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Spinal Cord Stimulator for Treating Chemotherapy-induced Peripheral Neuropathy

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Background: Chemotherapy-induced peripheral neuropathy (CIPN) is not only one of the most common adverse experiences of cancer survivors, but it is also one which has the greatest effect on quality of life. Ultimately, CIPN can lead to unwanted modification of treatment such as chemotherapy dose reductions or termination of treatment altogether.

Case Report: We present a case of a 47-year-old man with severe bilateral CIPN resistant to conservative management, who was successfully treated with spinal cord stimulation.

Conclusion: Spinal cord stimulation can be an effective treatment for CIPN resistant to conservative management.

Key words: Spinal cord stimulator, chemotherapy induced neuropathy, peripheral neuropathy

BACKGROUND

Chemotherapy-induced peripheral neuropathy (CIPN) is not only one of the most common adverse experiences of cancer survivors with rates ranging from 40%-70% (1), but it is also one which has the greatest effect on quality of life. It is associated with worsening depression, fatigue, insomnia, and other symptoms (2). Ultimately, CIPN can lead to unwanted modification of treatment such as chemotherapy dose reductions or termination of treatment altogether.

There is considerable variability in the severity of CIPN among patients (3). The severity depends on the regimen used and duration of therapy. The development of CIPN can cause severe pain and can be hard to treat with medications. In addition, it can affect the quality of life for cancer survivors and limit their activities (4-6). The most common presentation of CIPN is a pure sensory neuropathy that is symmetric in nature. Typical symptoms include numbness, loss of proprioception sense, tingling, pins and needles sensation, hyperalgesia or allodynia in the hands or feet in a stocking-glove distribution (7).

Treatment for CIPN is poorly understood at best. A recent systematic review of available CIPN treatments found "insufficient evidence to confirm the efficacy of central nervous system drugs" for CIPN (8). Despite this, opioids remain the front line therapy for CIPN as many patients require them to control their pain. The only nonopioid drug that has proven effective is duloxetine (9). Anticonvulsants such as carbamazepine (10) and pregabalin (11) have both been studied and results have failed to support their use in CIPN. Chemo-protectant agents have had similarly dismal results. Amifostine, an organic triphosphate, has produced conflicting results, but a systematic review of existing studies ultimately demonstrated that it was not effective in treating CIPN (12). Nimodipine, a calcium channel blocker, was studied via a randomized, double blind study and actually demonstrated such inferior outcomes related to neurotoxicity that the study was terminated (13). The narrative is the same for other known neuroprotectants such as: neurotropin and diethyldithiocarbamate (14, 15). Finally, although multiple "natural" approaches

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have been undertaken to try to treat or prevent CIPN, no statistically significant evidence has been generated to support or recommend the use of such therapies. As of now, there is also no known way to prevent CIPN.

Most treatment plans for refractory CIPN are multimodal in nature. Exercise should be encouraged since emerging studies have elucidated data which support the notion that exercise may actually protect against CIPN and that it may also help in the repair process once CIPN develops (16-18). In addition, pain modulation should be addressed through less commonly considered avenues such as acupuncture and spinal cord electrical stimulation, to name a couple.

In fact, some of the most encouraging outcomes related to CIPN treatment have emerged from these less popular avenues. Specifically, studies around the use of spinal cord stimulation . Spinal cord stimulation was first reported to provide meaningful relief for CIPN in 2004. Since then it has been found to be highly effective in multiple cases (19-21). Even more, all of these case reports demonstrate long-term pain reduction with an absence of major, intolerable side effects.

Here we present a case of CIPN resistant to conservative management that was treated by spinal cord stimulator implant with improvement in pain and function. Consent was obtained to discuss this anonymous case to help further CIPN treatment for the future.

CASE PRESENTATION

A 47-year-old man presented with severe bilateral CIPN in both hands. He had been treated with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) for 8 cycles for his diffuse B-cell lymphoma. He presented to the pain clinic 8 years later after failing conservative management. His management included hydrocodone/acetaminophen 10 mg/325 mg, 3 tabs daily; gabapentin 1200 mg 4 times daily; duloxetine 90 mg daily; cyclobenzaprine 10 mg daily; lidocaine patches; and weekly physical therapy. The pain made the patient unable to use his hands for activities of daily living. After exhausting all traditional treatment modalities, the patient opted to have a spinal cord stimulator trial. This trial was very successful in decreasing the patient's pain by approximately 80% and improved his ability to use his hands.

We then proceeded to place the permanent implant. First, an epidural needle was placed at the T1-T2 interspace on the right side and again at T4-T5 on the left. Next, we placed 2 linear 8-contact epidural electrodes to the C4-C5 area (Fig. 1). The intraoperative complex programming was PW 450 on both sides, rate 45 on both sides, Rt. Amp 2.8 v, It. Amp 3.2 v. Conventional stimulation was used.

