

SPINAL CORD STIMULATION FOR COMPLEX CHRONIC PAIN FOLLOWING EXTENSIVE PLEURAL MESOTHELIOMA AND SUBSEQUENT POST-THORACOTOMY PAIN SYNDROME

Jay Karri, MD, Harsha R. Kannan, DO, George Polson, MD, and Brian Bruel, MD

Background: Cases of malignant pleural mesothelioma and subsequent post-thoracotomy pain syndrome include pain that remains daunting and clinically challenging to manage. These presentations of pain are quite medically complex and etiologically multifactorial in nature. This challenge often yields poorly effective approaches, highlighting the need for new effective treatment including interventional procedures – especially in the context of increased cancer survivorship rates.

The objective of this case report is to present the efficacious use of spinal cord stimulation as an alternative interventional approach to the management of complex pain syndromes, particularly in the case of a malignant pleural mesothelioma and post-thoracotomy pain syndrome.

Case Report: The patient underwent successful trial and implantation of the spinal cord stimulator pulse generator under standard practices. The analysis of the procedure's efficacy was based on the patient's pain, monitored over appropriate follow-up and measured using the Visual Analog Scale as well the patient's own satisfaction. Upon successful completion of the trial and placement procedures, the patient experienced a significant reduction in pain that had been refractory to standard analgesic practices, thus allowing the patient to resume and improve functional capabilities.

Conclusions: Findings of this report are limited to this case, warranting further studies exploring its efficacy and reproducibility. As presented through our experience in this case, there is potential for the use of neuromodulatory techniques in the context of cancer-related pain syndromes, offering a promising avenue for a clinically challenging condition.

Key words: Cancer pain, interventional pain, mesothelioma, neuromodulation, pain, pain rehabilitation, pain syndromes, post-thoracotomy pain syndrome, spinal cord stimulation

BACKGROUND

Patients with malignant pleural mesothelioma (MPM) are often burdened with chronic pain that is mixed nociceptive and neuropathic in nature (1,2). Localized tumor infiltration of the chest wall and thoracic organs confers somatic and visceral types

of pain, respectively. Moreover, involvement of intercostal nerves and proximal nerve roots can also produce neuropathic pain. Unfortunately, up to half of those patients with MPM who undergo surgical debulking are also burdened by post-thoracotomy

From: Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, TX

Corresponding Author: Jay Karri, MD, E-mail: jay.karri@bcm.edu

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

Conflict of interest: Dr. Bruel has an advisory relationship with Medtronic Inc. for their cancer pain, pain management, and restorative therapies committees. He is a paid consultant for Medtronic Inc. and Jazz Pharmaceuticals PLC. He has received in-kind contributions from Medtronic Neuromodulation. Drs. Karri, Kannan, Polson have no conflicts of interest to disclose.

Accepted: 2020-11-04, Published: 2021-05-31

pain syndrome (PTPS) – a challenging postoperative chronic pain syndrome itself (1,2).

Collectively, patients with MPM and subsequent PTPS suffer from a complex mixed nociceptive-neuropathic pain syndrome that is clinically challenging to treat (1-3). This challenge is secondary to not only the severity of this phenomenon, but also due to the unclear and likely multifactorial etiologies underlying this condition. Despite the causal mechanisms, studies have shown that most patients with either MPM or PTPS are not often effectively managed with standard analgesic approaches, and chronic opioid regimens remain controversial or suboptimal (1-3). Consequently, effective pain management in patients affected by both conditions concomitantly is even further challenging to attain.

There exists some evidence that suggests efficacy of radiotherapy for treating pain in patients with MPM (1,2). However, response rates in patients are variable, and radiotherapy has been found to impart side effects associated with the treatment itself. Previously, more aggressive interventions such as cordotomies were even considered to be choice treatments. Despite the continued emergence of neuromodulation interventions, including spinal cord stimulation (SCS), there exists a paucity of evidence for their use in chronic pain syndromes in patients with cancer (2,3). To our knowledge, evidence of successful interventions exists as case reports discussing the efficacious treatment of chronic pain in the setting of a malignancy and subsequent PTPS, but remains limited in the literature (4,5). Early exploration of SCS postulated a gate control theory-mediated reduction in nociceptive pain, but further studies have remained limited in demonstrating the efficacy of SCS in nociceptive pain states, even demonstrating that there is no effect on nociceptive pain (6,7). However, the literature is robust in demonstrating the role of SCS in neuropathic pain, mixed nociceptive-neuropathic pain states, and chronic pain (7-9). We present below a novel case of complex chronic pain in a person with extensive local MPM involvement and subsequent PTPS that is successfully treated with SCS. Of note, our local institutional review board policy does not require committee approval for fewer than 3 cases reported.

