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# Successful Treatment of an Intractable Postherpetic Neuralgia (PHN) Using Peripheral Nerve Field Stimulation (PNFS)

Surjya Prasad Upadhyay, MD, Shiv Pratap Rana, MD,  
Seema Mishra, MD, and Sushma Bhatnagar, MD

Postherpetic neuralgia (PHN) is a chronic neuropathic pain syndrome that arises as a sequel of herpes zoster eruption. The treatment of postherpetic neuralgia is medically challenging and often frustrating in some situation as the exact mechanism of neuralgia is poorly understood and multiple and complex pathophysiology is postulated requiring poly pharmacy, which itself leads to many side effects. Here, we present a successful management of supra-orbital PHN using peripheral nerve field stimulation (PNFS), which was refractory to the

commonly used pharmacological treatment. After successful trial stimulation, permanent stimulator was placed successfully, patient medication were tapered off within 2 weeks. At present, patient is in 8-week poststimulation with excellent pain relief, without any side effect.

**Keywords:** postherpetic neuralgia (PHN); neuropathic pain syndrome; supra-orbital neuralgia; immunocompromised; polypharmacy; peripheral nerve field stimulation (PNFS)

## Introduction

Postherpetic neuralgia (PHN) is a sequel of herpes zoster infection that often leads to intractable chronic neuropathic pain. Postherpetic neuralgia has been defined in different ways, recent data support the distinction between acute herpetic neuralgia (within 30 days of rash onset), subacute herpetic neuralgia (30-120 days after rash onset), and postherpetic neuralgia (defined as pain lasting at least 120 days from rash onset).<sup>1,2</sup> Etiology of pain is well known; the recrudescence of dormant varicella-zoster virus initiates an inflammation of sensory ganglia and peripheral nerves, inducing abnormal nociceptors sensitization and central

hyperexcitability.<sup>3</sup> Pain of PHN may persist for months to years or even lifelong after healing of the herpetic eruptions.<sup>1,4</sup> Management of PHN is medically challenging as the pathophysiological mechanism involved in pain are multiple and complex needing polypharmacy. Pharmacological treatment of PHN often has limited success.<sup>5</sup> The main reason behind the failure of pharmacological treatment are potential ineffectiveness and risks of pharmacotherapy<sup>6</sup>; second, most of the drugs used to treat PHN act in the central nervous system (CNS), leading to intolerable side effects like dizziness, lethargy, nausea, and vomiting, which limit the doses' increment to achieve the therapeutic concentrations in the target organs<sup>7</sup> and third, the comorbidity in the elderly persons, especially of the cardiovascular system and CNS making them prone for troublesome adverse events or side effects.<sup>8</sup> To avoid these disadvantages, various nondrug therapies were tried and are evolving to treat chronic neuralgia including transcutaneous electrical nerve stimulation (TENS),<sup>9</sup> acupuncture,<sup>10</sup> spinal cord stimulation,<sup>11</sup> and peripheral nerve fields stimulation (PNFS).<sup>12</sup>

From the Departments of Anaesthesiology and Pain and Palliative Care, Dr. BRA Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi, India.

Address correspondence to: Sushma Bhatnagar, Departments of Anaesthesiology, and Pain and Palliative Care, Room No-242, 2nd Floor, Dr. BRA Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi, India; phone: (981) 132-6453; e-mail: shumob@yahoo.com.

Peripheral nerve fields stimulation is emerging as one of the successful treatment method for varieties of chronic neuropathic pain. No systemic effects or side effects with PNFS have been reported so far. We are reporting a case of intractable postherpetic neuralgia refractory to pharmacological treatment, which was successfully treated using PNFS.

## Case History

A 55-year-old male, a known case of coronary artery disease with post angioplasty 7 years ago, was diagnosed to have multiple myeloma in 2002. After 3 cycles of chemotherapy, he underwent stem cell transplantation in 2003 for multiple myeloma. He was alright for 4 years when he developed herpes zoster eruption in his left supraorbital region in November 2007. He received treatment for his painful vesicular eruption of the herpes zoster with both systemic and local acyclovir along with other supportive measures including analgesics, antibiotics, and pregabline for neuropathic component. Although the herpetic eruption disappeared in 2 weeks, painful electric-like sensation and shooting pain supervened in the distribution of the vesicular lesions with severe allodynia. The patient's day-to-day activity was severely hampered; he was unable to touch his affected area and used to spend many sleepless nights. His allodynia was so severe that even blowing air from fan used to provoke his painful neuralgia. Initially, he was treated with pregabline in incremental dosage starting with 150 mg per day, though the initial response were promising with pain relief up to 50%; but after 2 to 3 months, both the intensity and frequency of pain increased to a much greater extent and it continued increasing even after addition of amitryptaline (50 mg/day) and fentanyl patches (25 µg/h) along with pregabline (Lyrica; 600 mg/day). He had never achieved more than 50% pain relief and was not satisfied at all with the treatment method. Moreover, he was experiencing number of side effects like somnolence, giddiness, and inability to concentrate. This painful neuralgia was affecting a lot his daily activities of living, leading to anger and frustration. Before jumping into PNFS, we thought to perform diagnostic block of left supraorbital nerve with local anaesthetic (0.25% bupivacaine 2 mL). Patient was given local blocks for 3 consecutive days, which provided excellent pain relief. Encouraged by these diagnostic blocks, he was

