Nerve Ultrasound Findings before and after Surgery in a Patient with Charcot-Marie-Tooth Disease Type 1A and Comorbid Carpal Tunnel Syndrome

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Abstract
The diagnosis of comorbid carpal tunnel syndrome (CTS) in patients with Charcot-Marie-Tooth (CMT) disease is challenging due to the overlapping symptoms and inconclusive electrodiagnostic studies (EDX). This case report is aimed at illustrating the value of ultrasound (US) in a patient with CMT1 disease and comorbid CTS. A 28-year-old woman presented with symptoms of painful paresthesia and weakness of both hands. EDX demonstrated a demyelinating sensory-motor polyneuropathy in the upper and lower extremities, consistent with CMT1 disease. US showed an increased cross-sectional area (CSA) of the median nerve at the carpal tunnel inlet (CTI) with a significant drop in the diameter within the carpal tunnel, confirming concurrent CTS. Genetic testing confirmed PMP22 duplication consistent with CMT1A. Bilateral carpal tunnel releases were performed with partial symptom resolution within 3 weeks. Postoperative EDX demonstrated improved motor conduction across the wrist, but the sensory potentials continued to be unrecordable. US showed a significant reversal of the diameter-drop of the median nerve within the carpal tunnel and decrease in CSA at the CTI. US imaging is a valuable technique for identifying comorbid CTS in patients with CMT and directing appropriate treatment.

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Introduction

Charcot-Marie-Tooth (CMT) disease is the most common inherited neuropathy which is characterized by progressive weakness in the distal limb muscles and sensory disturbances with a prevalence of 1 in 2,500 individuals [1]. The autosomal dominant duplication of the PMP22 gene on chromosome 17p is identified in 70–80% of CMT cases (CMT1) [2]. Electrodiagnostic studies (EDX) in CMT1 are characterized by a demyelinating motor-sensory neuropathy with motor nerve conduction velocity (MNCV) in upper extremity nerves <38 m/s, while the axonal forms of CMT tend to have MNCV >38 m/s [1].

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy, affecting 3–6% of adults [3]. While the prevalence of CTS in CMT disease is unknown, it has been estimated that 5.8% of patients with inherited neuropathies have concurrent CTS [3]. EDX are often used to confirm entrapment of the median nerve at the carpal tunnel by documenting focal slowing of motor and sensory conduction across the area of the carpal tunnel. Diagnosis of CTS in the setting of CMT1 disease may prove challenging due to overlapping clinical symptoms (numbness, pain, or weakness of the hands) and the significant slowing of median nerve motor conduction. The criteria utilized to diagnose CTS are less dependable when demyelination associated with a polyneuropathy complicates the interpretation of EDX findings [2]. In severe CTS, there may be retrograde slowing of motor conduction or loss of compound muscle action potentials (CMAP) and sensory nerve action potentials (SNAPs), making EDX findings nondiagnostic. Under these scenarios, use of ultrasonography (US) imaging of the median nerve has been found to be a highly useful technique to confirm CTS [4]. This case report illustrates the diagnostic value of US in a patient with CMT1 disease and comorbid CTS. EDX and US findings prior to and following bilateral carpal tunnel releases (CTR) are documented.

Case Description

History, Radiological Imaging, and Physical Examination

A 28-year-old woman (body mass index: 53.8 kg/m²) reported an 11-year history of neck pain, bilateral arm pain, as well as burning sensations of both hands. The paresthesia affected all the fingers and involved the forearms and upper arms when severe. She also experienced pain and paresthesia of the feet. Her physician was initially concerned about cervical radiculopathy; a noncontrast cervical MRI demonstrated a small-disc herniation at C7-T1, without significant foraminal narrowing. Treatment included physical therapy, gabapentin 100 mg 3 tablets per day, and meloxicam 15 mg 1 tablet per day, which provided improvement of her neck pain, but the painful paresthesia of the upper extremities persisted. She was subsequently referred for EDX.

Salient findings on clinical examination included bilateral pes cavus and diminished pinprick and light touch sensations over the plantar and dorsal aspects of the feet as well as over all digits in both hands. Weakness of the intrinsic hand muscles was noted, more prominently of the abductor pollicis brevis bilaterally. Extensors of the toes were also weak with atrophy of the extensor digitorum brevis bilaterally. There was also weakness of the tibialis anterior bilaterally. Ankle reflexes were absent bilaterally; knee reflexes were normal. Upper extremity reflexes were normal. The patient was unaware of a similar problem in other family members, but after further inquiries, it was confirmed that there was a positive family history for CMT disease.

EMG/NCV of the Arms and Legs and US

Nerve conduction abnormalities are summarized in Table 1. The CMAPs did not show dispersion on proximal stimulation. Needle electromyography revealed decreased motor
unit recruitment and increased polyphasic units (wide duration and large amplitude) in the distal muscles in upper and lower extremities bilaterally; proximal muscles showed a normal pattern. The abnormalities were suggestive of demyelinating motor-sensory polyneuropathy in the upper and lower extremities consistent with CMT1A disease. The loss of SNAPs and motor unit abnormalities were thought to be related to secondary axonal loss.

The US study was performed using a GE LOGIQ machine (GE Healthcare; Chicago, IL, USA) with a linear array transducer of 8–18 MHz, according to our lab protocol [4]. The findings included increased cross-sectional area (CSA) of the median nerves at the carpal tunnel inlet (CTI) bilaterally with a mildly increased CSA in the forearms (Fig. 1, Table 1). The median nerve diameter within the carpal tunnel showed a significant decrease (Fig. 2) bilaterally. These findings suggested significant entrapment of the median nerves at the carpal tunnel.

