



Pulsed Radiofrequency Therapy for Relieving Neuropathic Bone Pain in Cancer Patients

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Metastatic bone pain is among the most commonly reported pain conditions in cancer patients and pharmacological therapy frequently fails to provide satisfactory pain relief. Pulsed radiofrequency (PRF) is a minimally invasive procedure and may be an effective alternative. However, there is little published data evaluating PRF treatment of metastatic pain. PRF therapy of select lumbar dorsal root ganglia was performed on two patients suffering from uncontrolled metastatic lumbar bone pain. After PRF therapy, the patients reported markedly improved back pain, and the effect lasted for months until they deceased. No complications or adverse events were noted from this minimally invasive procedure. PRF may be considered a potential intervention in treating certain neuropathic cancer pain conditions.

Key words: Pulsed radiofrequency, neuropathic bone pain

INTRODUCTION

Despite the lack of well-designed trials supporting its use, there is published evidence indicating that pulsed radiofrequency (PRF) may effectively manage certain chronic neuropathic pain conditions when other treatments have failed. PRF has been repeatedly demonstrated to be a safe procedure with minimal side effects when performed by a well-trained and experienced practitioner.¹ Potential reported benefits include reduced post-amputation stump pain,² chronic radicular pain,³⁻⁵ certain neuropathic pain conditions,⁶⁻⁸ and shoulder arthropathic pain.⁹

The first step in managing metastatic bone pain is conservative treatment with high doses of opioid analgesics and other medications, such as biphosphates (alendronic acid). Besides, radiotherapy can serve as an adjunct to pharmacologic analgesia for relieving metastatic bone pain.^{10,11} The pump implantation is primarily considered an interventional

treatment. However, there are few published studies evaluating metastatic pain treatment with PRF.¹² Particularly, seldom reports of PRF for metastatic spinal bone pain which is one of the most common causes of pain in cancer patients, and pharmacological therapy frequently failed to provide satisfactory pain relief in these patients. We presented two cases of patients suffering from intractable resting neuropathic bone pain that failed to respond to multiple medications, chemotherapy, and radiotherapy, but satisfactorily responded to PRF therapy targeting the lumbar dorsal root ganglion (DRG).

CASE REPORTS

Case 1

A 47-year-old woman, was diagnosed with cervical squamous cell carcinoma, liver metastasis, and hydronephrosis following concurrent chemo-radiation therapy, which failed to halt disease progression. She began experiencing low back pain with progressive numbness and soreness over the left lower limbs for 6 months. Subsequently, heterogeneous retroperitoneal masses destroying the L2-3 vertebrae were found. The patient described the pain as a sharp, shooting, and burning sensation. She also experienced several neuropathic pain symptoms including allodynia, numbness, and hyperalgesia, as well as lower limb swelling. Palliative radiotherapy and multimodal analgesia did not relieve her lumbar vertebral pain (visual

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analogue scale [VAS]: 9/10). Her analgesia regimen comprised a fentanyl transdermal patch 75 mcg/h q3d and numerous oral medications: Tramadol 37.5 mg, acetaminophen 325 mg q6h, gabapentin 300 mg tid, oxcarbazepine 300 mg bid, and clonazepam 2 mg qn. In addition, she received intravenous tramadol 100 mg or nalbuphine 10 mg q4-6h as needed for breakthrough pain. We performed fluoroscopy-guided PRF using a NeuroTherm NT1000 (NeuroTherm, Inc., Middleton, MA, USA) radiofrequency generator [Figure 1].^{13,14} In the surgical suite, the patient was placed in a prone position, and the lumbar region was wiped with betadine and aseptically draped with sterile towels. The skin was anesthetized with 2% lidocaine administered subcutaneously. A 22-gauge, 10 cm radiofrequency cannula with a 5 mm active tip was inserted percutaneously at the lumbar spine. The introducer needle was withdrawn, and the RF electrode was advanced. Selective sensory nerve stimulation (50 Hz) showed concordant pain <0.5 V, which confirmed the PRF electrode location. Motor nerve stimulation was tested at 2 Hz to exclude an uncorrelated nerve. After stimulation and fluoroscopic confirmation, PRF was administered at 60 V and 42°C for 6 min at each site. After receiving the left percutaneous PRF DRG at L2, her severe back pain markedly improved (VAS: 2/10), and the effect lasted for approximately 4 months until she deceased. Her only remaining chronic analgesics were fentanyl transdermal patch 25 mcg/h, oral gabapentin 300 mg nightly and rarely, additional medications for breakthrough pain following the procedure. Oswestry low back pain and disability questionnaire scores also improved from 56 points to 40 points after treatment.

