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Peripheral Nerve Stimulation for Arm Pain in an Adolescent Girl with Ewing Sarcoma as Bridge Therapy to Chemotherapy: A Case Report

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Background: Cancer commonly presents discomfort from abnormal cell growth in healthy tissue and is often inadequately managed. Peripheral nerve stimulation (PNS), mainly for non-cancer chronic pain, has emerged as a minimally invasive option for neuropathic cancer-related pain when conventional methods fail. Limited research, primarily in adults, has focused on PNS in the non-oncological population.

Case Report: A 14-year-old adolescent girl with a history of obesity, diabetes, and Ewing sarcoma in her left proximal humerus experienced severe pain, initially rated at 10/10. After undergoing ultrasound-guided left suprascapular PNS as a 60-day bridge therapy to chemotherapy, her pain improved to 3/10 at lead removal and remained at 4/10 at 3 months postremoval.

Conclusion: PNS is a promising and less invasive neuromodulation approach for managing tumor-related bone pain. Our case study illustrates the effectiveness of PNS placement for significant pain reduction, although limitations, such as delayed response and the need for further randomized-controlled studies, are acknowledged.

Key words: Neuromodulation, peripheral nerve stimulation, Ewing sarcoma, arm pain, bone pain, chemotherapy, teen, adolescent

BACKGROUND

The most common and dreaded symptom linked to cancer is pain that arises from the abnormal proliferation of malignant cells in otherwise healthy tissue, whether directly or indirectly (1). It has been shown with significant evidence that cancer pain is frequently undertreated in a wide range of clinical settings and care models (2).

Options like opioids, intrathecal pumps, steroid injections, radiofrequency ablation, and chemical neurolysis of sympathetic nerves, along with accompanying visceral afferent fibers have emerged as appealing for managing pain in these individuals; however, these all come with their own indications, side effects, and risks (3).

Opioids in 10%–15% of cases fail to achieve an acceptable level of pain relief, and that is if patients can succumb to their fears as a large number of patients are afraid of taking opioids due to worries of addiction, side effects, and developing tolerance to them (3,4).

Corticosteroids are utilized to relieve pain associated with space-occupying lesions and are commonly employed in cases where there is a possibility of inflam-

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mation and edema occurring in confined areas, including intracerebral, pelvic, retroperitoneal, and spinal malignancies. They frequently serve as a temporary measure while awaiting more definitive treatments such as radiotherapy; however, steroid injections may have contraindications, including conditions like uncontrolled diabetes mellitus or ongoing immunotherapy (3,5).

Neuromodulation techniques are more commonly used in non-cancer, chronic, neuropathic pain syndromes, such as complex regional pain syndrome or posttraumatic neuralgia. Peripheral nerve stimulation, specifically, has been proposed as a cost-effective, low-risk, and minimally invasive option for those who do not respond well to conservative first-line management. Consequently, it has become an emerging therapy that is found to an be effective technique for neuropathic cancer pain management (4). Preliminary evidence suggests that percutaneous peripheral nerve stimulation (PNS) can temporarily offer pain relief for patients experiencing acute postoperative or posttraumatic pain, neuropathic pain, phantom limb pain, and low back pain. A case series performed by Mach et al (6) examined PNS as a bridge therapy to radiation treatment in patients with multiple myeloma with osteolytic bone lesions resulting in 70-80% complaining of bone pain and decreased quality of life. Following PNS therapy, their low back pain secondary to myeloma-related spinal lesions was effectively treated (7).

Yet, there are limited studies evaluating using PNS in patients with cancer other than the Mach, et al, an additional retrospective review performed by Sudek et al (8), and now our case report demonstrating its use in this population. Furthermore, using PNS f for treating pain in children has not been well-studied; to our knowledge, our case study is the first.

Herein we report the case of an adolescent girl with intractable left proximal humeral pain secondary to Ewing sarcoma. Her options for various pain management regimes were limited due to her comorbidities. Implanting percutaneous electrodes for 60 days decreased her pain significantly, thereby allowing her to complete adjuvant chemotherapy following the electrodes' removal.

CASE PRESENTATION

A 14-year-old girl with a history of obesity (body mass index [BMI, kg/m^2] of 34), diabetes (hemoglobin A1C 6.5), and newly diagnosed Ewing sarcoma of the left proximal humerus as seen on x-ray (Fig. 1) presented with severe, excruciating pain. On the numeric rating scale, she initially reported a 10/10 in her left arm. Physical exam was notable for pain to palpation of the left humeral head accompanied by swelling and pain with active range of motion in all directions. For pain relief, she tried tramadol 50 mg 3 times a day as needed, and hydrocodone/acetaminophen 5mg/325mg by mouth 3 times a day as needed without any alleviation. Furthermore, due to her history of diabetes mellitus, she was unable to undergo steroid injections.

