References

1. Perper Y. On the spinal cord injury during attempted cervical interlaminar epidural injection of steroids. Pain Med 2019;20(4):854–5.
2. Landers MH. Spinal cord injury during attempted cervical interlaminar epidural injection of steroids. Pain Med 2018;19(4):652–7.
3. International Spine Intervention Society. Cervical interlaminar epidural access. In: Bogduk N, ed. Practice Guidelines for Spinal Diagnostic and Treatment Procedures. 2nd ed. San Francisco: International Spine Intervention Society; 2013.
4. Landers MH, Dreyfuss P, Bogduk N. On the geometry of fluoroscopy views for cervical interlaminar epidural injections. Pain Med 2012;13(1):58–65.
5. Perper Y. On the geometry of fluoroscopy views for cervical interlaminar epidural injection. Pain Med 2012;13(11):1520–1.
6. Perper Y. Contrast spread technique. Pain Med 2015; 16(4):827–8.
7. Perper Y. Contrast spread technique: Evolution. Pain Med 2016;17(7):1385–6.
8. Bogduk N, ed. Practice Guidelines for Spinal Diagnostic and Treatment Procedures. 2nd ed. San Francisco: International Spine Injection Society; 2013.

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Letters to the Editor

Chemotherapy-Induced Peripheral Neuropathy Treated with Dorsal Root Ganglion Stimulation

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Dear Editor,

Different chemotherapeutic drugs can induce peripheral neuropathy as a side effect. Chemotherapy-induced peripheral neuropathy (CIPN) predominantly affects small-diameter nerve fibers, causing burning pain, hyperesthesia, and later on loss of pain and temperature sensations [1]. The most common causative drugs are taxanes, platinum compounds, vinca alkaloids, epothilones, bortezomib, and thalidomide [1]. Conventional treatment options for CIPN include antidepressants, anticonvulsants, and physical therapy. More recently, neuromodulation has emerged as a possible treatment option for CIPN [2,3]. Dorsal root ganglion (DRG) stimulation may be a particularly useful neuromodulation treatment modality considering the fact that CIPN substantially affects neurons at the DRG as the DRG is not protected by the blood–brain barrier [1].

A 52-year-old female presented at our institute with neuropathic pain in the bilateral feet and her left lateral lower leg. At presentation, she described the pain as burning and rated the pain 8/10 on the visual analog scale (VAS). Her physical exam revealed a loss of pinprick sensation, two-point discrimination, proprioception, and allodynia to light touch in the bilateral feet to the ankles. The pain significantly interfered with her daily activities and prevented her from standing longer than 15 minutes. She had developed this pain after being treated with high-dose thalidomide (100–150 mg daily) for several years for severe cutaneous lupus erythematosus. With her rheumatologist and neurologist, she had previously tried muscle relaxants (carisoprodol and methocarbamol), neuropathic pain medications (gabapentin, pregabalin, amitriptyline, and duloxetine), medical marijuana, and opioids (tramadol, tapentadol,

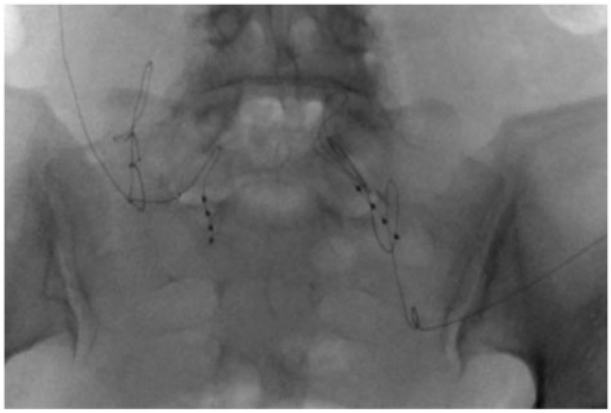

Figure 1. Anterior/posterior fluoroscopic view of the bilateral dorsal root ganglion stimulation electrodes (Axium, Abbott, Chicago, IL, USA) on the S1 level.

tylenol-codeine, and hydrocodone) without effective relief of pain. We proposed a DRG stimulation trial as an off-label option considering the patient's persistent debilitating CIPN and failure of other treatment modalities. DRG stimulation is currently only FDA approved for treatment of complex regional pain syndrome, but its use has been reported in a variety of other neuropathic chronic pain conditions [4]. VAS pain score and health-related quality of life (EuroQol [EQ-5D], 36-Item Short Form Survey [SF-36]) were measured preoperatively and at follow-up as part of standard of care.

