Successful Treatment of Charcot-Marie-Tooth Chronic Pain with Spinal Cord Stimulation: A Case Study

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**Objectives:** Charcot-Marie-Tooth (CMT) disease is one of the most common hereditary neuropathies affecting one in 2500 people in the United States. CMT disease is associated with moderate to severe chronic extremity pain. We present the case of a young man with chronic intractable lower extremity pain associated with CMT disease treated with spinal cord stimulation (SCS).

**Materials and Methods:** This was an Institutional Review Board-approved case study involving a 37-year-old man diagnosed with CMT disease with pain of more than 20 years. He was implanted with an SCS device and patient pain and quality of life was assessed one and six months later using the SF-McGill Pain Questionnaire, Visual Analog Scale, Oswestry Disability Questionnaire, Pain Disability Index, and SF-36. Baseline measures were obtained retrospectively. Qualitative data were collected from the medical record.

**Results:** SCS was effective in decreasing pain, improving quality of life and reducing medication consumption at both one and six months post-implant. In addition, the patient was satisfied with SCS treatment.

**Conclusion:** SCS produced favorable results in a patient with CMT and should be considered a treatment option for pain resulting from this condition.

**Keywords:** Charcot-Marie-Tooth disease, chronic pain, neurostimulation, peripheral neuropathy, spinal cord stimulation

**Conflict of Interest:** Ioannis M. Skaribas, MD, DABA is a paid consultant of St. Jude Medical Neuromodulation Division, and Stephanie Washburn, PhD is an employee of St. Jude Medical Neuromodulation Division.

**INTRODUCTION**

Spinal cord stimulation (SCS) is becoming an increasingly popular tool for the treatment of chronic, intractable pain, with an estimated 40,000 SCS systems implanted every year worldwide (1). The basic premise underlying SCS was proposed in 1965 by Melzack and Wall (2). Their theory, known as the “gate control theory,” postulates that activation of large diameter, myelinated primary afferent fibers suppresses the response of dorsal horn neurons to input from small, unmyelinated primary afferents. The first application of the “gate control theory” was put into practice by Shealy and colleagues (3) when they electrically stimulated the dorsal columns to treat chronic, intractable pain. SCS is currently used to treat a variety of pain conditions, including diabetic neuropathy (4), failed back surgery syndrome (5–8), complex regional pain syndrome (9–11), phantom limb pain (12), ischemic limb pain (13), refractory unilateral limb pain syndrome (14), postherpetic neuralgia and acute herpes zoster pain (15).

Another pain condition that is a potential candidate for SCS treatment is Charcot-Marie-Tooth (CMT) disease, which is associated with moderate to severe chronic extremity pain. CMT disease is one of the most common hereditary peripheral neuropathies affecting one in every 2500 people in the United States and an average of 2.6 million people worldwide (16). The disease is progressive as peripheral nerves degenerate and denervated muscles begin to atrophy causing patients to slowly lose function of their hands and feet. Foot-drop, foot bone abnormalities, high arches and hammertoes, as well as balance problems, problems with hand function, occasional lower leg and forearm muscle cramping, loss of reflexes, and scoliosis are characteristic of CMT disease (16). Many patients also develop sensory deficits and neuropathic pain similar to that seen in complex regional pain syndrome and postherpetic neuralgia (17), making CMT a potential candidate for treatment with SCS. To date, there have been no reported cases of SCS treatment for pain relief associated with CMT disease in the United States. We present here a case study of SCS for the treatment of pain related to CMT disease.

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CASE REPORT

The case of a 37-year-old man with bilateral lower extremity and right buttock pain resulting from CMT is presented. The patient has suffered from chronic intractable pain of the lower extremities for more than 20 years. Restless legs and inability to sit due to buttock pain further complicated his condition. Prior to presentation to the clinic, the patient had tried numerous pharmacological agents, including heavy narcotics with marginal response. The patient was taking Tramadol 300 mg three times a day, Mirapex 5 mg three times a day, Vicodin 7.5/750 mg three times a day, Norco 10/325 mg three times per day, Lyrica 600 mg/day, Neurontin 3600 mg/day, and Actiq 200 mg/day at the time of the first assessment. He had undergone extensive therapy with intravenous Ketamine infusions. The response from these infusions was adequate as described by the patient; however, very short lived. The patient had also received epidural steroid injections with limited success. One of the major concerns of the patient was that he was taking potentially toxic doses of acetaminophen in the form of Vicodin every four hours. SCS treatment was recommended after all other treatment options had been exhausted based on the treatment continuum which places SCS in the last tier of advanced pain therapies. This tier consists of SCS, implantable drug pumps, and surgical intervention and is recommended only after all other treatment options, including physical therapy, nerve blocks, and opioids have failed. The patient was being treated for depression; however, he passed the psychological assessment that is recommended prior to SCS trial and was therefore considered a viable candidate for the treatment.

