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Prolonged Dorsal Root Ganglion (DRG) Trial Adequately Treats Neuropathic Pain Due to Malignant Invasion of the Lumbosacral Plexus: A Case Report

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Background: Pain control remains a challenge for patients suffering from acute malignancy-induced pain. Dorsal root ganglion (DRG) stimulation, normally indicated for chronic pain syndromes, may be an effective tool against neuropathic pain in the setting of tumor invasion.

Case Report: A 63-year-old woman with a past medical history significant for stage 1A endometrial adenocarcinoma status post robotic total hysterectomy and a recently diagnosed presacral mass (high-grade undifferentiated squamous carcinoma) presented for neurosurgical evaluation due to subacute onset of urinary retention, constipation, weight loss, and left lower-extremity pain associated with dysesthesia and impaired gait. Magnetic resonance imaging demonstrated direct invasion of the inferior sacrum and moderate spinal canal stenosis. After a multimodal regimen failed, the inpatient pain service was consulted for consideration of advanced modalities. Since the patient experienced relief from an epidural steroid injection (ESI), the team placed DRG trial leads proximal to the sacral mass at the left L5 and S1 DRGs. The patient had an immediate postoperative pain reduction of 75% to 90%. The primary team and family elected for a prolonged trial (> 7 days) as the patient's neuropathic pain was significantly improved until the patient expired 22 days post placement.

Conclusion: To the best of our knowledge, this is the first DRG trial used to treat refractory, acute cancer-related pain.

Key words: Acute pain, cancer, case report, dorsal root ganglion stimulator, DRG trial, lumbosacral plexus, malignancy pain, neuromodulation, neuropathy, pain

BACKGROUND

Malignancy-related pain is amongst the most reported symptoms when it comes to evaluation of cancer patients. More than 60% of cancer patients suffer from pain, and for one-third of this population, pain is insufficiently controlled (1). Inadequate pain control has been an unfortunate consequence of poor patient-provider communication, ineffective treatment, and a limited understanding of multimodal pain management. Opioid therapy has been regarded as the most effective and mainstay treatment for acute and terminal cancer pain (2). However, patients often cannot tolerate the adverse effects including constipation, nausea, and sedation. Furthermore, concerns about tolerance, dependence,

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and addiction limit the utility of opioids for chronic pain management (3). In well-selected patients, intrathecal drug delivery systems have demonstrated significant pain control, reduced side effects, trends to improved survival, and cost-effectiveness compared to conventional medical therapy (4,5). Neuromodulation has become increasingly popular for treatment of chronic neuropathic pain. Traditional dorsal column stimulation has been used to treat postlaminectomy syndrome and complex regional pain syndrome (CRPS) and was recently approved in the United States for diabetic peripheral neuropathy (6). Dorsal root ganglion (DRG) stimulation is a more localized modality for delivering electrical energy to specific spinal roots to modulate pain signaling. It has been used to treat chronic neuropathic pain for similar indications as dorsal column stimulation. We present a case report in which DRG stimulation is applied acutely and demonstrate that it may be an effective tool against neuropathic pain in the setting of tumor invasion.

CASE REPORT

We present a 63-year-old woman with a past medical history significant for stage 1A endometrial adenocarcinoma status post robotic total hysterectomy who had a fall 2 months prior to presentation, with subsequent development of left gluteal and labial numbness. She presented for neurosurgical evaluation of subacute onset of urinary retention, constipation, weight loss, and radiating left lower-extremity pain associated with dysesthesia and impaired gait.

Physical exam findings were significant for urinary retention and constipation. Musculoskeletal evaluation of lower extremities included: 5 of 5 strength grossly in the right knee extension/ flexion vs 4+ of 5 on the left, 5 of 5 ankle dorsi and plantar flexion bilaterally; attempts at hip flexors, hip extensors, hip abductors, and hip adductors all elicited pain, limiting the motor exam. Focal sensory deficits in the posterior left gluteal area to the left posterior thigh, and plantar arch of the left foot, were also appreciated. The remaining sensory exam of the left lower extremity was normal.

A combination of nonsteroidal anti-inflammatory drugs, opioids, and gabapentin were ineffective in controlling her pain, which progressively worsened. Initial computed tomography (CT) imaging showed a left-sided lumbosacral cyst vs mass involving the sciatic notch, with evidence of invasion that was suspicious for malignancy. An interventional radiology biopsy showed an undifferentiated squamous cell carcinoma with sacral invasion. Subsequent CT of her pelvis showed a left-sided lumbosacral 13.9 x 6.3 x 6.3-cm mass (Fig. 1). Neurosurgical and colorectal surgery services were consulted for resection planning with the oncology service on board to guide neoadjuvant therapy. Radiation therapy was initiated, and the patient was started on immunotherapy with pembrolizumab to slow tumor progression. Palliative care and interventional pain service were consulted for inpatient management of her intractable pain. The patient's pain remained refractory despite multimodal treatments including high-dose opioids, patient-controlled analgesia pumps, ketamine infusion, and epidural steroid injections (ESI). Since the patient experienced transient, yet significant relief from ESI, the inpatient pain service decided to trial DRG stimulation.

