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Efficacy of High-Frequency Spinal Cord Stimulation in Idiopathic Asymmetrical Small-Fiber Neuropathy Case Report

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Background: Small-fiber neuropathies (SFNs), affecting thinly myelinated Aδ fibers and unmyelinated C fibers, often manifest with sensory or autonomic symptoms in varied patterns. Diagnostic tools comprise skin biopsy, quantitative sensory, autonomic testing, and biochemical markers. Spinal cord stimulation (SCS), particularly high-frequency SCS, has emerged as a pivotal therapeutic intervention.

Case Report: This study delves into a 49-year-old woman diagnosed with idiopathic asymmetrical SF peripheral neuropathy, examining her 12-month postoperative trajectory after SCS implantation. Postsurgical assessment revealed substantial improvements: baseline pain (Numeric Rating Scale 7) decreased to 4 at 3 months, indicating reduced intensity; Oswestry Disability Index improved from 38% to 4%, highlighting enhanced functionality; Patient-Specific Questionnaire 3 average score dropped from 35 to 2, indicating improved outcomes in specific pain-related concerns.

Conclusions: This case report underscores the efficacy of SCS in managing idiopathic asymmetrical SFN, demonstrating significant symptomatic relief over a 12-month postoperative period.

Key words: Small-fiber neuropathy, spinal cord stimulation, HF10 SCS, idiopathic asymmetrical small-fiber neuropathy, pain management

BACKGROUND

Small-fiber neuropathy (SFN), a condition characterized by painful burning sensations in the feet, is often seen in the elderly and is commonly caused by diabetes mellitus or associated with impaired glucose tolerance and metabolic syndrome (1). SFN is characterized by dysfunction and degeneration of thinly myelinated Aδ and unmyelinated C fibers, leading to length-dependent neuropathic pain symptoms. This can be spontaneous or triggered by innocuous stimuli; while the underlying cause is often unknown, immunologic mechanisms and inflammatory modifications in nerves may contribute to the condition (2). Pure SFN often requires specific diagnostic tests that are not widely available. This case report highlights the importance of using objective diagnostic tests, such as skin biopsy, quantitative sensory testing, and nociceptive evoked potentials, to definitively diagnose pure SFN. A study (3) found that

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the SFN Symptoms Inventory Questionnaire showed good accuracy in diagnosing pure SFN, suggesting it could be used as a screening tool to identify patients who require further diagnostic tests.

SFN can have various etiologies, including diabetes mellitus, alcohol withdrawal, viral infections (such as COVID-19), genetic mutations (e.g., SCN9A), and autoimmune processes (4,5). In patients with diabetes, SFN can manifest as mixed neuropathy, affecting both large myelinated Aβ fibers and small myelinated Aδ and unmyelinated C fibers (3). Early detection of SFN is crucial, as it can help reduce unhealthy lifestyles associated with a higher incidence of the disease. Skin biopsy is a useful method for confirming SFN, which is a leading cause of neuropathic pain and can cause disability and impair quality of life; early detection can reduce the incidence of the disease (6). Diagnostic tests for large-fiber neuropathy are not effective in capturing SF dysfunction, so skin biopsies stained with PGP 9.5 [protein gene product 9.5] are recommended as the objective test for SFN. Fibromyalgia (FM) patients often have symptoms that overlap with SFN, and skin punch biopsy can be used to quantify SF pathology in FM, providing better classification and guidance for patient care (7).

Accurate quantification of peripheral neuropathy is crucial for identifying at-risk patients, predicting deterioration, and evaluating new therapies. Conventional methods and tests primarily assess large-fiber dysfunction, limiting early damage to SFs. They also fail to demonstrate nerve regeneration and repair. Noninvasive techniques, like corneal confocal microscopy, offer in vivo imaging of corneal nerve fibers, allowing for early detection of nerve damage and assessment of neuropathic severity and repair. Corneal confocal microscopy has also been used as a noninvasive imaging technique to identify early SFN (8). Figure 1 illustrates a patient presenting with asymmetrical SFN. Afflicted individuals manifest symptoms, such as pain, sensory loss, and hypersensitivity, to temperature variances (cold, warm), tactile stimuli, or pinpricks in nonlength-dependent SFN.