The patient underwent a SCS trial using two percutaneous 4-contact leads placed bilaterally (Quattrode™, St. Jude Medical Neuromodulation Division, Plano, TX, USA) on July 17, 2008. During the five-day trial period, the patient’s pain, measured using a Visual Analog Scale (VAS), was decreased from 7.5 to 2, a greater than 50% reduction. The patient was then deemed a suitable candidate for permanent implantation and permanent percutaneous 8-contact leads (Octrode™, St. Jude Medical Neuromodulation Division, Plano, TX, USA) and a conventional implantable pulse generator (IPG; Genesis™, St. Jude Medical Neuromodulation Division, Plano, TX, USA) were implanted under fluoroscopy on July 22, 2008. The leads were bilaterally placed 3 mm from the anatomic midline at T9 (Fig. 1). Initial programming occurred at the time of permanent placement. The IPG was set at a pulse width of 338 μsec, amplitude of 6.8 mA, and frequency of 80 Hz with an anode at contact 3 and a cathode at contact 4. The patient returned to the clinic one month and six months after the permanent implant and pain and quality of life (QoL) were assessed using the SF-McGill Pain Questionnaire, VAS, Oswestry Disability Questionnaire, Pain Disability Index (PDI), and SF-36. Baseline measures were obtained retrospectively by asking the patient to recall events prior to implantation. Qualitative data were collected from the patient’s medical record.

The patient’s pre-implant VAS score was a 7.5 out of 10. The VAS score had decreased to 5.1 out of 10 one month following SCS treatment and was further reduced to a score of 3 out of 10 at six months post-implant (Fig. 2).

The patient described his pain as throbbing, shooting, sharp, cramping, gnawing, tiring-exhausting, fearful, and cruel-punishing on the SF-MPQ. The majority of these descriptors were rated as moderate to severe in intensity. One month following SCS treatment, only the cruel-punishing pain component remained severe in intensity. At six months post-implant, the patient described his pain as cramping, aching, and tire-exhausting, two of which were described as mild in intensity. Only cramping was described as moderate in intensity. Figure 3 depicts the sensory, affective, and total SF-MPQ score at baseline, one month, and six months post-implant. At baseline, the sensory component of the SF-MPQ score was a 10 and the affective component was a 6, resulting in a total score of 16. The overall score has been reduced to 13 at the one-month time-point. This reduction resulted from a 3-point decrease in the sensory score. At six months, the sensory score had been further reduced to a score of 3 and the affective component score had been reduced to 1, resulting in an overall score of 4.

The PDI scores are shown in Figure 4. The patient’s PDI score was 56 out of 70 prior to SCS treatment. The patient indicated that all family/home responsibilities, job activities, and sexual behavior were totally disrupted or prevented by his pain by assigning them all scores of 10. Recreation which includes hobbies, sports, and leisure time, and all social activities were also severely impacted by pain, indicated by a score of 9 and 8, respectively. Self-care and life support activities were only moderately impacted, with the patient assigning scores of 4 and 5, respectively. One month following SCS implantation, the PDI score had decreased to 48, however; the...
The patient still indicated that family/home responsibilities and sexual behavior were totally disrupted by his pain. At six months the score had significantly decreased to 19 and family/home responsibilities and sexual behavior were only moderately impacted by his pain (ranking reduced to 5). Self-care, eating, sleeping, and breathing were no longer impacted by pain.

