Case Report

Efficacious Dorsal Root Ganglion Stimulation for Painful Small Fiber Neuropathy: A Case Report

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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.

Manuscript received: 01-29-2016
Revised manuscript received: 03-25-2016
Accepted for publication: 03-29-2016

Free full manuscript: www.painphysicianjournal.com

Small fiber neuropathy is a disorder of the peripheral nerves with typical symptoms of burning, sharp, and shooting pain and sensory disturbances in the feet. Pain treatment depends principally on the underlying etiology with concurrent administration of antidepressants, anticonvulsants, opioids, and topical treatments like capsaicin and local anesthetics. However, treatments for pain relief in these patients frequently fail. We describe the first case of intractable painful small fiber neuropathy of the foot successfully treated with spinal cord stimulation of the left L5 dorsal root ganglion.

A 74-year-old man presented at our clinic with severe intractable pain, dysesthesia, and allodynia of the left foot caused by idiopathic small fiber neuropathy, confirmed by skin biopsy. His pain score was 8 on a standard 0 – 10 numeric rating scale. As the pain was not satisfactorily controlled by conventional therapy, dorsal root ganglion stimulation was proposed to the patient and, after informed consent, a specifically designed percutaneous stimulation lead was placed over the left L5 dorsal root ganglion and connected to an external neurostimulator. After a positive trial of 10 days, a permanent neurostimulator was implanted. Twenty months post-implantation the patient continued to experience stimulation-induced paresthesia covering the entire pain area and reported a pain rating of 4.

Results from the case report demonstrate that the dorsal root ganglion is a promising neural stimulation target to treat neuropathic pain due to intractable small fiber neuropathy. Prospective controlled studies are warranted to confirm the efficacy of this treatment as an option for the aforementioned condition.

Key words: Dorsal root ganglion stimulation, small fiber neuropathy, neuropathic pain

Pain Physician 2017; 20:E459-E463

Small fiber neuropathy (SFN) is a disorder of the peripheral nerves that affects thinly myelinated Aδ and unmyelinated, nociceptive C nerve fibers. Typical symptoms affect the lower limbs in a distal-to-proximal gradient and are burning, sharp, and shooting pain in the feet, sensory disturbances, and in some cases autonomic dysfunction. Symptoms mostly worsen during periods of rest and at night (1). SFN might be acquired secondary to a variety of diseases including diabetes mellitus, HIV infection, or chemotherapy. However, in up to 50% of cases of painful SFN, an underlying cause cannot be identified (2). The diagnosis of SFN is often challenging because the small fibers are undetectable to routine neurophysiological nerve conduction studies. Tests such as quantitative sensory testing (QST) and laser Doppler flowmetry may help to confirm the diagnosis. Biopsy at the ankle showing reduced intraepidermal nerve fiber (IENF) density is however the most reliable technique to diagnose SFN to date (3). Pain treatment depends principally on the underlying etiology with concurrent administration of antidepressants,

anticonvulsants, opioids, and topical treatments like capsaicin and local anesthetics. However, treatments for pain relief in these patients frequently fail (1).

Spinal cord stimulation (SCS) is used to treat chronic, intractable neuropathic pain when conventional therapies have failed and has been shown to be effective in patients having a variety of neuropathic pain conditions, including complex regional pain syndrome (CRPS), failed back surgery syndrome (FBSS), and diabetic polyneuropathy (4-6). Dorsal root ganglion stimulation (DRGS) is a relatively new mode of SCS with selective stimulation in specific dermatomes and has demonstrated neuropathic pain relief for groin pain, CRPS, and pain of the limbs and trunk (7-10). DRGS may offer several potential benefits over conventional SCS, including lack of postural effects, lower therapeutic power demands, and selective stimulation in the dermatomes and therefore the ability to reach areas like the feet that are typically difficult to reach using conventional SCS (7). In this report we describe a first case of successful treatment of intractable painful SFN with left L5 DRGS. The patient gave permission to publish this case report.

Case Report

A 74-old man (retired pilot) presented at our clinic with burning and shooting pain in his feet that had progressively worsened in the past 6 years. The pain was predominantly localized on the dorsal side of his left foot and he experienced allodynia, hypoesthesia, and dysesthesia in the same region. The pain increased especially at rest and at night, which led to sleep disturbances. The patient reported a pain score of 8 out of 10 at rest and a pain score of 2 – 3 during the day on a standard numeric rating scale (NRS, 0 = no pain; 10 = extremely painful).