When it comes to treatment, there is limited research focused on SFN. However, some studies have explored the effectiveness of certain medications. Management of SFN involves treating the underlying cause and addressing associated neuropathic pain, with various options, such as antidepressants, anticonvulsants, opioids, topical therapies, and nonpharmacologic treatments, although limited data specifically for SFN exist. In a study (9) examining SFN, gabapentin and tramadol were effective. Intravenous immunoglobulin (IVIG) therapy has shown promise in managing SFN-related pain (2). IVIG modulates the immune system and reduces inflammation, relieving SFN patients. Other treatment approaches include symptomatic pain management with medications, such as tricyclic antidepressants, anticonvulsants, and topical agents (2,10,11).

Spinal cord stimulation (SCS) has been shown to be an efficacious and cost-effective treatment for many chronic neuropathic pain conditions (12). SCS has been shown to be a safe and effective treatment for intractable painful diabetic neuropathy. The effectiveness of 10 kHz SCS has been observed in various conditions, including painful diabetic neuropathy, where it has shown promise in pain reduction and possible neurological improvements (13). A study (14) found that 10 kHz SCS was a safe and effective treatment for painful diabetic neuropathy. Additionally, 10 kHz SCS has been utilized to salvage nonresponsive low-frequency SCS trials, indicating its potential as an alternative when traditional SCS proves ineffective (15). The underlying mechanism of action of high-frequency SCS at 10 kHz (HF10 SCS) remains unclear, and further research is needed to understand its physiological effects (16).

One study (17) reported successful treatment of SFN pain using multiple SCSs. This case report describes the use of multiple SCSs to treat widespread SFN pain in a patient. The patient experienced significant pain improvement and reported excellent pain relief, allowing him to increase his activity and attend graduate school full time (17). Another case study (18) showed successful treatment of intractable SFN with SCS of the left L5 dorsal root ganglion. The patient experienced significant pain relief and paresthesia after the implantation of a neurostimulator. This indicates that the dorsal root ganglion is a promising target for treating neuropathic pain caused by SFN (18).

Here, we report the case of a 49-year-old female musician with asymmetrical SF peripheral neuropathy (SFPN) with multisite involvement. Despite past medication challenges, a successful SCS implant significantly alleviated pain in her feet, hands, and her facial pain. At 12 months postimplantation, the patient experienced substantial pain reduction, ceased gabapentin use, and resumed professional activities. Residual mild symptoms were managed with occasional medications, with notable postsurgical site sensations addressed through daily antihistamines.

CASE PRESENTATION

In adherence to ethical standards, informed consent has been obtained from the patient, as is required for studies involving humans. A 49-year-old woman diagnosed with asymmetrical SFN presented with multisite neuropathic pain. The patient's past medical history included Hashimoto's disease and SFN. The diagnosis of SFN was established through a comprehensive diagnostic approach. A neurologist conducted a nerve biopsy and nerve conduction study to assess nerve function and structure. Additionally, a magnetic resonance imaging of the entire spine and brain was performed to rule out other potential causes. Despite diligent evaluation, the etiology of SFN remained unknown. Despite her medical conditions, she remained functional and worked as a musician, playing the saxophone and piano, and teaching music. However, her sensory issues began affecting her work, making her consider alternative professions.

Clinical Presentation

She primarily complained of:

1. Burning pain in the bilateral soles of her feet, more intense on the left side, radiating up the posterior left leg. This pain had intensified in the past year, exacerbated by stress and anxiety over the last 3 months. The patient developed hypersensitivity, with difficulty tolerating socks and shoes.
2. Burning sensation beginning in the distal fingers and spreading to her hands, again more pronounced on the left side. This resulted in