CASE

Patient History

We present the case of a 78-year-old man with a history of right-sided sarcomatoid MPM with extensive

local involvement of the parietal and visceral pleura, lung parenchyma, pericardium, and diaphragm. His initial surgical management approximately 5 years prior to presentation included a right-sided thoracotomy with rib resection, extrapleural pneumonectomy with omental flap to a bronchial stump, diaphragmatic and pericardial resection and reconstruction, and intraoperative chemotherapy. Subsequently, he underwent 2 cycles of premetrexed and cisplatin chemotherapy approximately 3 to 4 years prior. Following the extensive surgical and medical management, the patient was deemed cancer-free but was left functionally depleted secondary to chronic mixed nociceptive and neuropathic pain along his right thoracic and upper abdominal wall. Of note, the patient's chronic pain was thought to be oncogenic rather than postsurgical in origin given that it was present even prior to his debulking surgery.

Previous Pain Interventions

Prior to initial presentation to our clinic, the patient underwent multiple multilevel intercostal nerve blocks that only provided temporary analgesia ranging from 1 to 2 weeks. Unfortunately, he did not obtain effective analgesia with numerous pharmacological agents including scheduled gabapentin, duloxetine, and as needed tramadol. He was unable to tolerate opioid medications due to adverse effects. Our initial interventions were right-sided transforaminal epidural steroid injections to the T5-T7 vertebral levels. Following only temporary relief, we then performed right-sided radiofrequency ablations to the T5-T7 spinal nerves, which provided good relief for approximately 6 months. However, given the recurrence of pain, the patient wished to pursue other, more long-lasting modalities. Therefore, a plan was made to pursue a SCS trial.

SCS Trial

The patient was placed in a prone position and underwent general anesthesia. Standard sterile protocol was used to prepare the lumbar area. Using fluoroscopic guidance and loss-of-resistance technique, the T12/L1 interspace was identified and 2 paramedian 14-gauge Tuohy needles were advanced along anesthetized tracks toward the epidural space. The 2 SCS leads (Abbott, St. Paul, MN) were advanced superiorly via the Tuohy needles to the midline T1 level and the right paramedian T1.5 level. Following brief sedation interruption, intraoperative lead placement confirmed replacement of the pain with mild paresthesias. The Tuohy needles

were then withdrawn, the SCS leads anchored, and the incision sutured. At the 10-day postprocedural follow-up, the patient reported an 80% improvement in his pain (Visual Analog Scale score decreased from 10 to 2) and wished to pursue pulse generator implantation. His SCS trial leads were then removed in the interim.

Pulse Generator Implantation

Following the aforementioned preprocedural practice, SCS leads were once again placed at the midline T1 level and the right paramedian T1.5 level. Analgesic benefit was confirmed with the patient after a brief sedation interruption. Subsequently, a horizontal skin incision was made along the right paraspinal flank area and blunt dissection was used to create a pocket along the dorsal fascia. A tunneling device was then used to transport the 2 SCS leads subcutaneously from their paramedian anchor sites to the newly created dorsal pocket. Both incision sites were irrigated with a sulfamethoxazole-trimethoprim solution and then filled with 1 g of vancomycin powder split between sites. Final anteroposterior fluoroscopic imaging was collected and confirmed appropriate placement of the left midline T1 and right paramedian SCS leads between T1 and T2 (Fig. 1). The SCS pulse generator was then anchored to the underlying fascia and the incision was approximated with sutures.

Postprocedural Clinical Course

The patient was seen in the clinic 4 weeks after SCS pulse generator implantation and endorsed significant pain relief, once again reporting an approximately 80% improvement in pain from baseline (Visual Analog Scale decreased from 10 to 2). He was extremely happy with his results and reported marked functional improvement in his ability to move and change positions without inciting the previously demonstrated chronic pain. Of note, a plan was also made for the decreased use of his as-needed tramadol medications.

DISCUSSION

With ever-increasing precision therapies and evidence-based management for cancer, there exists a correlated increase in cancer survivorship. Concurrently, emerging sequelae of cancer disease, such as refractory complex chronic pain syndromes, are increasing in prevalence (3). Unfortunately, given the relative novelty of these conditions compounded by their complexity, managing such afflicted patients

can often be clinically challenging (1-4). The use of innovative pain interventions, such as SCS, for such chronic complex pain conditions has been relatively underreported (3-5).

In the aforementioned case, the patient's chronic complex pain is likely multifactorial secondary to the localized MPM involvement, treatment with platinum-based chemotherapy, and extensive surgical debridement leading to PTPS (1,2). Localized spread of intrathoracic cancers can cause infiltration into the thoracic wall. This degree of bony involvement, as with the ribs, can cause periosteal inflammation – a previously demonstrated etiology of severe cancer-mediated somatic nociceptive pain. Additionally, involvement of intercostal nerves serves to further propagate this pain (1,2). When managed with surgical debulking, the aforementioned localized inflammation is heightened along the periosteal-intercostal nerve interface and thus mediates PTPS when dysregulated for a prolonged period of time.