Fairbank and colleagues (18) interpret “percentage of disability” scores in the following manner for the Oswestry Disability Index: 0–20%—minimal disability; 20–40%—moderate disability; 40–60%—severe disability; 60–80%—crippled; 80–100%—bed bound (or exaggerating symptoms). The patient received a score of 30 on the Oswestry Disability Index prior to SCS implantation. A score of this magnitude put him into the “crippled” category proposed by Fairbanks and colleagues. The Oswestry Disability Index score was only slightly reduced to 28 at one month post-implant; however; even this 2 point decrease was enough to move the patient into a lower category of disability. By six months post-implant the Oswestry Disability Index score had significantly decreased to a score of 12 and the patient had moved into the “moderate disability” category (Fig. 5). One of the most significant improvements in the patient was the ability to tolerate pain without pain medication. He had stated that pain killers only gave him moderate relief from pain prior to SCS treatment. Additionally, the patient experienced dramatic functional improvements in his sexual activity, and his ability to effectively sit, stand, and sleep.

The SF-36 is a 36-item tool for measuring health-related QoL from the patient’s point of view. The items on the questionnaire are scored and divided into eight subscales. A higher score in each subscale indicates greater health-related QoL. Six of the eight subscales were positively impacted after one month of SCS treatment (Fig. 6). Scores on the physical functioning and vitality sections remained unchanged. After six months of treatment, all eight had increased, indicating greater QoL on each component of the scale. The most improvement was seen on the Role-Emotional subscale, with a baseline score of 9.2 and an increase to 44.2 at six months.

Overall, the patient is very satisfied with the results of SCS treatment and has not experienced any adverse events. He reports 80–90% effectiveness of SCS and an “incredible change” in lifestyle, characterized by “being more active and enjoying life.” He reports dramatic improvement in his QoL with the ability to exercise on a treadmill on a daily basis, tolerate prolonged sitting, work for long hours, and improved mood. In addition, the patient reports no symptoms related to Restless Leg Syndrome after the implantation and clinical assessment by the physician shows improvements in the patient’s spasticity associated with CMT disease.

DISCUSSION

Until very recently, little attention has been given to pain associated with CMT and therapies have been limited to rehabilitation, walking aids, counseling, over-the-counter medications, and a combination of narcotic and non-narcotic pharmacological agents. Physical therapy and exercise programs targeting the specific
needs of this patient population aim to maintain a level of function and to avoid disease progression and further muscle loss. Other conservative treatments such as biofeedback, acupuncture, and massage have also been used. Anticonvulsants such as Lyrica, Gabapentin, NSAIDS including COX-2 inhibitors, Carbamazepine, corticosteroids, as well as hydrocodone and propoxyphene have all been used with various responses and side-effects that are not always acceptable or tolerated by the patients. Stronger opioids such as morphine, oxycodone, hydromorphone, and fentanyl have also been used when other medications have failed to provide relief. However, these stronger opioids have more severe side-effects and pose the risk of dependence. Currently, an adequate treatment option for pain associated with CMT has not been identified and it is clear that other treatment options should be explored.

Neurostimulation has been used extensively for the treatment of intractable torso and extremity pain both neuropathic, as well as, nociceptive for more than three decades. It has been demonstrated clinically that neuropathic pain arising from peripheral neuropathies, such as occipital neuralgia, brachial plexopathy, diabetic neuropathy, multiple sclerosis, complex regional pain syndrome type I (RSD) and type II (causalgia), ischemic neuropathies, and pudendal neuralgia have been managed with SCS with good results when other therapies have failed (19–21). Today SCS is recognized as “an established treatment for chronic neuropathic pain, which can arise after nerve or nervous system injury” according to the combined position statement released by the Neuromodulation Therapy Access Coalition that represents five of the most prominent national and international pain societies (22). To date in the United States, there has been no published literature concerning the use of SCS for CMT pain. An extensive literature review by the authors failed to produce any bibliographic evidence of any type other than a Japanese article dating back to 1984. In that article SCS was carried out in 11 cases of intractable pain, one of which was a patient with CMT pain. The results were encouraging (23). There have been no studies looking at CMT pain and SCS since. That is not to say that this technology has not been used prior to this study for CMT patients with chronic pain. Communication with leaders in the field of neuromodulation reveals several anecdotal series.