Under fluoroscopic guidance, 4 contact leads were placed within the left L5 and S1 interlaminar window via an antegrade left-sided paravertebral approach (Fig. 2). The leads were secured with a superior loop of the lead wire above the level of the foramen to the level of the disc above. A similar loop was created inferior to the foramen within the epidural space to create a figure of 8 to ensure stability. The patient was awake to confirm the presence of stimulation, and spinal needles were removed under fluoroscopic guidance to minimize the risk of lead migration. During the immediate postoperative period the patient experienced some incisional pain and posterior thigh pain, which were relieved with positional changes. Twenty-four hours postoperatively, the patient reported relief of her pain from a severity of 8 of 10 to 2 of 10.

The DRG trial's effectiveness was initially observed via the patient's subjective pain reduction and objective decrease in daily opioid usage. Efficacy was confirmed by immediate increase in pain to 10 of 10 severity associated with an increase in opioid requirement when the stimulator was briefly turned off. The decision was made to prolong the trial to 14 days as opposed to the typical 7 days, given the positive effect on treating the patient's pain. Although the intractable left lower buttock and extremity pain was initially alleviated, within a few days, the patient began to complain of intra-abdominal pain consistent with the anatomical location of her mass. Interval imaging of the tumor revealed a substantial increase in tumor size (2.9-cm increase in width over one month). Radiation therapy was discontinued given its ineffectiveness in controlling