In our presented case, where a rib resection and extensive surgical debulking were performed, the severity of PTPS was likely exacerbated, especially in the setting of a malignancy infiltrating the thoracic wall. The complexity of this pain condition was evident by the patient's being refractory to multiple interventional pain procedures. However, the efficacy and promise of neuromodulation in

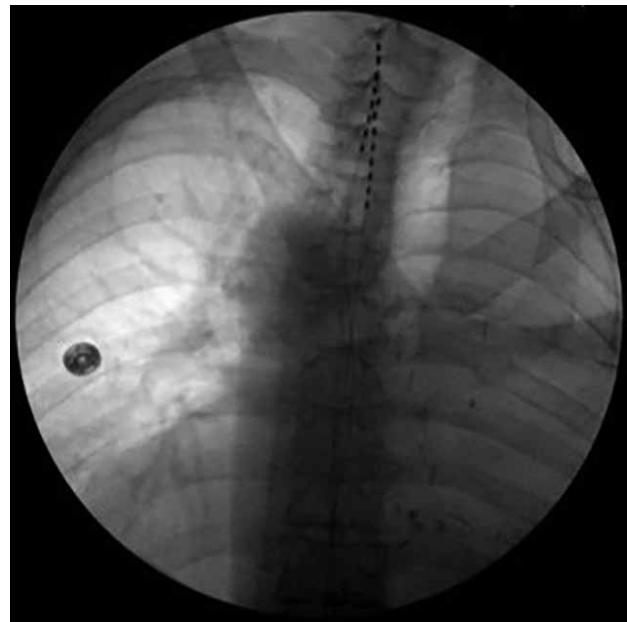


Fig. 1. Fluoroscopic image of reported patient's upper thoracic level spinal cord stimulator lead placement

such clinical contexts is demonstrated by the high degree of analgesic benefit obtained with SCS implantation despite the complexity and chronicity of the patient's pain syndrome. Overall, there was pain relief with both nociceptive and neuropathic pain components. One of the most marked aspects of the trial was a significant reduction in pharmacologic pain interventions, particularly in reference to tramadol. Subsequently, there was an overall decreased level of sedation. The overall pain relief led to increased mobility. Given the extensive involvement of the MPM across the thoracic wall and the anatomically-related thoracotomy for tumor resection,

ultimately with disease progression we were unable to distinguish pain generators as separate entities, which may be a focus of future studies.

Given the current lack of evidence for treatment options for patients refractory to standard pharmacological interventions, this case report was intended to add to the literature our clinical experience with successful neuromodulation in the cancer context. Future studies exploring pathophysiological mechanisms of complex chronic pain syndromes following cancer treatments and the role of neuromodulation in treating such affected patients are necessary.

REFERENCES

1. MacLeod N, Kelly C, Stobo J, et al. Pain in malignant pleural mesothelioma: A prospective characterization study. *Pain Med* 2016; 17:2119-2126.
2. Hochberg U, Elgueta MF, Perez J. Interventional analgesic management of lung cancer pain. *Front Oncol* 2017; 7:17.
3. Burton AW, Fanciullo GJ, Beasley RD, Fisch MJ. Chronic pain in the cancer survivor: A new frontier. *Pain Med* 2007; 8:189-198.
4. Graybill J, Conermann T, Kabazie AJ, Chandy S. Spinal cord stimulation for treatment of pain in a patient with post thoracotomy pain syndrome. *Pain Physician* 2011; 14:441-445.
5. Wininger KL, Bester ML, Deshpande KK. Spinal cord stimulation to treat postthoracotomy neuralgia: Non-small-cell lung cancer: A case report. *Pain Manag Nurs* 2012; 13:52-59.
6. Vannemreddy P, Slavin KV. Spinal cord stimulation: Current applications for treatment of chronic pain. *Anesth Essays Res* 2011; 5:20-27.
7. Chodakiewitz J, Chodakiewitz Y, Bicalho GC. Multi-target neurostimulation for adequate long-term relief of neuropathic and nociceptive chronic pain components. *Surg Neurol Int* 2013; 4:170. doi:10.4103/2152-7806.110676.
8. Dones I, Levi V. Spinal cord stimulation for neuropathic pain: Current trends and future applications. *Brain Sci* 2018; 8:138. doi:10.3390/brainsci8080138.
9. Maheshwari A, Pope JE, Deer TR, Falowski S. Advanced methods of spinal stimulation in the treatment of chronic pain: Pulse trains, waveforms, frequencies, targets, and feedback loops. *Expert Rev Med Devices* 2019; 16:95-106. doi:10.1080/17434440.2019.1567325.