits. Most patients will preserve their ambulatory status but may go on to require assistive devices, most commonly only requiring ankle-foot orthotics (AFO). A small subset of patients will require a wheelchair. Life expectancy is similar to that of the general population, although some may become disabled due to distal muscle weakness and deformity.

IMAGING STUDIES

Imaging studies are of no efficacy for diagnosis but can play a key role in treatment decisions. Diagnostic testing begins with nerve conduction studies (NCS)/electromyography (EMG) and is the mainstay for diagnosis. Patients with CMT show low nerve conduction velocities with prolonged distal latencies. Testing can differentiate axonal versus demyelinating diseases, helping to differentiate the varying subtypes of disease. Sural nerve biopsy can be performed and has a high specificity, but is rarely required. Genetic testing is also available but is used more for determining inheritance patterns for family planning.

TREATMENT

Supportive therapy is the mainstay for treatment of CMT. Care requires a multimodal approach, involving neurologist, genetic counselors, physical and occupational therapists, in addition to treating orthopeadic surgeon. The goals of therapy are to maintain strength while minimizing pain and sensory disturbances, in order to preserve maximal function and independence for activities of daily living. Physical therapy focuses on heel cord stretching for ambulation and AFO's. Crutches or wheelchairs may be required. Occupational therapy may also be utilized to assist the patient with adaptive equipment.

Indications for surgical intervention are dictated by the degree of deformity and impairment. Flexible forefoot deformities may be addressed with soft tissue reconstruction, potentially combining plantar fascia release, tendon transfers and Achilles tendon lengthening. As the deformity becomes more rigid, valgus producing calcaneal osteotomy may be required for hindfoot varus with dorsiflexion osteotomy of a plantarflexed first ray. In the setting of

arthritic changes, fusions may be indicated. Lesser toe deformity may also need to be addressed. Treatment for each patient must be individualized.

CONCLUSION

CMT is a common and debilitating disease with profound manifestations in the foot and ankle. It is a hereditary neuropathy that results in a distal weakness and can progress to a fixed, complex cavus deformity. Treatment is multifactorial. With supportive care and appropriate surgical interventions, patients can expect to live a full and productive life.

Written by Donald Covell, MD
Reviewed by Thomas Dowd, MD
Last reviewed June 2015