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CASE REPORT

High-frequency spinal cord stimulation for treating pain in the lower limbs accompanied by bilateral para-anesthesia: A case report

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ABSTRACT

A 46-year-old female patient experienced severe pain in both lower limbs following a traffic accident in 2008. The pain mainly presented in her feet; she also experienced sensory impairment, convulsions, and exercise function disorders. She was diagnosed with neuropathic pain, and no medicine had any remarkable effect. Therefore, spinal cord stimulation (SCS) was performed in October 2019. Her pain did not reduce after the initial adoption of conventional SCS until the application of high frequency SCS (HF-SCS). At the 6-month follow-up, the pain in her lower limbs was considerably reduced, lower limb motor function was slightly improved, and muscle twitching in both feet disappeared.

1 Introduction

Neuropathic pain is always intractable despite different kinds of available medicines. Spinal cord stimulation (SCS) has been used in the treatment of neuropathic pain as a minimally invasive, invertible therapeutic method with implanted equipment and highly sophisticated techniques for more than 50 years [1]. For conventional low-frequency SCS (LF-SCS; 30–300 Hz), the patient needs to report coverage of the pain position by stimulation-evoked paresthesia for pain relief [2, 3]. However, a noteworthy feature of the high-frequency (HF) SCS (> 500 Hz, most often 10 kHz) is that it can provide analgesic effects without the manifestation of paresthesia or other abnormal sensations

along with the stimulation [4]. Traditional LF-SCS is ineffective in some patients with neuropathic pain [5], especially those with imperceptible stimulation-evoked paresthesia caused by physical sensory impairment. However, HF-SCS may be helpful and may result from different mechanisms between LF-SCS and HF-SCS. In addition, HF-SCS may also promote the motor function of the limbs. Here, we report a neuralgia patient with bilateral para-anesthesia and twitching of both the feet to achieve HF-SCS.

2 Case report

The patient was a 46-year-old female who had experienced pain, sensory denervation, partial

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motor disturbance, twitching of the bilateral feet, and dysfunctions of excretion resulting from the spinal conus injury caused by a fracture of L1 vertebral body in a car crash 12 years previously. Although she had received timely surgical treatment, those complications did not disappear. The myodynamia of bilateral gastrocnemius was grade 3. Achilles reflex was decreased. The catheterization was continuous because of dysuresia, and she had chronic, long-standing dyschezia. More importantly, she had severe pain in both feet that negatively influenced her ability to perform activities of daily living. Her pain presented as a pinprick sensation that is considered a symptom of neuropathic pain. Sometimes, the pain score (visual analogue scale, VAS) could reach 10. Oral medication (total daily dose of tramadol was 200 mg for 11 years, total daily dose of gabapentin was 2700 mg for 10 years), paravertebral nerve blockers (2 doses of 0.125% ropivacaine combined with 40 mg of methylprednisolone), or injections of sacral

canal steroids (a single dose of methylprednisolone was 40 mg) was not able to alleviate her pain effectively.

Therefore, SCS was performed to achieve pain relief. The patient was unable to perceive stimuli in the area of pain during the SCS procedure. Therefore, the electrodes (PINS®, China) were implanted into the thoracic epidural space (at the level of T9–T11) as per the anatomical definition (Fig. 1). The patient could experience paresthesia of electrical stimulation in the thighs and calves. During the first week of SCS treatment, there was no reduction in pain for the conventional LF-SCS patterns with frequency 30–100 Hz. However, the application of 1 kHz HF-SCS in the patient produced an analgesic effect after 3 days. Finally, follow-up was continued for 6 months, and her feet pain reduced substantially; she discontinued oral painkillers. Moreover, the twitching in her lower limbs was reduced, and lower limb motor function was slightly improved.

