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Effects of Novel Dual Peripheral Nerve Stimulator Therapy: A Case Report

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Background: Peripheral nerve stimulators (PNS) are currently used for refractory cases of neuralgia, and are associated with single manufacturer use. This is the first case report describing the novel scenario where a patient received 2 neuromodulation devices from 2 different manufacturers.

Case Report: We present a 32-year-old woman with spinal muscle atrophy type 2 who received a permanent PNS implant for chronic neuralgia. She experienced gradual treatment failure over 6 months, but continued to have pain relief with subsequent nerve blocks to the same nerves. She underwent semipermanent PNS placement to those same nerves. After the semipermanent PNS was removed, she experienced new, unexpected symptoms after trying to use her permanent PNS again.

Conclusion: Instances of multiple PNS treating the same area in patients is likely going to be a recurring scenario. More research will be needed to document the potential effects that dual neuromodulation therapy may have.

Key words: Case report, chronic pain, dual therapy, peripheral nerve stimulator

BACKGROUND

Peripheral nerve stimulators (PNS) have been trialed in clinical practice as far back as the 1970s (1). Despite case studies showing favorable responses, its invasiveness and high complication rates due to hardware failure severely limited its use. Technological advances in both real-time imaging and PNS devices have mitigated many of these problems, allowing for much more targeted and precise therapy. However, there remains limited evidence to recommend the routine use of PNS outside of treatment for refractory neuropathic pain (1).

Many case reports detail ultrasound-guided PNS implantation at a variety of locations. Studies have reported that up to two-thirds of patients with peripheral neuropathic pain have attained 50% pain relief for up to one year (1,2). Case reports discussing PNS implants focus on a single manufacturer. We describe the unique symptoms experienced by a patient who received a permanent PNS implant to the left lower extremity from one manufacturer, followed by a temporary PNS implant from a different manufacturer to the same extremity without removal of the former.

This manuscript adheres to the applicable EQUATOR guidelines.

The patient herself has provided verbal and written consent to publish this case report and written HIPAA authorization has been obtained.

CASE

A 32-year-old, wheelchair-using woman with a history of spinal muscle atrophy (SMA) presented to the clinic with worsening left lower leg pain for the past 5 years. She reported sharp and intermittent pain in her left sole that radiated to her left posteromedial calf and worsened when sitting down. She described numbness in her posteromedial thigh, calf, and foot; the numbness was worse on the plantar surface. Tramadol, baclofen, gabapentin, oral ketamine, and lidocaine patches did

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not provide her with adequate relief. As a result, the patient agreed to a diagnostic nerve block, with the eventual goal of pulsed radiofrequency ablation.

An ultrasound-guided left femoral nerve block in clinic with 0.25% ropivacaine, provided her with 100% relief for one day to the posteriormedial calf. A subsequent injection of 1% lidocaine, 0.25% ropivacaine, and 40 mg of methylprednisolone to the saphenous and posterior tibial nerves provided relief to the posteriormedial calf and sole for one week. Pulsed radiofrequency ablation did not have any benefit. Given her history of refractory neuralgia localized to the saphenous and posterior tibial nerve distributions, the patient was deemed appropriate for neuromodulation trial.

The patient received a StimWave (Curonix, Pompano Beach, FL) trial implant, and reported 100% pain relief in her left leg for her one-week trial. She elected to proceed with the permanent StimWave implants to her left saphenous and posterior tibial nerves and underwent uncomplicated StimWave PNS placement with ultrasound guidance, confirmed with fluoroscopy (Fig. 1). She returned one week later to the clinic, with almost complete resolution of her left leg pain.

Six months after her initial StimWave PNS placement, the patient noted that her pain had progressively worsened and her allodynia had also returned. She continued to receive some relief from her PNS on the highest setting, although it was noticeably less than before. She