The neurological examination was normal. His medical history was significant for hyperlipidemia, left common carotid artery stenosis, coronary artery disease, and a depressive disorder. His medications included oral daily doses of aspirin 100 mg and atorvastatin 20 mg. Atorvastatin, because of its known potential side effects of myositis and myalgia, was stopped for 2 weeks, but the symptoms did not improve. In 2010, lumbar magnetic resonance imaging (MRI) demonstrated a mild spinal stenosis without radicular compression. Electromyographic assessment performed in 2010 and 2011 showed no signs of sensitive or motoric polyneuropathy of the large fibers. In 2011, the patient scored 7 out of 21 on the Hospital Anxiety and Depression Scale (HADS), which is considered normal (11). QST, performed in 2011 according to the protocol of the German Research Network on Neuropathic Pain (12), revealed dysesthesia, thermal hypoesthesia, and hypoalgesia to pinprick on the left foot and an increased vibration detection threshold. Laser Doppler flowmetry did not show any flare response as expression of disturbed C-fiber function and blood tests revealed normal full blood count, renal and thyroid function, glucose levels, ferritin, folic acid, and vitamin B12. Other serologies, including antineutrophil cytoplasmic antibody, antinuclear antibody, hepatitis C, human immunodeficiency virus (HIV), and paraneoplastic antibodies were negative. Finally, vascular disturbances of the leg were excluded, and in March 2014 a biopsy of the skin confirmed the diagnosis of SFN via pathological reduction of intraepidermal unmyelinated nerve fibers. There was no history of SFN in his family.

Over the course of 6 years the pain of his previously undiagnosed SFN was neither satisfactorily controlled by optimized doses of multiple medications including gabapentin, pregabalin, duloxetine, amitriptyline, mirtazapine, lidocaine patches, topical capsaicin 8%, and cannabis, nor by treatment with a transcutaneous electrical nerve stimulation (TENS), physical therapy, acupuncture, and a corticosteroid infiltration at the level of the first ray of the left foot. Only ice packs and pressure applied on his left foot provided some relief at night.

As the pain was not satisfactorily controlled by conventional therapy, neuromodulation was considered. DRGS was chosen because of its known selective stimulation in the dermatomes and therefore the ability to reach areas like the feet that are typically difficult to reach using conventional SCS. Informed consent was obtained. The left L5 dorsal root ganglion (DRG) was chosen because the pain was predominantly felt in the dorsal side of the patient's left foot. On April 7, 2014, a quadripolar DRGS lead (Axium™ Neurostimulator System, Spinal Modulation, Inc., Menlo Park, CA, U.S.A.) was placed percutaneously according the procedure described by Liem et al (7). Access to the contralateral epidural space was achieved using a 14-gauge, 10-cm Tuohy needle applying a loss of resistance technique. The lead was advanced under fluoroscopic guidance in an anterograde fashion and steered into the medial aspect of the left L5/S1 intervertebral foramen over the left L5 DRG (Figs. 1,2). The lead was connected to an external trial neurostimulator, stimulation was initiated, and stimulation-induced paresthesia covered the entire

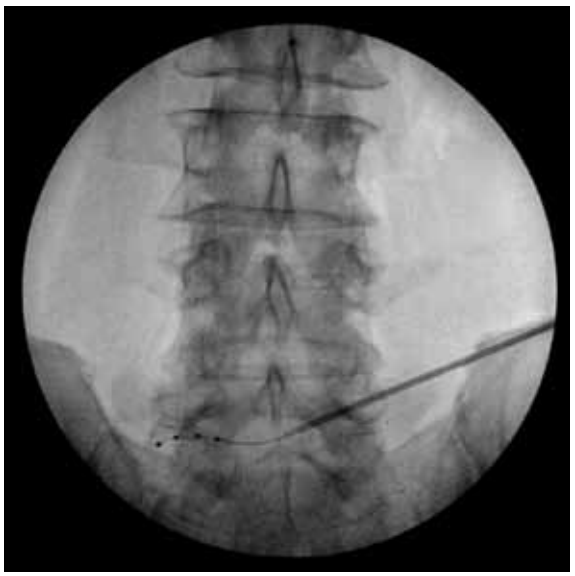

Fig. 1. *Lead placement at the left L5 DRG.*

pain area on the dorsal site of the left foot. During 10 days of the trial period, the patient reported a pain score of 3 out of 10 on the NRS at rest (an improvement of 62.5%). Having completed a successful trial, the implantable neurostimulator was placed in the patient's abdominal wall (pulse width: 670 μs; frequency: 40 Hz; amplitude: 1.88 mA). Two months post-implantation, the patient still experienced complete pain coverage, graded his pain as 2 out of 10 on the NRS during stimulation (an improvement of 75% from baseline), and improved on all domains of the McGill Pain Questionnaire (MPQ). Also the degree of disability, as measured by the Oswestry Disability Index (ODI), was reduced substantially (Table 1). In addition, the patient reported that his sleep quality had improved and that he no longer needed to apply ice packs on his left foot to alleviate the pain before going to bed. To describe his feelings, the patient stated "now it's paradise." The device was used 24 hours a day. The patient reported resumption of pain within minutes when the neurostimulator was switched off. At the 6 month follow-up the patient still reported a pain rating of NRS 2 and at the 12 and 20 month follow-up he reported a pain rating of 4. The augmentation in NRS of 2 points could possibly be explained by progression of the SFN. However, the patient was completely satisfied with the pain relief from stimulation, did not need additional pain treatment, and reported his Global Impression of Change (GIC) on all the above-mentioned time points as "much improved." The improvement on the MPQ and the degree of disability measured by the ODI remained stable.