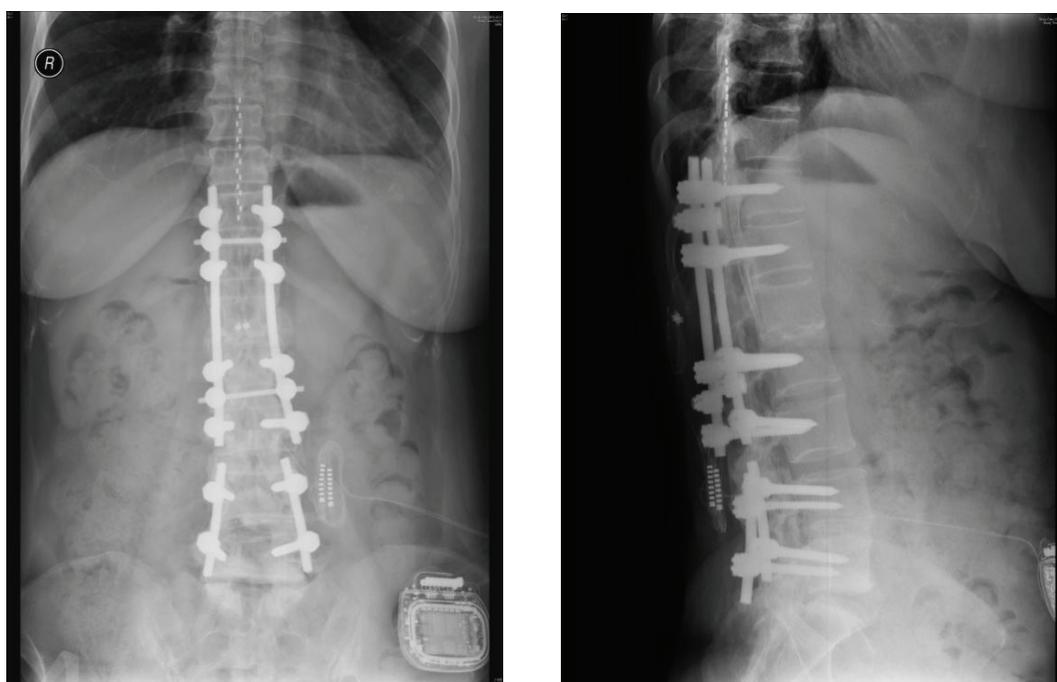


Fig. 1 The radiography images showing the implant position of the spinal cord stimulation electrodes, and the internal fixations for L1 vertebral body fracture and L4 spondylolisthesis.

3 Discussion

The conventional LF-SCS depends on the patient's perception of electrical stimulation [2, 3]. This patient could not report the stimulation-evoked paresthesia due to loss of sensation in her feet. Thus, we were unsure of the effectiveness of conventional LF-SCS in the beginning. Then, the electrodes with both low- and high-frequency stimulation parameters were implanted. It was not surprising that the traditional LF-SCS did not relieve the feet pain in the patient. However, HF-SCS became an option for achieving pain relief and later proved effective. This may be because of the different mechanisms of LF-SCS and HF-SCS.

It has been demonstrated that the analgesic effect of conventional LF-SCS may be related to the activation of dorsal column collaterals secondary to the induction of the release of inhibitory neurotransmitters, notably γ -aminobutyric acid (GABA), acetylcholine (ACH), and serotonin (5-HT) [6–10]. The LF-SCS can cause GABA release in the dorsal horn (DH), mainly activating GABA-B receptors and decreasing the release of excitatory amino acids from the hyperactivity of wide dynamic range (WDR) neurons in the superficial laminae of the corresponding DH [6, 11, 12]. In addition, the investigators also used rat models of painful neuropathy and confirmed that LF-SCS induced cholinergic neurons to release ACH in the DH and activate M4 and M2 muscarinic type receptors after nerve injury [8, 9]. Moreover, the DH could be activated by orthodromic low-frequency stimulation, inducing descending inhibition via the serotonergic and noradrenergic pathways. The neuronal circuitry in the brainstem (particularly in the rostroventromedial medulla) may release 5-HT and NE that inhibit DH through dorsolateral funiculus [13].

The conventional LF-SCS has a very close relationship with the activation of the dorsal columns (DCs).

HF-SCS has been available for many years; however, it has been reported rarely [14]. HF-SCS is demonstrated to have superior analgesia effects in a few clinical trials [15–17]. HF-SCS involves the use of kilohertz tonic stimulation without paresthesia that is superior to low-frequency tonic SCS in treating neuropathic pain. It was applied to DH in animal models and in clinical trials that might provide a local conduction block and effective pain relief [18–20]. HF-SCS would lead to the generation of quickly reversible conduction block along with several nodes of Ranvier via the inactivation of sodium channels in several animal models [19, 21]. However, recent simulation models *in silico* displayed that conduction block thresholds are almost beyond the clinical amplitude range that matches with other research results about an original augment in action potential firing called the onset response before HF-SCS induced a conduction block. This onset response has the ability to increase the WDR activity and results in discomfort during the first few moments of HF-SCS in animal models [22]. Instead, HF-SCS treatment has effectively alleviated pain in patients who have not reported paresthesia or other subjective perceptions [23]. These results suggested that HF-SCS-induced analgesia may have no connection with the activation or conduction block of fibers in DCs. Therefore, more complex and delicate analgesia mechanisms may be involved. A recent study suggested that HF-SCS can attenuate extracellular regulated protein kinase (ERK), c-Jun N-terminal kinase (JNK), and p38 activation in the spinal DH and in the dorsal root ganglia, providing effective treatment for spared nerve injury (SNI)-induced neuropathic

pain in rats [24]. Other studies have shown that the superficial neurons of the DH might be directly inhibited by effective HF-SCS [25]. This may be a possible reason why the patient achieved pain relief with HF-SCS.

In this patient, lower limb pain was considerably reduced after HF-SCS that also helped in the regulation of muscle movements. Recent studies on the use of HF-SCS in respiratory muscles have shown that HF-SCS induced considerable activation of the inspiratory or expiratory muscle via very low stimulus currents [26, 27]. Nonetheless, it remains unclear what mechanism of HF-SCS regulates limb muscles functions.

Currently, it is suggested that HF-SCS be applied with low amplitude (below the paresthesia threshold) to prevent an uncomfortable experience [28]. Therefore, if the pain is associated with loss of sensation and is not relieved with conventional low-frequency stimulation, HF-SCS treatment may be a good alternative.

4 Conclusion

In conclusion, we would like to share this case about the experience of SCS for severe refractory neuropathic pain with sensory impairment. HF-SCS may be a reasonable choice in special patients such as the present patient.

Consent

The patient agreed the doctors could use and publish her disease related article with personal information deleted.

Conflict of interests

The authors declare that they have no conflict of interests.

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