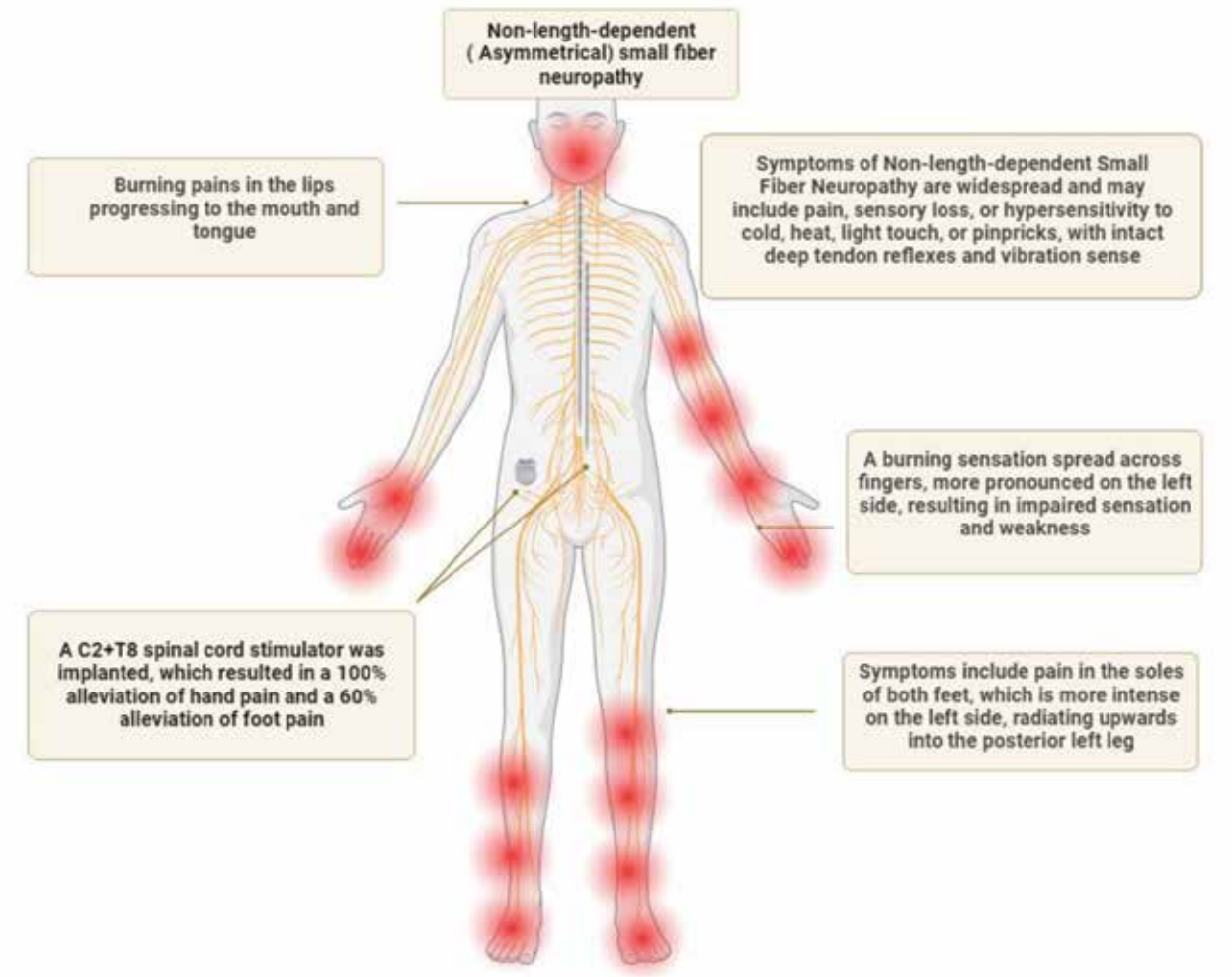

Fig. 1. Patient exhibit pain, sensory loss, or hypersensitivity to cold, warm, touch, or pinpricks in nonlength-dependent SFN. The SF function of one or more nerves may be reduced or increased in a patient. SFN, small-fiber neuropathy; SF, small-fiber.

sensation loss and weakness, causing her to drop objects.
3. Development of burning pain in the lips, progressing to her mouth and tongue.

Pharmacological History

Previous medications administered included Lyrica and Cymbalta. Both were discontinued due to severe side effects, with Lyrica causing a heavy sensation in the head and Cymbalta triggering increased suicidal ideation and depressive moods. Gabapentin cream was also ineffective. The patient was, however, on a regimen of gabapentin (1,000 mg thrice daily), Zoloft (150 mg daily), cannabidiol oil, and Panadol. Notably, the high dose of gabapentin led to a series of side effects, such as fatigue, forgetfulness, and difficulties in finding words.

