

EPIDURAL SPINAL CORD STIMULATION HELPS RESTORE LOCOMOTION IN AN INDIVIDUAL WITH SUBACUTE COMBINED DEGENERATION: A CASE REPORT

Ornella Bricoune, MD¹, Martin Myers, MD^{1,2}, James Warren, MD³, and Charles Brock, MD²

Background: Subacute combined degeneration (SCD) of the spinal cord with corticospinal tract involvement can impair motor functions below the level of the lesion.

Case Report: A 63-year-old man developed progressive bilateral lower extremity weakness marked by difficulty standing for more than a second and the inability to ambulate, causing him to become wheelchair-bound. He was diagnosed with SCD. His vitamin B12 level was corrected and he underwent physical therapy. Despite these interventions, he experienced an overall deterioration in his strength examination. He later underwent an epidural spinal cord stimulator trial with pulsed electrical stimulation. With this, he experienced improvement in his lower extremity strength and regained the ability to ambulate independently. Permanent leads were placed with the retained faculty to ambulate with the stimulator turned on.

Conclusion: Epidural spinal cord stimulation (SCS) has the potential to improve motor function and restore locomotion in individuals with spinal cord injury from SCD.

Key words: Case report, epidural spinal cord stimulation, spinal cord injury, subacute combined degeneration

BACKGROUND

Spinal cord injuries (SCI) encompass a broad range of both traumatic events and diseases and leave tens of thousands of individuals yearly in permanent need of assistance to conduct basic activities of daily living (ADL). The National Spinal Cord Injury Statistical Center reports about 17,730 new SCI cases each year. Due to advances in biomedical engineering and targeted therapies, it has become apparent that neuromodulatory interventions may offer a new array of treatments for previously irremediable neurological damage, including SCI. Amongst those targeted treatments, epidural spinal cord stimulation (SCS), performed in a certain algorithm that is respectful of the body's proprioceptive signal firing rate paired with

rehabilitation, has already shown promising results (1-4). But while most of the current studies have focused on traumatic causes of SCI, few have observed the effects of SCS on alternative causes of paraplegia. In this article, we report the case of a man with a chronic T10 level SCI of Asia Impairment Scale (AIS)-Grade C secondary to subacute combined degeneration (SCD) with involvement of the corticospinal tracts, who incidentally regained the ability to ambulate without an assistive device from a wheelchair-bound state following the implantation of an epidural spinal cord stimulator.

Methods

We report the case of a 63-year-old man with chronic

From: ¹University of South Florida Health Morsani College of Medicine, Department of Neurology; ²James A. Haley Veteran's Hospital; ³ Apollo Pain Management, Apollo Beach

Corresponding Author: Ornella Bricoune, MD, E-mail: ornella@usf.edu

Disclaimer: There was no external funding in the preparation of this manuscript.

Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Patient consent for publication: Consent obtained directly from patient(s).

Accepted: 2022-10-20, Published: 2022-12-31

lower back pain from a military injury over 20 years prior with a known chronic bilateral L5-S1 radiculopathy who developed progressive bilateral lower extremity sensory loss and weakness in 2011. He was initially evaluated in February 2013, at which time he was noted to have normal tone and muscle bulk. His strength testing was 3/5 with right hip flexion, and 2/5 with knee extension and flexion, dorsiflexion and plantarflexion; 4/5 with left hip flexion, and 4-/5 with left knee extension and flexion, dorsiflexion and plantarflexion. His lower extremities showed spasticity with 3+ reflexes at the bilateral patellar and Achilles tendons with bilateral ankle clonus. He had a sensory level to pinprick at T10 and decreased sensations to sharp/dull, cold, and vibratory stimuli up to the level of his mid shins symmetrically bilaterally. He was able to stand for about a second unassisted and was mostly wheelchair-bound. He also had a neurogenic bladder and required intermittent straight catheterization. Magnetic resonance imaging (MRI) of his thoracic spine showed a nonenhancing subtle signal abnormality which was most prominent in the dorsal cord from T6-7 to T7-8. At the time, his serum vitamin B12 level was 170 pg/mL. He was diagnosed with subacute combined degeneration with clinical dorsolateral spinal cord involvement and started on vitamin B12 supplementation with cyanocobalamin intramuscular injections. He also underwent regular physical therapy for strength and gait training.

With the normalization of his serum vitamin B12 level and initial extensive rehabilitation, his strength examination improved slightly, however he remained unable to stand for more than a few seconds or to ambulate independently. In November 2019, he had increased tone, more prominently in his right leg, and decreased bulk in his legs bilaterally. His strength testing was 5/5 with right hip flexion, knee extension and flexion; 2/5 dorsiflexion and plantarflexion; and 3/5 with left hip flexion, 4/5 strength with knee flexion, and 2/5 with knee extension, and ankle movements. His deep tendon reflexes were 3+ in the patellar and Achilles reflexes with crossed adductor responses bilaterally. He also had nonsustained ankle clonus with more beats of clonus in his right ankle than in his left. His sensory examination was unchanged. The improvements observed in his proximal right leg strength were attributed to his increased tone, while the degradation in his left leg strength was felt to be related to lower-back pain and deconditioning.

