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Case Report

Charcot-Marie-Hereditary Neuropathy: A Dental Disorder

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ABSTRACT

Charcot-Marie-Tooth disease (CMT) is a hereditary neuropathy affecting the peripheral nervous system due to genetic mutations impacting the myelin sheath or axon. The main types include CMT 1 (demyelinating), CMT 2 (axonal), and CMTX (X-linked CMT). Symptoms progress insidiously, starting with foot deformities and weakness in the lower limbs, potentially advancing to the upper limbs. Diagnosis involves clinical evaluation, electro diagnostic tests and genetic testing. Treatment aims to manage symptoms. This case discusses a 66-year-old man with flaccid tetra paresis and glove-and-stocking hypoesthesia, with a family history of CMT. Electromyography indicated predominantly axonal sensorimotor polyneuropathy, leading to a diagnosis of CMT 2. He is being treated in primary care with physiotherapy focused on functionality and gait. The late diagnosis stemmed from the patient underestimating his symptoms. CMT is challenging to diagnose in primary care, highlighting the need for collaboration with neurology and thorough assessments to manage the condition effectively.

Keywords: Charcot-Marie-Tooth; Axonal; Demyelinating; Genetic mutations, Physical medicine; Rehabilitation

INTRODUCTION

CMT is a group of hereditary neuropathies affecting the peripheral nervous system, caused by genetic mutations that impair the structure and function of the myelin sheath or the axon. It is one of the most common hereditary neurological disorders, presenting with different types and subtypes that vary depending on the affected genes, inheritance patterns, age of onset and electrophysiological findings [1-4]. CMT type 1 (CMT 1), inherited in an autosomal dominant pattern, is characterized by demyelinating pathology (myelin sheath abnormalities) and typically has an early onset, usually in childhood. Most mutations in individuals with CMT 1 are caused by duplication of the *PMP22* gene or point mutations in *GJB1* or *MPZ*. Nerve Conduction Velocity (NCVs) is moderately reduced, and a distinctive feature is the presence of hypertrophic nerves, palpable or visible, especially at the elbow, due to thickened myelin sheaths. The most common subtype, CMT1A, results from a mutation in the *PMP22* gene [1,2]. CMT type 2 is less common than CMT 1 and is associated with axonal pathology. It is also autosomal dominant, with typical onset between the second and third decades of life, leading to less disability and sensory loss compared to CMT 1 [1]. Nerve conduction velocity (NPV) is normal or slightly reduced, with the most common mutation found in the *MFN2* gene [1]. CMTX combines both demyelinating and axonal pathologies and follows an X-linked inheritance pattern, with more severe symptoms in males. The onset typically occurs in the first or second decade of life, with a slight reduction in nerve conduction velocity. Mutations in the *Cx32* gene are responsible for causing CMT1X, CMT 3 or Dejerine-Sottas disease, is a severe form of CMT with autosomal dominant or recessive inheritance, characterized by demyelinating pathology [1,2]. It usually begins in infancy, presenting with hypotonia, feeding difficulties, severe motor and sensory impairments, and a profound reduction in nerve conduction velocity. This rare condition may result from mutations in the *PMP22, MPZ,* and *EGR2* genes [1,2]. CMT 4 encompasses various subtypes of demyelinating and axonal neuropathies with autosomal recessive inheritance. Symptoms typically begin in childhood, primarily with leg weakness, and

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progress to the point where many patients lose the ability to walk by adolescence. CMT 4 causes severe motor and sensory impairments, with a moderate reduction in nerve conduction velocity [1,2]. Most individuals with CMT develop symptoms during the first or second decade of life, although the onset is insidious and slow in progression, making it difficult to pinpoint the exact age of onset. CMT is characterized by progressive foot deformities such as high arches (pes cavus) and hammer toes, muscle weakness and atrophy in the extremities, initially in the lower limbs, loss of tendon reflexes, reduced sensation, and difficulties with fine motor skills. Muscle atrophy in the legs can lead to the characteristic "inverted champagne bottle" shape [1-4]. Symptoms usually start in the lower extremities but can progress to the upper limbs and include difficulties walking or running, frequent tripping, falls and ankle sprains. The disease progresses gradually and in some cases, tremors may occur, along with impaired vision and hearing. The severity of symptoms varies significantly, even among family members with the same genetic mutation, ranging from mildly symptomatic cases to severe manifestations [3]. Diagnosis begins with a thorough clinical evaluation, including medical history, family background, and a neurological exam. Additional tests, such as nerve conduction studies, Electromyography (EMG), genetic testing and nerve biopsies, may be required. EMG and NCV tests are essential to confirm the presence of neuropathy and distinguish between demyelinating and axonal forms of CMT. These tests are also useful for screening asymptomatic family members [1-4]. A reduced muscle action potential along with preserved conduction velocity suggests axonopathy, while a profound reduction in conduction velocity supports the diagnosis of demyelinating pathology. In some cases, both demyelinating and axonal neuropathies may coexist [1-4]. Thus, the diagnosis of CMT involves a combination of clinical presentation, electro diagnostic testing and genetic analysis [1-4]. There is no cure for CMT, and treatment focuses on symptom management and rehabilitation, as there are currently no effective disease-modifying therapies to alter its natural progression. Treatment typically involves a multidisciplinary healthcare team, including neurologists, physiatrists, orthopedic surgeons, podiatrists, physical therapists, and occupational therapists [1,2]. Physical therapy plays a vital role in treatment, helping to improve muscle strength, flexibility, and joint range of motion, balance, and cardiorespiratory fitness. Key components of physical therapy include stretching, resistance and aerobic exercises, and in some cases, early use of orthoses or orthopedic devices, such as special shoes to correct foot deformities and assist walking, may be necessary. In more advanced cases, canes or crutches may be needed to stabilize walking. Additionally, splints can be used to improve hand dexterity, and occupational therapy can assist with daily activities [1,2]. Physical therapy also prevents contractures and musculoskeletal deformities, addressing fatigue and pain associated with CMT [5]. However, the concept of "overuse weakness" remains debated, as exercise may potentially exacerbate muscle weakness in some cases [1,2]. In cases of progressive deformities, such as pes cavus, ankle contractures, hip dysplasia, or scoliosis, orthopedic surgery may be required. Supervised exercise programs and core muscle strengthening, along with balance training, are recommended to slow the progression of weakness. Foot deformities are a significant source of disability in CMT and can worsen over time, even with physical therapy and orthotic use [1,2]. It is important to encourage patients to remain active, maintain a healthy weight and avoid neurotoxic medications that could worsen their neuropathy. Genetic counseling is also recommended to address family planning concerns and the progression of the disease [1,6].