Clinical Examination and Treatment

Upon initial examination, there was significantly reduced sensation in the left foot and some desensitization in the right foot. Despite these sensory issues, strength in the upper limbs was normal. Before undergoing an SCS trial, the patient underwent other interventional treatments. These included lumbar sympathetic block and T2 sympathetic ganglion block, which were administered with no discernible effectiveness. Despite these prior interventions, the patient's symptoms persisted, leading to the consideration of SCS as a potential therapeutic option. Considering the patient's symptoms and her nonresponsiveness to previous treatments, an SCS trial was proposed. After discussing the potential outcomes and benefits, the patient was keen and was scheduled for the procedure.

SCS Pretrial Assessment

The patient's primary diagnosis was SFN pain. Her pain sites were identified as feet, legs, hands, face, tongue, and lips. Despite her pain, she reported no trouble sleeping. Mood disturbances were controlled with Zoloft, and she had a strong support system at home. The patient hoped to reduce her gabapentin intake posttrial.

SCS Trial and Implantation

Following a successful pretrial assessment, the patient underwent the SCS trial. During percutaneous lead placement for SCS, the process begins with preparing the patient's skin and draping it in a sterile fashion. Local anesthesia is then administered at the intended needle insertion site. Under fluoroscopic guidance, the needle is inserted at an angle of 45° into the posterior ligamentous complex at the desired vertebral level. After confirming entry into the epidural space, the lead is slowly advanced through the needle, with the stylet fully inserted for optimal steering. Care is taken to avoid using non-Nevro Corp needles (Redwood City, CA), inserting the lead at angles exceeding 45°, or damaging existing leads when inserting a second lead. During the 14-day trial, employing various waveform modalities, including tonic and burst under Nevro Corp's approval (Redwood City, CA), remarkable pain alleviation was achieved in a patient suffering from bilateral hands and feet pain. During SCS lead placement, one lead is positioned along the midline from C1 to C5, while the second lead is situated mid T8 to T10. By precisely positioning the leads, clinicians aim to provide effective relief for both hands and feet. Lead placement at C2 and T9/T10, with stimulation intensity set at 0.6 mA for the hands and 1.5 mA for the feet, yielded significant improvements. Stimulation at C2 notably reduced burning sensations in the hands and improved sensory function in the fingertips, alongside diminished facial symptoms. Similarly, stimulation at T9/T10 resulted in a substantial reduction in burning pain in the feet, coupled with a decrease in ice-block sensations. SCS was the best therapy used. During the trial, a 10 KHz SCS waveform was performed. Permanent implantable pulse generator (IPG) and lead implantation occurred 8 weeks after a successful 2-week trial. Lead placed at C2 and T8 during SCS trial, resulting in a 100% relief in hand pain and a 60% relief in foot pain.

The results were promising. The patient reported a significant reduction in pain in her feet, and the burning sensation in her hands diminished. Two weeks post-SCS trial, there was notable relief in the feet, hands, and mouth. An IPG with one lead at the C2 level and another lead at the T8 level was implanted, and subsequent assessments showed progressive improvement in pain, with significant relief in hands and feet. The patient's quality of life improved noticeably, with increased activity levels. Anterior-posterior and lateral x-rays confirmed no lead migration.

Three-Month Follow-up

Three months postimplantation, the patient walked into the clinic, visibly improved and smiling. She reported an 80% improvement across pain, sleep, and function. The nerve pain in her arms had almost entirely subsided, and her feet were much more comfortable.

The burning sensation in her tongue remained, albeit at a manageable level. However, she still expressed concerns regarding the side effects of her medication, gabapentin, which she hoped to reduce or eliminate. The medical team provided her with a reduction schedule and continued monitoring her progress. Medication was tapered down, with the patient eventually stopping gabapentin completely. While she still had occasional flare-ups, her overall quality of life and functionality had significantly improved.

Six-Month Follow-up

Six months following SCS implantation, significant progress in symptom management was noted. The usage of gabapentin was ceased entirely, and the pain management was primarily through paracetamol and ibuprofen taken as needed. Residual symptoms included a burning sensation in the feet, tongue, and hands. However, these symptoms were occasionally accentuated during flare-ups. The patient's face showed no signs of pain, and the burning sensations persisted in her tongue but only when she consciously pondered over them. A constant yet mild burning pain was reported in the left foot, though she could now comfortably wear shoes. Some postsurgical itchiness and numbness were observed at the surgical site, which the patient managed with daily fexofenadine doses.