Case 2

A 49-year-old man, suffered from middle and lower back pain for 7 months. Pancreatic cancer with multiple bony metastasis from the L1 to L4 vertebrae, liver metastases, peritoneal carcinomatosis, and severe ascites were diagnosed after numerous examinations. He similarly described his pain as a sharp, shooting, and burning sensation. Neuropathic pain symptoms including allodynia, numbness, and lower extremity hyperalgesia were also noted. Because of the abdominal and back pain severity, a percutaneous L1 and L2 vertebroplasty was performed using bone cement, and the patient was administered radiotherapy. His analgesic regimen comprised fentanyl transdermal patch 50 mcg/h q3d; several oral medications, including tramadol 100 mg q6h, gabapentin 600 mg tid, clodronate disodium 400 mg bid, and imipramine 25 mg qn; and intravenous morphine 5 mg q4h as needed for breakthrough pain, with no relief. A left percutaneous PRF at the L1-L4 DRG was performed, as discussed previously in case 1 [Figures 2-4]. Immediately, his severe back pain became manageable, until he deceased 1 month later. His

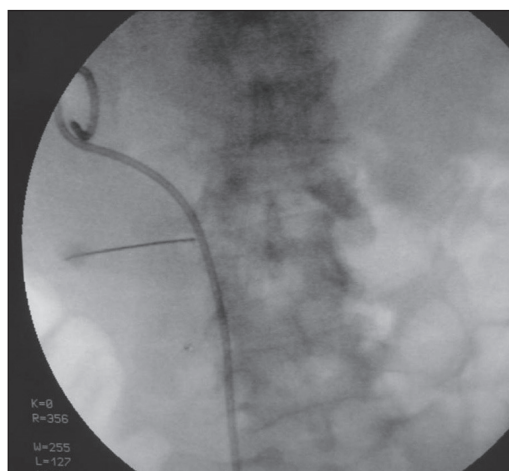


Figure 1. Pulsed radiofrequency therapy of the left L2 dorsal root ganglion



Figure 2. Percutaneous vertebroplasty performed on a patient. The patient is placed in the prone position, and percutaneous vertebroplasty is performed at the L1 and L2 vertebrae (black arrows)



Figure 3. Pulsed radiofrequency therapy of lumbar dorsal root ganglion denervation performed on patient

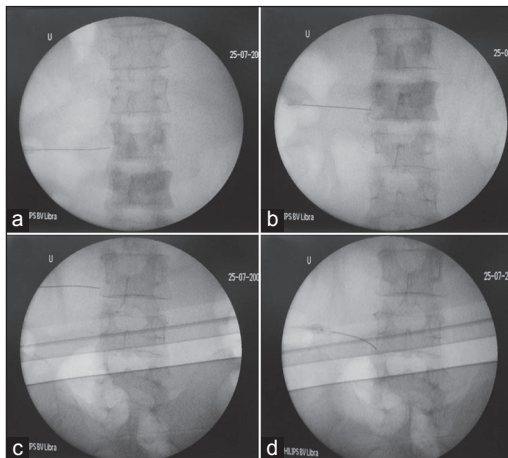


Figure 4. Fluoroscopy-guided pulsed radiofrequency therapy of lumbar dorsal root ganglion denervation at L1-L4. Electromagnetic field targeting L1 (a), L2 (b), L3 (c), and L4 (d) vertebrae

chronic pain medications were reduced, and included only fentanyl transdermal patch 25 mcg/h and oral gabapentin 300 mg tid; he seldom requested additional medication to relieve breakthrough pain after receiving PRF therapy. His Oswestry Low Back Pain and disability questionnaire scores also improved from 57 to 41 points after PRF treatment.