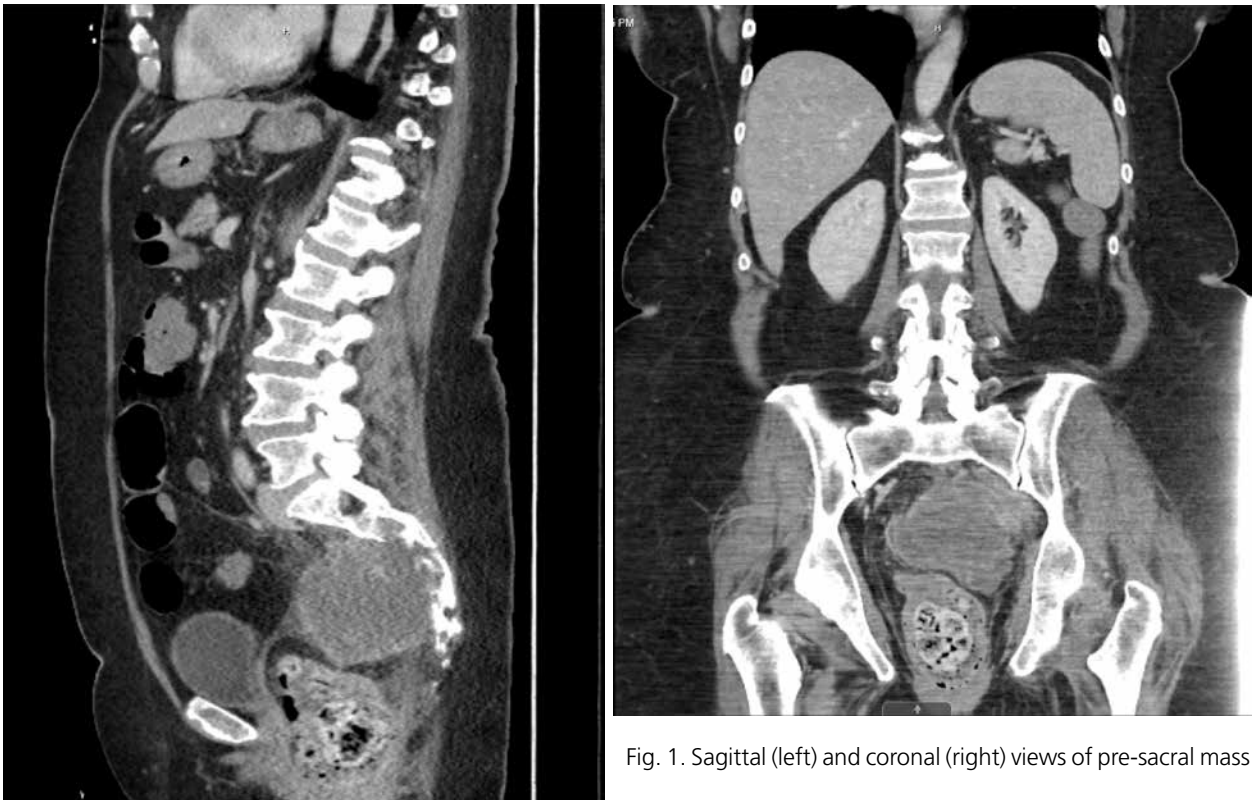

Fig. 1. Sagittal (left) and coronal (right) views of pre-sacral mass

tumor burden. The alleviation of her lower extremity pain likely unmasked the preexisting intra-abdominal disturbance that now plagued her. Given the morbid clinical course and ineffective treatment measure, the patient made the decision to transition to comfort care. Her daily opioid requirement slowly increased and her DRG trial leads remained in place to treat her neuropathic pain. The patient expired at 22 days post DRG lead placement without evidence of infection or lead migration.

DISCUSSION

Lumbosacral plexopathy (LSP) refers to an injury of the lumbosacral plexus supplied by the ventral lumbar and sacral rami. It is often associated with low back and leg pain spanning several dermatomes. Typically, the diagnosis of LSP requires a thorough clinical evaluation due to a wide differential. However, in the setting of a malignant invasion, our patient's diagnosis was rather brisk as the aggressive carcinoma was causing severe localized pain. In cases of tumor compression, the L4-S1 segment is commonly affected (> 50% of cases) followed by the L1-L4 segment (31%) and pan-plexopathy (about

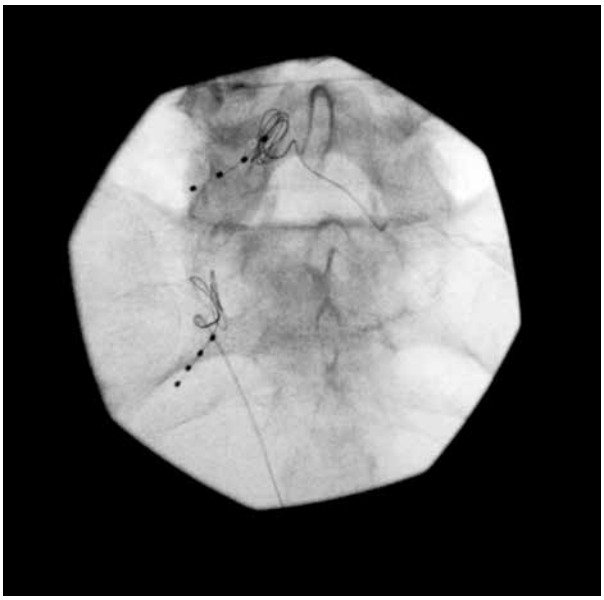

Fig. 2. Left L5 and S1 DRG leads
Abbreviation: DRG, dorsal root ganglion

10%). In one study, most patients had local compression or an invading abdominopelvic neoplasm present, which were associated with poor prognosis; at 42 month follow-up, 86% of patients diagnosed with LSP secondary to malignancy had expired (7). The prognosis for neoplastic LSP is morbid, thus making quality of life a priority for patients suffering from malignancy-related pain. Pain caused by tumor compression is best treated by tumor resection for decompression, but this is not always possible. Our patient was not a surgical candidate and palliation of pain for potential discharge to home was the primary goal of the multidisciplinary team.

Fundamentally, pain is sensed by afferent peripheral nerves (e.g., A-beta and C fibers) and transmitted via the DRG to the dorsal horn of the spinal cord synapsing at wide dynamic range neurons before crossing over and traveling cephalad via the spinothalamic tracts (8). Traditional dorsal column stimulation has been the mainstay of neuromodulation technology for decades and has shown modest efficacy against chronic pain. Yet, due to the adjacent sensory fibers within the dorsal column that lie near the electrode's zone of effect, pain relief is often accompanied/replaced with paresthesia (9). Thus, results can be inconsistent and ultimately require specific mapping/programming unique to each patient (10). Recent trials have demonstrated superiority with high-frequency stimulation for leg and back pain compared to traditional stimulation, but high energy requirements likely call for more frequent charging by the patient (11).