At the 6-month assessment post-SCS intervention, significant improvements were observed compared to baseline measures. The baseline Numeric Rating Scale for pain was 7, notably reduced to 4 at the 3-month mark, indicating decreased pain intensity. Additionally, the baseline Oswestry Disability Index dropped from 38% to 4%, revealing a substantial improvement in functional ability. Moreover, the baseline Patient-Specific Questionnaire 3 average score decreased from 35 to 2, demonstrating enhanced patient-reported outcomes concerning specific pain-related concerns. This comparison highlights a positive trend showcasing reduced pain intensity, improved functionality, and better outcomes post-SCS implementation.

Twelve-Month Follow-up

The patient's subsequent visit to the Pain Management Centre for her annual review revealed continued progress. No facial pain was reported, and the mild burning sensation in her tongue persisted but was only evident when she consciously focused on it. The left foot's dull burning sensation remained constant but was manageable, and wearing shoes was no longer an ordeal. While her professional life saw her returning to regular working hours, she was also active in her daily living activities. The only consistent complaint she voiced was the residual itchiness and numbness at the implant site, still managed with daily fexofenadine. The advice of alternating fexofenadine doses (every other day) was reiterated to possibly counter any reaction.

From the patient's perspective, the journey post-SCS implantation has been transformative. At the 3-month follow-up, she experienced a remarkable 80% improvement in pain, sleep, and function. By the 6-month mark, the complete cessation of gabapentin and the adoption of paracetamol and ibuprofen as needed underscored the successful transition to alternative pain management. The 12-month follow-up confirmed sustained progress, with minimal complaints and a return to regular working hours. The patient's perspective reflects a substantial improvement in her quality of life, highlighting the positive impact of SCS on managing her SFN symptoms and providing hope for continued well-being.

DISCUSSION

SFPN is frequently found in patients with FM syndrome and interstitial cystitis/bladder pain syndrome (IC/BPS), suggesting a potential role in symptom development. SFPN can manifest in various ways, including microvasculopathy, which may lead to muscle aches, fatigue, abdominal pain, and gastrointestinal symptoms. A significant proportion of women with FM and IC/BPS have skin biopsy findings consistent with severely decreased superficial cutaneous nerve density, with various known causes, including genetic syndromes, metabolic disorders, and autoimmunity, but up to 50% of cases have no known cause, leading to decreased autonomic nerve fiber density and high levels of autonomic symptoms (19). SCS's efficacy is highlighted in this case, with the patient experiencing substantial symptomatic relief. While the implant successfully addressed major neuropathic pain points, residual symptoms like burning sensations and postoperative side effects were present but manageable. Regular monitoring and treatment adjustments, such as the fexofenadine regimen modification, emphasize a patient-centric approach.

CONCLUSIONS

This case report is of a patient with idiopathic, multisite, and asymmetrical SFN treated with SCS. SCS implants can be a valuable therapeutic approach for patients with

multisite neuropathic pain nonresponsive to traditional treatments. SFN is a disorder of the peripheral nerves that primarily or exclusively affects small somatic fibers, autonomic fibers, or both. It is often manifested by paresthesias (abnormal sensations) and can be confirmed through findings of SF dysfunction on neurologic examination. Treatment focuses on relieving neuropathic pain unless an underlying disease is identified (20). This case report underscores the potential of SCS as a viable intervention for refractory neuropathic pain. The patient's quality of life improved remarkably postimplantation, signaling hope for similar patients grappling with SFN. Over the span of the 12-month postimplantation period, the patient has shown marked improvement in her neuropathic pain symptoms and overall quality of life. The SCS intervention appears to have yielded significant therapeutic benefits, with minor and manageable side effects.

In this case report, HF10 SCS has demonstrated sustained effectiveness as a treating tool for SFPN pain. Its ability to rescue nonresponsive traditional SCS therapy and provide superior pain relief makes it a promising therapeutic option for chronic pain management. Regular follow-ups, personalized interventions, and patient feedback are paramount in ensuring sustained relief and optimizing patient care.