She underwent an ultrasound-guided left suprascapular PNS placement of the left suprascapular nerve as a 60-day bridge therapy to chemotherapy (Fig. 2). At one-week postprocedure her pain reportedly had improved to 8/10, and she was able to complete chemotherapy. She completed the full 60 days with good tolerance; the leads were removed without any reported adverse events. Her reported pain level at the initial removal was a 3/10. At her follow-up appointment 3 months post-lead removal, her pain was a 4/10.

DISCUSSION

Ewing sarcoma is a rare osseous, and more rarely soft tissue, cancer that can afflict children and adolescents, with approximately 80% being less than 20 years old. It commonly has a predilection for the trunk and long bones with the most common site being the femur followed by the humerus, tibia, and the forearm bones, often arising in the diaphysis rather than the metaphysis. The earliest symptom is pain, first being intermittent and mild, but rapidly progressing to a severe degree. The tumor itself can grow rapidly, extending past cancellous bone outside the cortex, further causing pain and swelling around the tumor (9).

PNS presents a promising neuromodulation approach that provides continuous electrical stimulation directly to the location of the most intense pain through electrodes inserted subcutaneously or percutaneously (10). It can be performed under local anesthetic without sedation and is an attractive choice for patients with cancer who have numerous medical conditions that make them suboptimal candidates for monitored anesthesia care or general anesthesia. While permanent neuromodulation devices like spinal cord stimulators have been employed in treating patients with cancer, PNS offers a less invasive and temporary alternative (11,12).

PNS's mechanism of action is founded on the theoretical framework known as the gate control theory, initially introduced by Melzack and Wall in 1965 (12) where

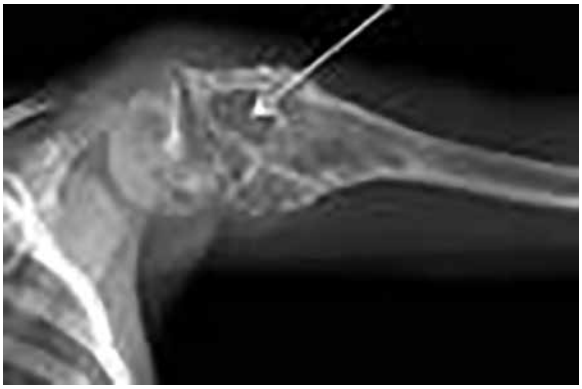

Fig. 1. X-ray showing the Ewing sarcoma of the left proximal humerus.

stimulation of inhibitory dorsal horn interneurons is initiated by the activation of Aβ fibers, which are characterized by their large diameter and low thresholds. These interneurons are involved in the processing and transmission of nociceptive information from Aδ and C nerve fibers, resulting in the ultimate inhibition of pain signals from the spinal cord to higher centers in the central nervous system (12).

It is not clear what is the exact mechanism of action behind PNS, but there are several proposed theories. According to Strand, et al (13), within the central nervous system, PNS has the potential to engage and regulate higher centers, including the dorsal lateral prefrontal cortex, somatosensory cortex, anterior cingulate cortex, and parahippocampal areas. Moreover, its neuromodulatory effects may also reach the spinal cord. Additionally, PNS can induce changes in endogenous neurotransmitter levels and affect the plasticity of N-methyl-D-aspartate pathways (13). Electrophysiological investigations have shown a decrease in abnormal discharges when PNS is employed (11). Swett, et al (14) looked to determine which central nervous system mechanism versus a conduction block in small peripheral diameter afferent fibers was responsible for producing pain relief in patients suffering from intractable pain of peripheral origin. In both human and animal studies, their findings revealed that the analgesic effects of PNS were evident at stimulus intensities above the perception threshold but below the pain threshold, thereby challenging the theory of PNS primarily interrupting nociceptive afferent nerve conduction to achieve its effects (14). Furthermore, research has demonstrated that PNS disrupts the transmission of nociceptive afferent fibers at a peripheral level, as illustrated by a