DRG stimulation is a recently approved therapy indicated for CRPS type I/II, causalgia, persistent postsurgical pain syndrome, and peripheral neuropathy for T10 and below vertebral levels. This technology localizes the therapy to specific spinal levels by taking advantage of basic anatomy and stimulating the DRG directly at the spinal levels of interest. This can be accomplished successfully with paresthesia-free stimulation and provides patients with a minimally invasive and safe therapy (12). Typically, eligible candidates for a DRG trial are experiencing pain due to one of the causes listed above, but here we alleviated our patient's malignancy-related neuropathic pain score by almost 90%. Furthermore, her daily opioid requirement was objectively decreased while the stimulator was turned on (Fig. 3). Unfortunately, due to aggressive disease progression, other cancer-associated (non-neuropathic) pain became more apparent and debilitating.

Several limitations must be considered before using this novel therapy in the treatment of acute cancer-related pain. The most significant is the accessibility and cost of this procedure. DRG stimulation requires advanced training by practitioners and this therapy is not readily available unless an interventionalist has acquired appropriate certification. Furthermore, DRG stimulation for a malignancy-related plexopathy is considered an

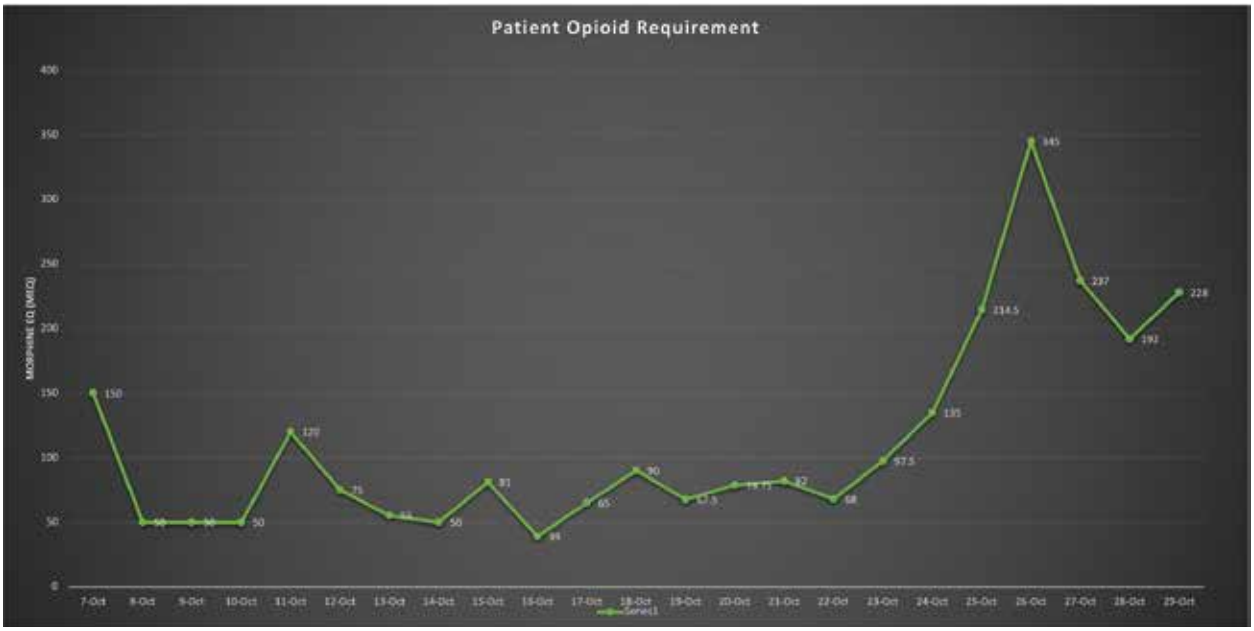

Fig. 3. Opioid requirement vs time

off-label use as it is only FDA-approved for CRPS and postlaminectomy syndrome (13). The cost-effectiveness of DRG vs traditional spinal cord stimulator (SCS) was analyzed with respect to quality-adjusted life years (QALYs) using data from the ACCURATE study superimposed with claims data (12). Although there is an initial premium in cost, over time the returns in quality of life give it superiority over traditional SCS. Additionally, the original battery used in the DRG systems has been replaced with more efficient and longer-lasting technology (14). Ultimately, as with intrathecal drug delivery systems, it is important to consider cost-effectiveness, risk vs benefit of implantation (e.g., anticoagulant dependence, anesthesia tolerance, nutritional status, etc.), and overall safety (4,5,15). This novel application has the potential to treat specific cancer-related neuropathic pain, but further research is needed to establish guidelines for its acute utility.

CONCLUSION

To the best of our knowledge, this is the first successful application of a prolonged DRG stimulation trial in the acute malignant pain crisis and comfort care setting. Cancer pain is often difficult to adequately control, and this demonstrates a new application for an interventional modality currently being used for chronic conditions. We highlight the versatility of this cutting-edge technology and hope it empowers the pain community to explore other avenues for both acute and chronic therapeutic use.

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