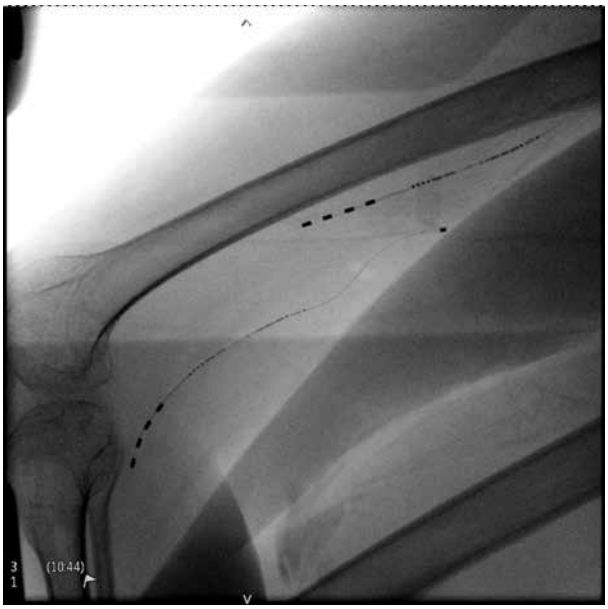

Fig. 1. Fluoroscopy after implantation of permanent StimWave PNS

resumed tramadol and lidocaine patches for additional pain relief. During this period, the patient also intermittently received ultrasound-guided, single-shot nerve blocks to the saphenous and posterior tibial nerves with 0.25% ropivacaine and 20 mg of methylprednisolone to control her pain along with her StimWave PNS.

During her follow-up clinic visits, the patient continued to express interest in neuromodulation therapy for her pain. Since the intermittent nerve blocks were successful in treating her pain, the decision was made to try an additional PNS system – the Sprint (Sprint, Cleveland, OH) semipermanent device. The device would be implanted to the same nerves treated by her StimWave PNS, with the hopes of enhancing her waning pain relief.

Prior to performing the procedure, it was noted that the StimWave and Sprint PNS devices may be close enough to interact with each other. There was a concern about the possibility of interference between the devices, and the potential repercussions that would have for the patient. Engineers from both StimWave and Sprint were consulted regarding proper placement. The Sprint chief engineer believed that there was a low risk of interaction between the devices, but expressed concern that the relative electromagnetic field of the StimWave 915 MHz transmitting coil could disrupt the normal operation of another PNS device if placed in close proximity. Thus, it should be physically separated from other PNS electronics.

At the start of the procedure, the patient's StimWave PNS was turned on to confirm proper functioning. The patient confirmed the sensation of her StimWave pattern, so she could make note of any change after the Sprint PNS was activated. The sciatic nerve lead for the Sprint PNS was then placed under ultrasound guidance, proximal to the StimWave PNS lead. Fluoroscopy was utilized to confirm that the Sprint PNS was not aimed at the coiled antennae of the StimWave PNS. Then, the intensity of the Sprint PNS was slowly increased until the patient could feel the paresthesia along the appropriate nerve distribution of her pain. The Sprint PNS was then turned off, and the StimWave PNS was turned back on. The intensity of the Sprint PNS was slowly increased again to ensure that there were no compounded stimulation or adverse effects experienced by the patient. She denied burning, pain, or discomfort with both devices at levels conducive to therapy. The Sprint lead was then deployed, secured, and implanted. Next, the saphenous nerve lead for the Sprint PNS was also placed

under ultrasound guidance distal to the StimWave PNS lead. Fluoroscopy confirmed that the Sprint PNS was not aimed at the coiled antenna of the StimWave PNS. The process was repeated to confirm that the patient experienced no burning, pain, or discomfort with both devices at levels conducive to therapy. The Sprint lead was then deployed and implanted successfully. The saphenous and posterior tibial StimWave PNS leads were reassessed after the procedure. It was noted that they were both intact and had not migrated since initial placement (Fig. 2).

At her one-week follow-up, the patient reported 100% pain relief with simultaneous use of the Sprint and StimWave PNS systems. At her one-month postoperative visit, her pain relief waned to 50% with use of both PNS systems.

About 2 months after her Sprint PNS implantation, she had turned off her StimWave PNS and was maintaining around 40% pain relief from the Sprint PNS alone. She noted that while her pain had improved, it had also spread proximally up her leg, further away from her PNS implants. During that visit, her Sprint PNS was removed in clinic without complication.

At her 4-month follow-up, the patient reported that her pain had gradually returned to its baseline, prior to the implantation of either device. She noted that for a few weeks after her Sprint removal, she maintained pain relief at around 40% to 50%. However, along with her recurrent pain, the patient reported a concerning new development – when she activated her StimWave device, instead of pain relief, it now increased her pain significantly. She described sharp, constant, and burning pain in her left heel and medial ankle, extending to the posterior aspect of her mid-calf. Three months later, she continues to report the same symptom, including the aggravation of pain with use of her StimWave PNS.

At her most recent follow-up visit, around 6 months after the removal of her Sprint PNS, the patient reported randomly turning on her StimWave, and no longer experiencing the previous pain exacerbation. She continued to receive minimal pain relief from the implant.