planned for trial PNFS. In the trial, PNFS- (Implantable Neurostimulator Synergy with octad lead, Medtronic, Minneapolis, MN) stimulating electrode (octapole) was placed subcutaneously from the left temporal region into his left supraorbital region. The other end of the stimulating lead was subcutaneously tunneled from temporal region to the posterior triangle of neck via the post auricular area. It was coiled and placed subcutaneously in the neck after connecting with another (external) stimulating electrode. The patient was given trial stimulation for 3 consecutive days via the external electrode that was connected with a stimulating machine at one end and the internal stimulating electrode at other end. During this trial phase, he attained 100% pain relief. After the successful trial stimulation, he was planned for placement of permanent stimulator. Initially, we thought to place the stimulator in his chest wall, but as the patient was a known case of coronary artery disease and might require pacemaker in future, we decided to place it over his abdomen. The external electrode was detached, the coil portion of the internal electrode lying in the neck was of sufficient length to reach the abdomen, it was subcutaneously tunneled via the neck and chest to abdomen, a small pocket was made subcutaneously in abdominal wall for the placement of stimulator, which was put in the pocket and secured with sutures after connecting with the internal stimulating lead. The whole procedure was done under local anesthesia and it was uneventful. A remote control system was provided to the patient for switching on, switching off, and changing stimulation magnitude. The patient was instructed to stimulate the stimulator initially for 2 to 3 hours for 3 times a day and switch off stimulation at night. Patient had achieved 100% pain relief from the first day onward. His drugs were gradually tapered off within 2 weeks. At present, the patient is in 8 weeks poststimulation, with 100% pain relief and without any side effects and complications.

## Discussion

The most well-established risk factors for development of PHN are old age, intensity of acute pain during vesicular eruption, severity of eruption, and a prodrome of dermatome pain before the onset of eruptions.<sup>13</sup> Patients with all of these risk factors may have as much as a 50% to 75% risk of persisting pain 6 months after the rash onset.<sup>13</sup> In patients

older than 50 years, 20% continue to report pain 6 months after the onset of the rash despite treatment with antiviral drugs.<sup>3</sup> Patients with PHN report constant burning, throbbing, or arching pain, intermittent sharp or shooting pain, and mostly tactile allodynia.<sup>3,14</sup> These symptoms may be explained by 3 distinct pathophysiological mechanisms: first, constant drive of input from abnormally hyperactive (irritable) anatomically intact primary afferent nociceptors results in central sensitization with marked allodynia but minimal sensory loss<sup>3,14,15</sup>; second, loss of C-nociceptive receptors and fibers initiate central sprouting of A $\beta$ -fibers, which in turn make contact with the receptors formerly occupied by C-fibers leading to hyperalgesia and allodynia<sup>3,16</sup>; and third, loss of both large and small diameter fibers generates spontaneous activity in deafferented central neurons, producing constant pain in a region of profound sensory deficits without allodynia, that is, anesthesia dolorosa.<sup>3</sup> These different mechanisms may coexist in individual patient. If we look at the risk factors for development of PHN, our patient bears most of the risk factors, being aged more than 50 years, was immunocompromised, had severe vesicular eruption, and had prodromal and neuropathic component at the time of vesicular eruption. Although he was treated with systemic antivirals and analgesics including anticonvulsant pregabalin from the time of initial eruption, he continued to have increasing symptoms of neuralgia, requiring increment of dosage of pregabalin and later addition of tricyclic antidepressant (amitryptalline) and strong opioid (fentanyl). Despite the polypharmacy, our patient had never achieved adequate analgesia; moreover, he was suffering from number of side effects like dizziness, inability to concentrate, and increased somnolence.

Various treatment modalities are postulated for management of PHN. Tricyclic antidepressants, the anticonvulsants gabapentin and pregabalin, controlled released oxycodone or morphine sulphate, tramadol, and lidocaine patches are all classed as moderate to highly effective.<sup>17</sup> Some evidence of efficacy was also found for topical capsaicin and aspirin creams and for intrathecally administered methylprednisolone.<sup>17,18</sup> Combination therapy is common, and the multiple putative mechanisms of neuropathic pain provide a rationale for this approach, but studies have not been conducted to examine its efficacy and safety.

Recently, there is a growing interest in spinal cord stimulation and PNFS in a variety of neuropathic conditions. Success with electrical stimulation of peripheral nerves has been reported in various painful neuropathic conditions in head and neck,<sup>12,19,20-22</sup> thoracic PHN,<sup>23</sup> and other varieties of painful conditions including diabetic neuropathy<sup>24</sup> and chronic visceral pain.<sup>25</sup> Encouraged with these results, we have also planned for PNFS of the supraorbital region for this painful neuropathic condition.

The mechanism of action of neurostimulation in subcutaneous tissue is postulated as similar to TENS or percutaneous electrical nerve stimulation (PENS)<sup>25</sup> and may alter local blood flow, block cell membrane depolarization and axonal conduction, affect neurotransmitters, and thereby similarly block or jam nociceptive input back at the spinal neurons. Peripheral nerve field stimulation may cause an increase in endogenous endorphins and other opiate-like substances, normalize nerve conduction velocity, and decrease conduction latency and the mechanical pain threshold. Further clinical study is needed to clarify the pathophysiology and mechanism of action of PNFS. Peripheral nerve field stimulation has potential advantages as a treatment for chronic pain where conventional pain management strategies have been disappointing. Advantages include reversibility, low morbidity without known side effects, minimally invasive implantation, percutaneous lead placement with the patient awake to confirm proper lead placement, and programmable stimulator systems to improve coverage and effectiveness of stimulation.

In summary, PNFS can be considered for treatment of intractable PHN when other pharmacological modalities have failed; further comparative study is needed to consider PNFS as effective and safe method of treatment for variety of chronic painful neuropathic conditions such as PHN.

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