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REFERENCES

1. Tavee J, Zhou L. Small fiber neuropathy: A burning problem. *Cleve Clin J Med* 2009; 76:297-305.
2. Geerts M, de Greef BTA, Sopacua M, et al. Intravenous immunoglobulin therapy in patients with painful idiopathic small fiber neuropathy. *Neurology* 2021; 96:e2534-e2545.
3. Galosi E, Falco P, Di Pietro G, et al. The diagnostic accuracy of the small fiber neuropathy symptoms inventory questionnaire (<scp>SFN-SIQ</scp>) for identifying pure small fiber neuropathy. *J Peripher Nerv Syst* 2022; 27:283-290.
4. Trevino JA, Novak P. TS. HDS and FGFR3 antibodies in small fiber neuropathy and dysautonomia. *Muscle Nerve* 2021; 64:70-76.
5. Abbott MG, Allawi Z, Hofer M, et al. Acute small fiber neuropathy after <scp> Oxford-AstraZeneca ChAdOx1-S</scp> vaccination: A report of three cases and review of the literature. *J Peripher Nerv Syst* 2022; 27:325-329.
6. Raicher I, Ravagnani LHC, Correa SG, Dobo C, Mangueira CLP, Macarenco RSES. Investigation of nerve fibers in the skin by biopsy: Technical aspects, indications, and contribution to diagnosis of small-fiber neuropathy. *Einstein (São Paulo)* 2022; 20:eMD8044.
7. Kelley MA, Hackshaw KV. Intraepidermal nerve fiber density as measured by skin punch biopsy as a marker for small fiber neuropathy: Application in patients with fibromyalgia. *Diagnostics (Basel)* 2021; 11:536.
8. Tavakoli M, Malik RA. Corneal confocal microscopy: A novel noninvasive technique to quantify small fibre pathology in peripheral neuropathies. *J Vis Exp* 2011; 47:2194.
9. Hovaguimian A, Gibbons CH. Diagnosis and treatment of pain in small-fiber neuropathy. *Curr Pain Headache Rep* 2011; 15:193-200.
10. Song P, Xu X. Reader response: Intravenous immunoglobulin therapy in patients with painful idiopathic small fiber neuropathy. *Neurology* 2021; 97:791-792.
11. Gibbons CH, Klein C. IVIG and small fiber neuropathy. *Neurology* 2021; 96:929-930.
12. Hayek SM, Veizi E, Hanes M. Treatment-Limiting complications of percutaneous spinal cord stimulator implants: A review of eight years of experience from an academic center database. *Neuromodulation* 2015; 7:603-609.
13. Wang D, Lee D, Lee K, Kagan ZB, Bradley K. 482-P: Behavioral assessment of 10kHz spinal cord stimulation–mediated pain relief in a rat model of painful diabetic neuropathy. *Diabetes* 2023; 72(suppl 1):482-P.
14. Galan V, Scowcroft J, Chang P, et al. 10-kHz spinal cord stimulation treatment for painful diabetic neuropathy: Results from post-hoc analysis of the SENZA-PPN study. *Pain Manag* 2020; 10:291-300.
15. Hasoon J, Robinson C, Urits I, Viswanath O, Kaye AD. Utilizing 10kHz stimulation to salvage a failed low frequency spinal cord stimulation trial. *Orthop Rev (Pavia)* 2023; 15:57624.
16. De Groote S, Goudman L, Peeters R, et al. Magnetic resonance imaging exploration of the human brain during 10 kHz spinal cord stimulation for failed back surgery syndrome: A resting state functional magnetic resonance imaging study. *Neuromodulation* 2020; 23:46-55.
17. Eckmann M, Papanastassiou A, Awad M. A unique case for spinal cord stimulation: Successful treatment of small fiber neuropathy pain using multiple spinal cord stimulators. *Case Rep Med* 2017; 2017:1-3.
18. Koetsier E, Regionale O, Lugano D, et al. Efficacious dorsal root ganglion stimulation for painful small fiber neuropathy: A case report. *Pain Physician* 2017; 20:E459-E463.
19. Wolff DT, Walker SJ. Small fiber polyneuropathy may be a nexus between autonomic nervous system dysregulation and pain in interstitial cystitis/bladder pain syndrome. *Front Pain Res (Lausanne)* 2022; 2:810809.
20. Lacomis D. Small-Fiber neuropathy. *Muscle Nerve* 2002; 26:173-188.