In September of 2020, he was referred to a pain

management specialist for severe lower-back pain which significantly impacted his ability to stand for any length of time and to sit comfortably in his wheelchair. He initially had bilateral L2-L4 medial branch and L5 dorsal rami radiofrequency ablations (RFA) with 100% pain relief and regained the ability to stand for a few seconds. MRI monitoring of his thoracic and lumbar spine done a month later showed improvement in his thoracic signal abnormality and redemonstrated his known L5-S1 radiculopathy. An epidural spinal cord stimulator trial with an Abbott model 3660 Proclaim™ XR 5 (Abbott Medical, Austin, Texas) was performed 2 months later for improved pain control. The stimulator was initially set on Program 1 which was characterized by intermittent dosage with a burst stimulation pattern of 30-second on-periods and 6-minute off-periods, but later self-adjusted by the patient to Program 3 characterized by intermittent dosage with a burst stimulation pattern of 30-second on-periods and 90-second off-periods. Both of these programs delivered stimulation in series of 5 pulses, with a ramp time of 4 seconds. Each pulse was set at a frequency of 40 Hz, an intraburst rate of 500 Hz, and a pulse width of 1000 μ s. Strength for all programs was set at a maximum of 1.5 mA with a step size of 0.05 mA and 30 steps in total, which can be independently adjusted by the patient. He reported similar pain relief as with the L2-5 RFAs, but also experienced marked improvement in his lower extremity strength with the ability to stand for prolonged periods of time and to ambulate independently. He therefore underwent permanent lead implantation 3 weeks later with Octrode 3186 percutaneous leads (Abbott Medical, Austin, Texas).

RESULTS

An updated physical examination done about 3 months later showed that he was deconditioned overall with bilateral 4+/5 strength with arm abduction and generalized decreased muscle bulk that was more prominent in his lower extremities, in keeping with his previous known wheelchair-bound status for over 7 years and lack of recent physical rehabilitation. With the stimulator turned off, his lower-extremity tone was increased. His examination showed 3/5 strength with right-sided hip movements, 4-/5 strength with knee extension and 4+/5 with knee flexion, and 2/5 strength with ankle movements. He had 1/5 strength with left hip movements, 3/5 strength with knee extension, 4/5 strength with knee flexion, and 2/5 strength with ankle

movements. His lower extremity deep tendon reflexes were also 3+ with prominent cross adductor responses. He had 5 beats of left ankle clonus and 6 beats of right ankle clonus. He was unable to stand or ambulate. He independently set his stimulator back on to program 3 and to a strength of 10 representing 0.5 mA, where he reported optimized results. With the simulator turned on, he remained spastic but with a relatively decreased tone in the lower extremities compared to when the stimulator was turned off. He had 4+/5 strength with hip, knee, and ankle movements bilaterally, and 5/5 strength with plantar flexion on the right. His reflexes were 3+ bilaterally at the patellar and Achilles tendons with mildly positive cross adductor responses. He had 2 beats of left ankle clonus and 4 beats of right ankle clonus. He was able to stand and ambulate independently with exaggerated lordosis, knee flexion, and a wide-based gait. His sensory examination was unchanged compared to prior examinations. His pain level was 0 of 10 throughout this examination.

DISCUSSION

While epidural spinal cord stimulators have mostly been used to help relieve pain in SCI, the evidence suggests a broader indication for those devices in neural repair. This example is in keeping with the current literature which suggests that in order to regain locomotion in SCI, stimulation protocols require dedicated implantable pulse generators that allow the delivery of SCS bursts with high-frequency resolution that are controllable in real time. An important observation is that this patient is only able to see motor benefits when the stimulator is turned on, and that these results are quasi-immediate. The current literature suggests that in order to achieve clinically significant results lasting beyond the effects of direct SCS, activity-based training is essential as it can modulate the properties of spinal circuitry and improve motor recovery (5-8).

Human studies have shown that intense activity-based interventions may reestablish access to residual descending input to the spinal circuitry, and result in plasticity after chronic motor complete SCI (3,9,10,). More controlled studies on severe SCI in rats also demonstrated that consistent cortical activation resulting from rehabilitative training, simultaneously with electrochemical modulation of the spinal cord, was crucial for promoting neural plasticity across the lesion and enabled functional recovery (11,12). Therefore, training-induced plasticity targets both the spinal circuitry below the level of injury

while also modulating the supraspinal structures and their connections to the spinal circuitry (13,14). This was further confirmed in different studies showing improved motor control of specific tasks, including locomotion, following cessation of SCS in individuals undergoing intensive physical rehabilitation (1,3,7,15). Repetition, variability, and volume in the trained motor pattern were found to be helpful for enhancing motor recovery (16-19).