CTR and Follow-Up

CTRs were performed by an open technique on both sides at a 2-week interval. The patient experienced improvement in the pain and paresthesia of the hands within 3 weeks postoperatively. Clinical findings were essentially unchanged at 3 months.

Postoperative EMG/NCV of the Arms and US

The upper extremity EDX and US were repeated 3 months after the CTR. The median nerves showed less marked decrease in distal motor latency and CMAP amplitude; the slowing of MNCV in the forearm remained unchanged. SNAPs could not be recorded as similar to preoperatively (Table 1). The US demonstrated a minimal change in the CSA of the median nerves at the CTI (Table 1). The most significant change was a reversal in the drop in diameter of the median nerve within the carpal tunnel (Fig. 2), resulting in a decreased maximum/minimum diameter ratio bilaterally. This finding suggested effective decompression of the

| Table 1. Electrodiagnostic and ultrasound findings pre- and post-carpal tunnel release in a patient with CMT disease |
|---------------------------------------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| **EMG/NCV** | **Right median nerve before CTR** | **Right median nerve after CTR** | **Left median nerve before CTR** | **Left median nerve after CTR** | **Right ulnar nerve before CTR** | **Left ulnar nerve before CTR** |
|---------------------------------------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Distal motor latency, ms | 10.6 | 8.6 | 10.4 | 8.2 | 6.5 | 6.3 |
| CV in forearm, m/s | 35.8 | 36.6 | 29.5 | 28.1 | 32.7 | 30.6 |
| Amplitude of CMAP, mV | 2.15 | 2.64 | 0.45 | 0.8 | 3.57 | 3.27 |
| Sensory latency, ms | NR | NR | NR | NR | NR | NR |
| Amplitude of SNAP, uV | NR | NR | NR | NR | NR | NR |
| US: CSAw, mm² | 19 | 16 | 18 | 17 | – | – |
| US: CSAf, mm² | 14 | 12 | 13 | 12 | – | – |
| Diameter ratio of median nerve within CT, max/min | 3.1/1.2 | 2.9/2.3 | 2.5/1.1 | 2.4/1.7 | – | – |

Lower extremities: no CMAP could be recorded over the extensor digitorum brevis on stimulation of the fibular nerve on either side. No CMAP could be recorded over the abductor hallucis on stimulation of the tibial nerve on either side. No SNAP could be recorded on stimulation of the superficial fibular and plantar nerves on either side.

EMG, electromyography; NCV, nerve conduction velocity; HRUS, high-resolution ultrasound; CTR, carpal tunnel release; CMAP, compound muscle action potentials; NR, not recordable (absent); SNAP, sensory nerve action potential.
median nerve at the carpal tunnel. The persistence of absent sensory potentials and the slow MNCV in the median nerves were presumably related to the underlying CMT1 neuropathy.

**Genetic Studies for CMT Disease**

The patient underwent genetic diagnostic investigation consisting of sequence analysis and deletion/duplication testing of 57 genes listed in the Invitae CMT Disease Comprehensive Panel. Based on validation study results, this assay achieved >99% analytical sensitivity and specificity for single nucleotide variants, insertions, and deletions <15bp in
length as well as exon-level deletions and duplications. This study uncovered a pathogenic PMP22 gene duplication, indicating a CMT1A subtype.

**Discussion**

No clear guidelines exist to confirm the additional presence of CTS in patients with concomitant CMT disease. Pantosyan and colleagues explored how effective the CTS symptom severity score performed as a diagnostic tool for CTS in the presence of CMT [3]. These authors reported that wrist splint therapy and/or surgery offered significant improvements in CTS symptoms as measured by the CTS symptom severity score [3].

EDX are valuable in differentiating CTS from CMT disease and reveal the extent, type, severity of the underlying condition, prognosis, and potential for recovery. However, conclusive diagnosis of CTS in patients with concomitant CMT by EDX findings is often difficult. Usual criteria like median-ulnar motor and sensory distal latency differences may still be helpful, but adequate data are unavailable that compare CMT1A patients with and without CTS. US has been found to be a valuable complement to EDX in situations where EDX fail to provide accurate localization and to differentiate chronic inflammatory demyelinating polyneuropathies from hereditary polyneuropathies. In CMT1A, the CSA often appears diffusely increased along the entire course of the median nerve [5]. Disproportionate enlargement of the median nerve at the CTI and/or carpal tunnel outlet suggests the additional presence of entrapment at the carpal tunnel, which is further substantiated by a drop in diameter within the carpal tunnel as in this patient.

Our report is the first case in the literature that highlights the pre- and postoperative US findings in a patient with CMT1A and comorbid CTS who underwent a bilateral CTR. Our case report illustrates the role of US in confirming the diagnosis of CTS when NCV is nondiagnostic, especially in the context of diffuse slowing of MNCV and absent SNAPs.

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**Statement of Ethics**

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. On November 15, 2021, the University of Louisville Institutional Review Board (IRB) determined that our project did not meet the “Common Rule” definition of human subjects’ research and did not require IRB review. The IRB number is 21.0916.

**Conflict of Interest Statement**

The authors have no conflicts of interest to declare.

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Author Contributions

Lisa B.E. Shields: data conception, design, acquisition, analysis, and interpretation; drafted the manuscript; critically revised the manuscript; and gave final approval; Vasudeva G. Iyer: data conception, design, acquisition, analysis, and interpretation; critically revised the manuscript; and gave final approval; Yi Ping Zhang: data conception, design, acquisition, analysis, and interpretation; critically revised the manuscript; and gave final approval; Christopher B. Shields: data conception, design, acquisition, analysis, and interpretation; critically revised the manuscript; and gave final approval.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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