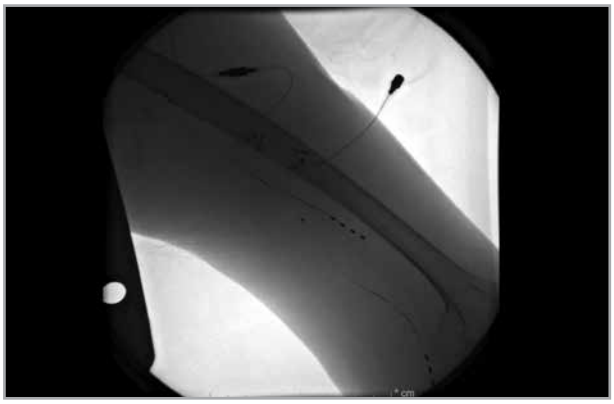

Fig. 2. Fluoroscopy after implantation of Sprint semipermanent PNS in relation to StimWave PNS
Abbreviation: PNS, peripheral nerve stimulator

DISCUSSION

Since the inception of nerve stimulation, Melzack and Wall's (3) gate control theory has been the most widely accepted explanation behind how electrical stimulation inhibits nociceptive transmission. More recent studies implicate both the peripheral and central nervous systems in contributing to the analgesic properties of PNS (4). The need for a permanent PNS to remain precisely adjacent to its target seems to favor the hypothesis that PNS disrupts nociceptive conduction. One study found that PNS may affect both biochemistry and electrophysiology of the surrounding environment. A recent review of neuromodulation documented downregulation of neurotransmitters, endorphins, and inflammatory mediators, as well as a reduction of ectopic discharges in nerves being treated with PNS (5).

The advent of newer models of temporary PNS, like the Sprint PNS, seems to suggest a more centrally acting mechanism for analgesia. Pain relief can persist up to weeks after PNS removal, as it did for our patient. One study hypothesizes that PNS may modulate the central nervous system by attenuating hyperalgesia in the brain, and improving endogenous pain inhibition in the spinal cord (6). It is unclear exactly how the central and peripheral nervous systems are affected by PNS, but studies examining laser cortical evoked potentials suggest that they work in tandem, with a potential predilection for the peripheral nervous system (6).

Although our patient's initial StimWave PNS was effective, its efficacy waned over time. PNS treatment failure is not uncommon, and is most often caused by lead migration. PNS systems placed in the upper and lower extremities are at higher risk for electrode displacement given their proximity to nearby tendons, nerves, and vascular bundles (7). However, our patient's history of SMA precludes extensive use of her extremities, reducing the risk of lead migration. Fluoroscopic results also confirmed proper placement without migration. Chronic inflammation and fibrous tissue growth can increase impedance, especially in implants

older than 6 months (8), which may explain her initial StimWave PNS treatment failure. Another possibility is that our patient had developed electrical tachyphylaxis and physical tolerance, which can be seen with central neuromodulation (9). However, this phenomenon is not well studied in peripheral neuromodulation, and seems less likely given our patient's recent renewed pain relief with her StimWave implant.

We had initially suggested dual PNS therapy in the hope that they may work synergistically to provide further pain relief for our patient. However, it seems that dual PNS can have unexpected and potentially dangerous interactions. The reason for our patient's pain currently being exacerbated with use of her StimWave PNS after Sprint PNS removal remains unclear. Worsening or aggravated pain is a cited risk of peripheral nerve stimulation, with some sources quoting complication rates of up to 20% (10). However, there are no documented cases that explore the potential causes or mechanism for this phenomenon. One article proposed another cause being stimulation of intended, and unintended, neurons (11). We considered the possibility that the Sprint lead may have migrated too close to the StimWave lead's transmitting coil, as the Sprint engineer had warned prior to the placement. However, that fails to explain why the patient continued to have pain even after her Sprint PNS leads were removed.

More research is needed regarding the exact mechanism behind why and how different PNS systems interact with each other. As the neuromodulation market expands, and an increasing number of patients seek further relief for their pain, there will invariably be more cases of patients trialing new systems with their legacy systems still intact. In the case of our patient, we were hopeful that combination therapy of both the StimWave and Sprint PNS systems would be synergistic, which was not the case. Whether that proves to be the exception or the rule regarding combination neuromodulation remains to be seen.

CONCLUSION

This is the first reported case of a patient who received both a permanent StimWave and temporary Sprint PNS with new, aggravated symptoms of pain when resuming use of her StimWave PNS. The advent of successful PNS case reports and trials has sparked a renaissance in neuromodulation therapy, with many companies scrambling to develop the gold standard treatment for refractory chronic pain. Instances of multiple devices treating the same area in patients is likely going to be a recurring scenario moving forward. More research is needed to identify the potential benefits and adverse effects that dual neuromodulation therapy may have, and guide physicians in counseling patients with refractory pain.

Contributions

All authors helped compile and draft the manuscript

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