With bilateral S1 DRG leads (Figure 1), we were able to get coverage of the dorsal and plantar aspect of the pain in her feet and of the pain that radiated up her left leg. During the trial, the patient reported complete relief of pain (0/10 on VAS) and was able to stand for prolonged periods of time for the first time in eight months. She decided to proceed with permanent stimulator implantation and continues to experience effective pain relief (1/10 on VAS) at five months postimplantation with concomitant improvement in quality of life (EQ-5D score: from 0.13 at baseline to 0.85; SF-36 physical component score: from 23 at baseline to 31; and SF-36 mental component score: from 7 at baseline to 59). The improved pain control allowed her to taper off her opioid medication and medical marijuana.

CIPN is becoming an increasingly common condition as a result of improving survival rates of cancer, combined with the high incidence of CIPN with certain chemotherapeutic drugs and the current lack of effective treatment options for CIPN [1]. Conventional stimulation of the dorsal column has been described as an interventional pain treatment option for CIPN [2,3], but it may be ineffective in the treatment of CIPN in focused distal dermatomes that are often affected. Upon literature review, we encountered one other case of DRG stimulation for CIPN: Finney and Helm [5] reported on the successful application of DRG stimulation for CIPN that occurred after treatment of rectal adenocarcinoma with oxaliplatin. Before any clinical studies, it has been speculated that DRG stimulation may be a treatment option for CIPN, as the DRG is often affected by the neurotoxicity of chemotherapy [1]. The neurotoxicity of thalidomide specifically has been shown to be affected at the neuronal cell bodies within the DRG [6]. In neuropathic pain models, it has been shown that nerve injury attenuates filtering of afferent pain signals at the T-junction in the DRG, allowing action potentials to propagate through the T-junction at a faster frequency, thereby increasing nociceptive signaling [7]. Additionally, following nerve injury, there is a substantial increase in ectopic activity generated by nociceptive neurons within the DRG [8]. DRG stimulation is thought to cause hyperpolarization of the neuronal cell bodies, resulting in a suppression of the ectopic firing from the DRG and increased filtering of afferent nociceptive input at the T-junction, overall reducing nociceptive signaling to the spinal cord [9].

In this case, bilateral S1 leads were sufficient to obtain coverage of the entire feet. This is inconsistent with the dermatomal distribution that is conventionally associated with the S1 nerve root. Others have similarly reported that S1 DRG stimulation can cause paresthesias in the entire foot [10], and this has been attributed to amplified secondary convergence of A delta and C fibers between adjacent DRGs under pathological conditions.

In conclusion, we treated a patient with refractory CIPN with DRG stimulation, resulting in substantial improvements in pain, quality of life, and reductions in pain medication dosages. Larger-scale prospective studies exploring the application of DRG stimulation in patients with CIPN may help corroborate a potential role for DRG stimulation in the treatment of CIPN.

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References

1. Gupta R, Bhaskar A. Chemotherapy-induced peripheral neuropathic pain. BJA Educ 2016;16(4): 115–9.
2. Cata JP, Cordella JV, Burton AW, et al. Spinal cord stimulation relieves chemotherapy-induced pain: A clinical case report. J Pain Symptom Manage 2004;27 (1):72–8.
3. Phan P, Khodavirdi A. Successful treatment of chemotherapy-induced peripheral neuropathy (CIPN) with spinal cord stimulation (SCS): Case reports. Cancer Res 2007;67(9 supplement):35.
4. Harrison C, Epton S, Bojanic S, Green AL, FitzGerald JJ. The efficacy and safety of dorsal root ganglion

stimulation as a treatment for neuropathic pain: A literature review. Neuromodulation 2018;21(3):225–33.
5. Finney J, Helm E. Dorsal root ganglion stimulation for chemotherapy-induced peripheral neuropathy: A case report. J Pain 2017;18(4):S89.
6. Cavaletti G, Beronio A, Reni L, et al. Thalidomide sensory neurotoxicity: A clinical and neurophysiologic study. Neurology 2004;62(12):2291–3.
7. Gemes G, Koopmeiners A, Rigaud M, et al. Failure of action potential propagation in sensory neurons: Mechanisms and loss of afferent filtering in C-type units after painful nerve injury. J Physiol 2013;591 (4):1111–31.
8. Amir R, Michaelis M, Devor M. Membrane potential oscillations in dorsal root ganglion neurons: Role in normal electrogenesis and neuropathic pain. J Neurosci 1999;19(19):8589–96.
9. Kent AR, Min X, Hogan QH, Kramer JM. Mechanisms of dorsal root ganglion stimulation in pain suppression: A computational modeling analysis. Neuromodulation. 2018;21(3):234–246.
10. Hunter CW, Yang A, Davis T. Selective radiofrequency stimulation of the dorsal root ganglion (DRG) as a method for predicting targets for neuromodulation in patients with post amputation pain: A case series. Neuromodulation 2017;20(7):708–18.