CASE PRESENTATION

A 66-year-old male was seen in a neurology consultation in 2003 for chronic flaccid tetra paresis with areflexia and stocking-glove hypoesthesia, without sphincter disturbances, and a positive family history. EMG revealed a predominantly axonal sensorimotor polyneuropathy. Based on the clinical presentation and EMG, he was diagnosed with CMT 2. The patient, a former football player, first experienced lower limb weakness at the age of 27 years, which gradually worsened, followed by weakness in hands, without sensory complaints. Currently, patient is independent in daily living activities, needing support only for long-distance walking, and on longer drives [4]. However, after a neurological evaluation, patient was advised to consult with the Institute of Mobility and Transport (IMT) to adopt strategies for safe driving. He reports no diplopia or dysphagia and has a family history of CMT (brother, aunt, and maternal grandfather). On physical examination, patient presented with grade dorsiflexion of the feet, weak patellar reflexes, and absent achilles reflexes. Patient also had marked atrophy of the first dorsal interosseous muscle in the hands, along with atrophy of the thenar and hypothenar eminences and less pronounced atrophy in the forearms. Additionally, patient exhibited hammer toe deformity, significant atrophy of the lower limbs, and absent vibratory sensation from the feet up to the joints. Patient showed reduced vibratory sensation in the hands, with compromised ability to perform a pincer grip. Patient gait demonstrated bilateral steppage. The patient is being followed in primary care, with physical therapy focused on improving functionality and walking ability (Figure 1).

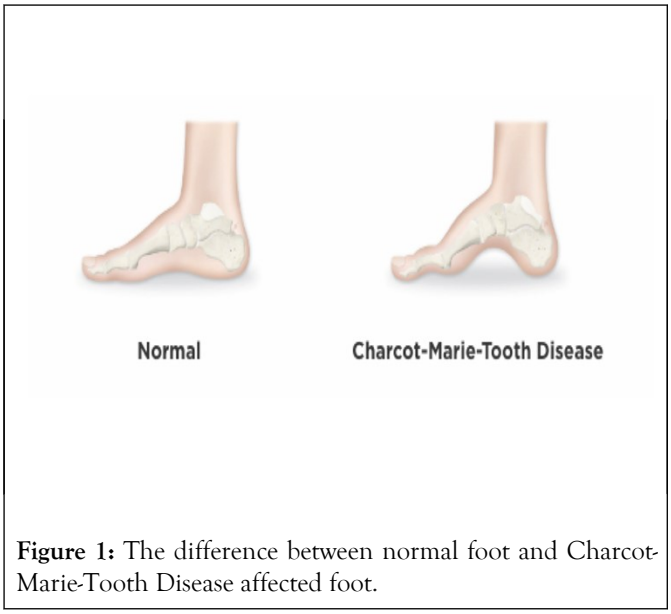

Figure 1: The difference between normal foot and Charcot-Marie-Tooth Disease affected foot.

RESULTS AND DISCUSSION

The delayed diagnosis was due to the insidious onset of the disease and the patient's initial underestimation of symptoms. CMT is challenging to diagnose in primary care, requiring collaboration with secondary care, particularly neurology. Managing neurological complaints in primary care demands a comprehensive medical history, a detailed physical examination, and consideration of differential diagnoses due to the complexity of the clinical picture. It is the family physician's role to initiate evaluation and request additional tests, such as EMG. Treatment for CMT is primarily rehabilitative and symptomatic, highlighting the important role of Physical Medicine and Rehabilitation (PMR) in disease management. Adaptive equipment is often necessary to facilitate daily activities.

CONCLUSION

CMT can significantly impact patient's daily routines, including activities such as driving, which may require adaptations or restrictions. The coordination of interprofessional care is essential for optimizing treatment and improving outcomes. While life expectancy is typically not affected, the disease tends to be more severe when it has an early onset. Regular assessments and interventions from an interprofessional rehabilitation team are key to maintaining independence, ensuring safe ambulation, and promoting functional capacity in patients.

CONFLICT OF INTEREST

None

CONFIDENTIALITY OF DATA

The authors declare that they have followed the protocols of their work center on the publication of data from patients.

PATIENT CONSENT

Consent for publication was obtained.

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