DISCUSSION

In malignant cancers that invade the skeleton, metastatic bone destruction leads to increased morbidity and impaired quality-of-life resulting from pain, fractures, and other skeletal related events.¹⁵ Not all patients with bone metastases exhibit these symptoms, but as many as two-thirds of affected patients experience severe pain, particularly patients in advanced disease stages.¹⁶ Pain caused by bone metastases can originate directly from bone, caused by direct invasion, microfractures, increased pressure on the endosteum, and periosteum distortion, or may also arise from nerve root compression or muscle spasm at the lesion. Bone pain is frequently caused by the release of chemical mediators that facilitate nociceptive conduction to the central nervous system. Metastatic bone pain is traditionally considered somatic, but recent experimental models describe a neuropathic component and even a unique mechanism, which may contribute to metastatic bone pain.^{17,18}

The conventional therapy for metastatic bone pain comprises multidisciplinary therapies such as radiotherapy applied to the painful area (or bones at high fracture risk), systemic treatment (hormone therapy or chemotherapy), and supportive care (analgesic therapy and bisphosphonates).¹⁹ Approximately 20-30% of patients treated with radiotherapy and analgesics may not achieve optimal pain relief. In these

patients, minimally invasive or noninvasive techniques may play an important role under certain circumstances.¹⁷ These techniques include vertebroplasty, balloon kyphoplasty, radiofrequency ablation, intrathecal pump implantation, and others. PRF has successfully treated a myriad of pain conditions, including cervical radicular pain, facial pain, trigeminal neuralgia, sacroiliac joint pain, facet arthropathy, shoulder pain, postsurgical pain, radicular pain, groin pain, and myofascial pain conditions.²⁰ Simopoulos *et al.* evaluated patients diagnosed with chronic lumbar radicular pain, and 2 months after receiving radiofrequency treatment, 70% of patients treated with PRF and 82% treated with pulsed and continuous radiofrequency (CRF) reported reduced pain intensity. The analgesic response averaged 3.18 months (± 2.81) in patients receiving PRF and 4.39 months (± 3.50) in patients receiving pulsed and CRF.⁴ However, there are no known studies evaluating the utility of PRF for treating neuropathic bone pain.¹² Reports investigating PRF treatment of metastatic spinal bone pain are particularly uncommon, despite this complication being one of the most commonly reported in patients diagnosed with cancer. In the two present cases, the pain relief was distinct and persisted approximately 1-4 months until the patients deceased.

In a study by Callstrom *et al.*, percutaneous computed tomography- and ultrasound-guided radiofrequency ablation reduced pain, improved quality-of-life, and reduced analgesic use in patients with skeletal metastases in numerous locations, including the tibia, talus, pubic symphysis, vertebral body, rib, ilium, and sacrum.²¹ In our cases, we focused on vertebral pain. Compared to ablation, PRF provides nerve-sparing therapy and is increasingly employed to treat chronic pain conditions using selective neuromodulation.¹ In contrast, CRF is particularly useful in creating neurodestructive lesions, such as facet joint denervation and trigeminal nerve ablation. However, its nonspecific effect limits CRF use when the motor nerves or spinal roots are involved; the potential neural damage risks deafferentation syndrome and other neurological sequelae. Neurodestructive procedures intended to relieve pain may actually increase pain; the complexity and plasticity of pain signaling pathways can cause significant neuroplastic changes following therapy.¹ Compared to CRF, PRF benefits from the absence of any mitochondrial degeneration or structural pathology in the cell or nuclear membranes, as observed in rat studies,²² and provides the option to repeat the procedure. Zeldin *et al.* reported the successful treatment of 3 patients suffering from uncontrolled vertebral and paravertebral metastatic pain using fluoroscopy-guided selective root ganglion

PRF.¹² In our cases, multiple medications, percutaneous vertebroplasty, and radiotherapy were performed, but were unsatisfactory. After PRF, a minimally invasive procedure, the patients reported satisfactory pain relief and improved daily life quality during the residual periods. Because of its safety and effectiveness, PRF may be an alternative strategy in treating neuropathic cancer pain.

DISCLOSURE

All authors declare no competing financial interests.

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