The patient continued to do well after the implant with the same reduction in pain scores as the trial. He

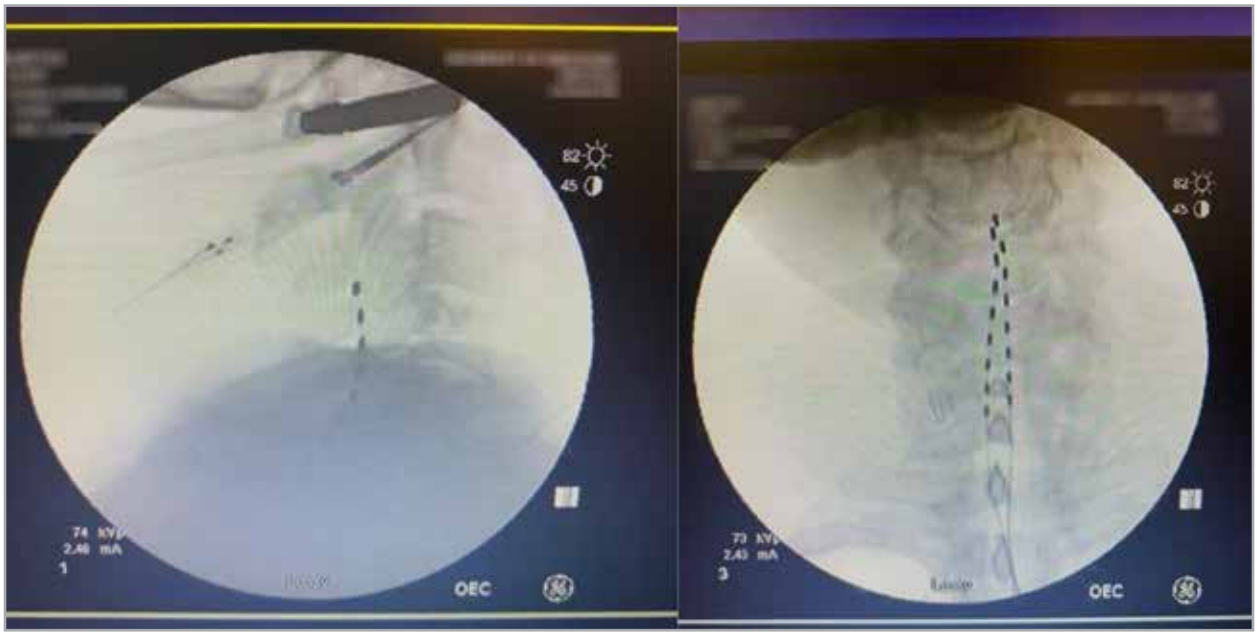

Fig. 1. Fluoroscopy after lead placement.

was able to use his hands and perform daily activities. He had a vast reduction in his medication dependence. His opioid usage was reduced by 66%, in addition to a 50% reduction in gabapentin dose. The patient still follows up in the pain clinic semiannually.

DISCUSSION

Some of the most common and effective chemotherapy agents available are also those most likely to cause CIPN. CIPN represents an important challenge due to the lack of effective treatment options paired with its often severe effects. Furthermore, there are no preventative treatments for CIPN (22).

With the development of newer and more targeted chemotherapy agents there was the hope that CIPN would be mitigated as a clinical problem. However, many of the older chemotherapy agents known to cause CIPN continue to be essential to cancer therapy. Furthermore, many novel agents also have CIPN as a dose-limiting side-effect, whether as a direct toxicity or secondary due to immune-mediated processes. With improved cancer treatments and longer survival, the late effects of CIPN continue to produce a significant burden of suffering for cancer survivors (3).

The use of spinal cord stimulators for cancer-treatment pain syndromes is a potentially effective modality that has not been heavily studied at this time. There has not been a single randomized, controlled trial assessing the efficacy of neuromodulation for cancer-treatment pain syndromes. Spinal cord stimulators are indicated for intractable neuropathic pain of the extremities and/or trunk and could be an important aspect to cancer-treatment-related pain syndromes with similar distributions. Other potential modalities may be paired, i.e., an intrathecal therapy may be used as an acute bridge to spinal cord stimulation for long-term neuropathic pain.

Efforts to find medications or therapies to prevent CIPN have not yielded any meaningful options. As research continues to address the issues surrounding CIPN, the burden felt by its victims has not been alleviated. It is well established that the pain associated with CIPN can be very resistant to conservative management and medications. What is known is that neuromodulation, such as spinal cord stimulation, can be an option for patients who have failed other modalities.

CONCLUSION

As discussed throughout this case report, CIPN is increasingly being recognized as one of the most common and most devastating adverse outcomes of chemotherapy treatment. Even worse, it has proven to be refractory to most of the preferred therapies associated with neuropathic pain. There are no proven preventative measures against CIPN, although exercise has shown some promise and should be encouraged.

In our experience with spinal cord stimulators in the non-cancer pain population in combination with the small amount of literature already published / our current case report, it seems highly likely that spinal cord stimulators can be an effective therapy for many of the challenging cancer-related neuropathic pain syndromes that are desperately undertreated and understudied.

This modality needs further research as it is currently limited by small numbers and the absence of randomized, controlled trials, but the existing evidence is promising.

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