In this case, the results observed were incidental, and strict parameters for monitoring improvement in motor functions were not clearly established. This patient's motor improvement was likely, at least in part, detrimentally affected by his observed overall physical deconditioning. More controllable and predictable results would likely be achieved with a standardized treatment approach that includes pre- and post-intervention physical rehabilitation. It is also important to note that the examinations performed between 2013 and 2019 were conducted by a different provider than those performed in 2020. There is therefore likely a degree of interrater variability justifying some of the differences observed between these examination findings. In this report, we emphasize a special focus on this patient's ambulatory status across all documented examinations for a more patient-centered method of assessing clinical significance, and on the observed changes in the examinations performed consecutively in 2020 with the stimulator turned off, then on, for a more exact comparative analysis of neurological function. This observation also suggests the use of a standardized physical examination protocol performed by trained examiners to help ensure interrater reliability in future studies. Another potential confounding factor was the treatment of his low-back pain by the SCS, however similar improvements in his motor functions were not observed after his bilateral L2-5 RFAs despite a reportedly similar pain improvement between these 2 procedures. Altogether, more controlled studies are needed with larger numbers of individuals with SCI encompassing a broader range of factors including age range, location/type of injury, and time since injury to help advance the field of neural repair and neuromodulation with SCS in SCI.

Acknowledgments

We would like to acknowledge Teresa Nelson, an Abbott representative, who provided technical assistance with the spinal cord stimulation system. No conflicts of interest were identified in publishing this case report.

REFERENCES

1. Formento E, Minassian K, Wagner F, et al. Electrical spinal cord stimulation must preserve proprioception to enable locomotion in humans with spinal cord injury. *Nat Neurosci* 2018; 21:1728-1741.
2. Gill ML, Grahn PJ, Calvert J, et al. Neuromodulation of lumbosacral spinal networks enables independent stepping after complete paraplegia. *Nat Med* 2018; 24:1677-1682.
3. Possover M. Recovery of sensory and supraspinal control of leg movement in people with chronic paraplegia: A case series. *Arch Phys Med Rehabil* 2014; 95:610-614.
4. Rejc E, Angeli C, Atkinson D, Harkema S. Motor recovery after activity-based training with spinal cord epidural stimulation in a chronic motor complete paraplegic. *Sci Rep* 2017; 7:1-12.
5. De Leon RD, Hodgson JA, Roy RR, Edgerton VR. Full weight-bearing hindlimb standing following stand training in the adult spinal cat. *J Neurophysiol* 1998; 80:83-91.
6. De Leon RD, Hodgson JA, Roy RR, Edgerton VR. Locomotor capacity attributable to step training versus spontaneous recovery after spinalization in adult cats. *J Neurophysiol* 1998; 79:1329-1340.
7. Rejc E, Angeli CA. Spinal cord epidural stimulation for lower limb motor function recovery in individuals with motor complete spinal cord injury. *Phys Med Rehabil Clin N Am* 2019; 30:337-354.
8. Rossignol S, Martinez M, Escalona M, et al. The "beneficial" effects of locomotor training after various types of spinal lesions in cats and rats. *Prog Brain Res* 2015; 218:173-198.
9. Gerasimenko YP, Lu DC, Modaber M, et al. Noninvasive reactivation of motor descending control after paralysis. *J Neurotrauma* 2015; 32:1968-1980.
10. Donati AR, Shokur S, Morya E, et al. Long-term training with a brain-machine interface-based gait protocol induces partial neurological recovery in paraplegic patients. *Sci Rep* 2016; 6:30383.
11. Asboth L, Friedli L, Beauparlant J, et al. Cortico-reticulo-spinal circuit reorganization enables functional recovery after severe spinal cord contusion. *Nat Neurosci* 2018; 21:576-588.
12. Van den Brand R, Heutschi J, Barraud Q, et al. Restoring voluntary control of locomotion after paralyzing spinal cord injury. *Science* 2012; 336:1182-1185.
13. Knikou M. Plasticity of corticospinal neural control after locomotor training in human spinal cord injury. *Neural Plast* 2012; 2012:254948.
14. Zewdie ET, Roy FD, Yang JF, et al. Facilitation of descending excitatory and spinal inhibitory networks from training of endurance and precision walking in participants with incomplete spinal cord injury. *Prog Brain Res* 2015; 218:127-155.
15. Wagner FB, Mignardot JB, Le Goff-Mignardot CG, et al. Targeted neurotechnology restores walking in humans with spinal cord injury. *Nature* 2018; 563:65-71.
16. Bigbee AJ, Crown ED, Ferguson AR, et al. Two chronic motor training paradigms differentially influence acute instrumental learning in spinally transected rats. *Behav Brain Res* 2007; 180:95-101.
17. Cai LL, Fong AJ, Otoshi CK, et al. Implications of assist-as-needed robotic step training after a complete spinal cord injury on intrinsic strategies of motor learning. *J Neurosci* 2006; 26:10564-10568.
18. Cha J, Heng C, Reinkensmeyer DJ, Roy RR, Edgerton VR, De Leon RD. Locomotor ability in spinal rats is dependent on the amount of activity imposed on the hindlimbs during treadmill training. *J Neurotrauma* 2007; 24:1000-1012.
19. Shah PK, Gerasimenko Y, Shyu A, et al. Variability in step training enhances locomotor recovery after a spinal cord injury. *Eur J Neurosci* 2012; 36:2054-2062.