Today there are major organizations representing patients with neuropathies and neuropathic pain. The National Institute of Neurological Disorders and Stroke (NINDS), as well as the Charcot-Marie-Tooth Association, fails to even mention SCS treatment for neuropathic pain, or to educate their members and make them aware of this technology. Compared with all the other methods for CMT pain relief, SCS presents itself as a possible method characterized by its overall safety and relative simplicity based on its use for other indications. Also, SCS is one of the very few modalities that offer a trial treatment period before the actual permanent implant procedure. Therefore, it may be considered a procedure that should be offered to CMT patients experiencing pain early on. Physicians involved in CMT patient care should be optimistic about the results of SCS on CMT pain and need to be further educated about this therapy option so the information can be passed on to their patients.

Although SCS is not a panacea, it has a clear role in the management of neuropathic pain and should be investigated further as a potentially safe and effective option for pain arising from CMT disease. This is the first case report of successful use of SCS for CMT chronic pain in the United States. We are in the process of collecting data for a case series report.

Authorship statements
Dr. Skaribas designed and conducted the study, including patient recruitment and data collection. Dr. Washburn assisted with data collection, performed data analysis, and prepared the manuscript draft with input from Dr. Skaribas. All authors approved the final manuscript. St. Jude Medical Neuromodulation provided funding for the study. Drs. Skaribas and Washburn had complete access to the study data. We would like to thank Dr. Tracy Cameron and Roni Diaz for their editorial support during the preparation of this manuscript.

How to Cite this Article:

REFERENCES
This is a straightforward report of a 37-year-old male with pain secondary to Charcot-Marie-Tooth disease that responded to spinal cord stimulation. A five-day trial showed a reduction in Visual Analogue Scale (VAS) pain scores from 9 to 2. The authors are to be commended on thorough quality of life (QoL) evaluations at 1- and 6-month post-operation visits. The only limitation, however, is that the baseline scores for each implemented scale were determined retrospectively after implant. The leads were placed 6 mm apart at T9, with stimulation settings at 338 μs, 6.8 mA, and 80 Hz. This led to a decrease in VAS scores from 7.5 (baseline) to 5.1 and then 3 at the 1- and 6-month visits, respectively.

As the authors also point out, this does not represent a completely novel treatment option. They are aware of a number of clinicians who have treated patients similarly with comparable results. However, all neuropathic pain syndromes are not alike and there is significant potential variability with respect to different neuropathic pain syndromes and their relative sensitivity to treatment with spinal cord stimulation. In my experience, post-herpetic neuralgia may respond differently than pain related to diabetic peripheral neuropathy; phantom limb pain may respond differently to spinal cord stimulation than pain from HIV-related peripheral neuropathy. Thus, this case report deserves publication not only to provide a contemporary literature reference for the successful treatment of pain related to Charcot-Marie-Tooth disease using epidural spinal cord stimulation. While in general, appendicular neuropathic pain is one of the pain categories most successfully treated with spinal cord stimulation, there has only been one specific case of pain related to Charcot-Marie-Tooth disease reported in the medical literature and that was 25 years ago. Furthermore, all neuropathic pain syndromes are not alike and there is significant potential variability with respect to different neuropathic pain syndromes and their relative sensitivity to treatment with spinal cord stimulation.

In my experience, post-herpetic neuralgia may respond differently than pain related to diabetic peripheral neuropathy; phantom limb pain may respond differently to spinal cord stimulation than pain from HIV-related peripheral neuropathy. Thus, this case report deserves publication not only to provide a contemporary literature reference for the successful treatment of pain related to Charcot-Marie-Tooth disease using spinal cord stimulation but also to suggest that neuropathic pain resulting from this specific mechanism of nerve injury may be amenable to treatment with this modality.

As the authors also point out, this does not represent a completely novel treatment option. They are aware of a number of clinicians who have treated patients similarly with comparable results. However, they have provided an important start in recording the details of their treatment of this specific disease. More unique to this case, and begging further investigation, are the implied effects on the treated patient’s restless leg syndrome (RLS) and spasticity. We are not aware of a literature addressing the use of SCS for RLS, and this would be an interesting avenue of further investigation. Spasticity has been addressed in the past with SCS in a number of conditions (1, 2), and some report successful treatment for over 2 years, but other authors have found that despite an initially high response rate, it is rarely effective for more than 6 months (3, 4), making us wonder if this would have continued in this patient with longer follow up.