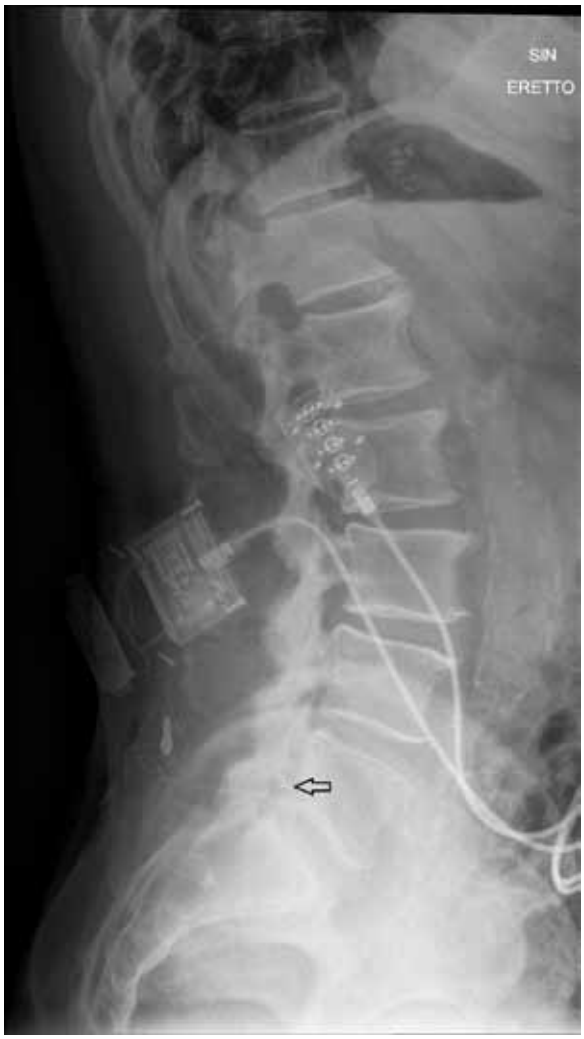

Fig. 2. *Lateral fluoroscopy of lead in the lateral epidural space near the left L5 DRG, seen as a white dots in the L5/S1 foramen (arrow) and external pulse generator during the test phase.*

Discussion

This is the first description of a successful case of intractable painful SFN treated with DRGS. The DRG is located between the dorsal root and the spinal nerve within the neural foramen and is composed of cell bodies of primary sensory neurons. It transduces pain to the central nervous system, and pathological changes in the DRG are described during chronic neuropathic pain

Table 1. *Pain and function are improved with DRGS.*

		Baseline	2 Month Follow-up	6 Month Follow-up	1 year Follow-up	20 Month Follow-up
Numeric Rating Scale (NRS)		8	2	2	4	4
McGill Pain Questionnaire Scores (MPQ)	Total Pain	2.55	1.45		1.05	1.09
	Continuous	2.83	1.67		0.83	0.83
	Intermittent	1.33	0.83		0	0.67
	Neuropathic	3.67	2.00		2.5	1.83
	Affective	2.25	1.25		2	1.5
Oswestry Disability Index (ODI)		32% (Moderate Disability)	8% (Minimum Disability)		12%	6%

states (13). Furthermore, it has recently been reported that mutations in sodium channels expressed in DRG neurons can induce hyperexcitability that contribute to the pathophysiology of painful small-fiber neuropathy (14). DRGS reduces excitability of sensory neuronal somata in the DRG in vitro, which suggests that it provides an analgesic effect by reducing somatic excitability (15). This may be the underlying beneficial analgesic effects that have been observed in our patient.

Although a case report is a report related to the care of an individual patient, it could be a source of new ideas in medicine, provide treatment guidance in clinical practice, and generate hypotheses for future clinical studies. To date, our patient remains satisfied with the DRGS and has not experienced any disturbances or complications related to the neurostimulator. We realize that this is a single case, but we consider the present results to be encouraging and the DRG to be a potential new neural stimulation target for reducing chronic intractable neuropathic pain due to SFN of the lower limbs. Keeping in mind appropriate patient selection and indication assessment, DRGS can be part of an overall treatment plan to manage difficult to treat neuropathic pain syndromes when conventional therapies have failed. Furthermore, we would like to remind the readers that SFN mostly affects the feet bilaterally (1), and although it is feasible to apply DRGS bilaterally as the neurostimulator can support up to 4 leads, the case made in this report applies to predominantly unilateral pain related to SFN. Prospective controlled studies (for both unilateral and bilateral SFN related pain) are needed to evaluate the efficacy of DRGS as a treatment option in SFN.

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