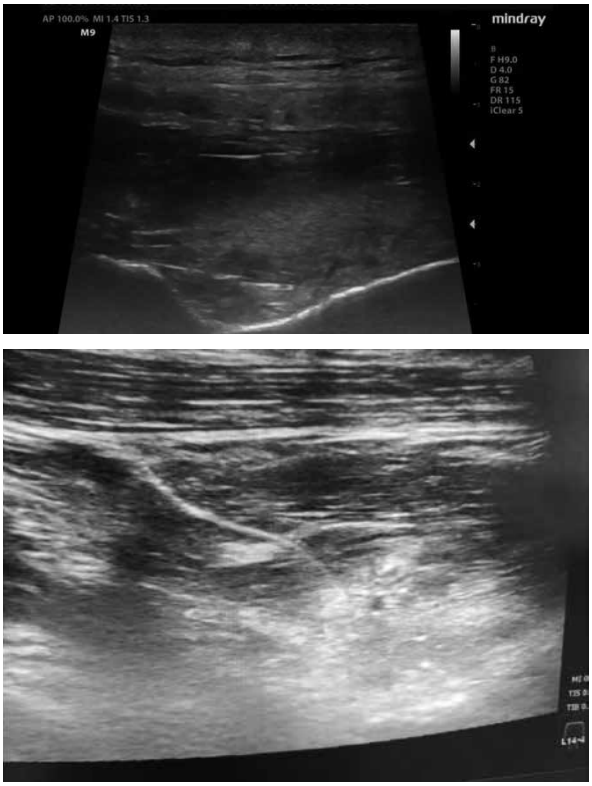

Fig. 2. Images of US guided suprascapular nerve PNS placement.

human study conducted by Torebjork and Hallin (15), where repetitive electrical stimulation of intact radial and saphenous nerves failed to excite A and C fibers.

Our patient underwent provisional (60-day), percutaneous PNS placement for managing pain. PNS's effectiveness can likely be explained by the retrospective review performed by Sudek, et al (7) whose findings suggest that PNS shows dual efficacy in addressing chronic degenerative joint disease among patients experiencing shoulder, knee, and lower back pain, regardless of any underlying cancer diagnosis, which can be observed in individuals with or without cancer-related conditions. The patient in our study was suffering from tumor-related bone pain. In their study (7), patients with tumor-related cancer pain reported the most significant reduction in pain scores. The patient who experienced the greatest degree of analgesia was treated for cancer-induced bone pain in concordance with previous literature on the successful use of PNS for chronic degenerative and traumatic shoulder pain (16,17). In the retrospective analysis (18), this was referring to a myelomatous lesion of the shoulder causing a

pathologic fracture of the humeral head, which shares many similarities to our patient with Ewing sarcoma of her left proximal humerus.

Mainkar, et al (18) conducted a case series in adults where PNS was applied to address cancer-related pain. They reported notable effectiveness when tumors had infiltrated or encircled peripheral nerves (18). Additional case reports examining adults have showcased PNS's application in managing neuropathic pain in the shoulder and upper extremities caused by metastatic lung cancer invading the brachial plexus (19,20). Sudek, et al's (7) findings further reinforce the utility of PNS in managing pain related to oncologic tumors.

CONCLUSION

Of note, our patient's pain at the one-week post-lead removal was 7/10. At 60 days and 90 days post-lead removal her pain was 4/10. Previous literature has indicated that, initially, some patients may not respond to PNS by the end of the 60 days; therefore, education is crucial for these patients regarding this delayed effect. Additionally, it can also be expected for patients to experience ongoing pain relief after the PNS device removal (7). Both of these were observed in our patient.

Although PNS is traditionally performed under ultrasound, a limitation in our study could be the inaccurate placement of leads for muscle group stimulation, as PNS placement under fluoroscopy has been shown to yield more precise lead placement (18). Especially in patients with distorted anatomy, fluoroscopy may be more beneficial to optimize lead positioning. Additionally, given that our study is a case report, it would be beneficial for more randomized controlled studies to be performed to examine the effectiveness of PNS in cancer-related bone pain, assessing the duration of pain relief in this population. In summary, percutaneous PNS stands out as a safe, long-lasting, and effective method for managing pain within this demographic. This report is, to our knowledge, the first documenting percutaneous PNS as an alternate therapeutic approach for an adolescent patient grappling with cancer-related bone pain refractory to conventional pharmacological treatments. The procedure demonstrates reliability and efficiency, yet further multicenter prospective studies are essential to validate these observations. Future research should aim to enhance patient selection criteria and delineate precise applications of PNS within the oncological domain.

Our patient reported good pain relief following percutaneous PNS. Before the intervention, her pain was intolerable; she could not undergo further oncological treatment for her cancer. Following PNS, her pain continued to be manageable as it was significantly reduced and continued to improve after starting chemotherapy treatments.

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