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Long-Term Evolution of an Ependymoma-Related Pain Syndrome Managed with Spinal Cord Stimulation: A Case Report

Mariano Fernandez Baena, MD, PhD, MsC, Laureano Delange Segura, MD, PhD, MsC, María Teresa Palomino Jiménez, MD, PhD, MsC, and María Luisa Rodríguez Padilla, MD, PhD

Background: Ependymoma is the most common spinal tumor in adults. Its treatment is surgical and consists of maximum possible tumor resection. Although the recurrence rate is low, painful sequelae are also common. Electrical spinal cord stimulation (SCS) has demonstrated efficacy in neuropathic and postsurgical pain, and the efficacy and duration of relief can be improved through the use of new modalities, such as burst stimulation.

Case Report: A 27-year-old woman with chronic severe painful sequelae in her lower limbs and thoracic region was found to be refractory to pharmacological treatment after total thoracic ependymoma resection. The successive use of spinal cord and/or peripheral nerve stimulation in tonic and burst modalities has provided consistent pain relief for approximately 10 years.

Conclusion: Our experience suggests that SCS, in its various modalities, can be an adequate and long-lasting therapy for patients with pain secondary to resection of spinal cord tumors.

Key words: Case Report, ependymoma, intramedullary tumors, neuropathic pain, spinal cord stimulation

BACKGROUND

Ependymomas represent 40% to 60% of all intramedullary tumors and are most common in the adult population (1). They originate from the uncontrolled proliferation of ependymal cells in the brain ventricles; these cells can be transported via the cerebrospinal fluid to other brain or spinal areas and rarely outside the central nervous system. The common symptoms are pain, dysesthesia, motor weakness, ataxia, and sphincter disorders, and are usually more severe at the thoracic level than at the cervical level.

The indicated treatment for ependymoma is surgery, consisting of maximum tumor resection, which in most cases is complete because the margins of these tumors are usually well-defined. Although the rate of tumor recurrence is low (4.2% after total resection), the morbidity related to neurological symptoms is significant, especially when it comes to pain. In a study of 100 patients undergoing ependymoma resection surgery, pain increased with respect to the preoperative situation by 6.8% and 10.3% in patients with cervical and thoracic tumors, respectively (2). Additionally, the appearance of neuropathic syndromes was between 19% (2) and 60% (3).

The analgesic action of spinal cord stimulation (SCS) is probably due to a combination of spinal and supraspinal mechanisms. At the spinal level, antidromic activation of the ascending fibers of the posterior cords is observed to occur; however, it could also be mediated by the interconnection between the fibers of ascending orthodromic pathways and descending serotonergic pathways that modulate pain. At the molecular level, spinal

From: Head of the Pain Unit, Hospital Regional Universitario de Málaga, Málaga, Spain

Corresponding Author: Mariano Fernandez Baena, MD, PhD, MsC, E-mail: mfbagp@gmail.com
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stimulation causes an increase in the γ-aminobutyric acid (GABA) and acetylcholine levels, and a decrease in the glutamate levels (4).

BurstDR™ (Abbott, Abbott, TX) stimulation was postulated for the first time in 2010 by De Ridder et al (5) and seems to be based on different mechanisms of action than those of traditional tonic pulses. In a rodent model, Crosby et al (6) demonstrated that this stimulation pattern also led to a decrease in wide dynamic range neuronal firing in the dorsal horns; however, this decrease was not related to the GABAergic mechanisms. On the other hand, different imaging procedures, including fEGM (7), PET-TC (8), and fMRI (9), suggest that the effects of burst stimulation may reach brain areas that are not affected by tonic stimulation, such as the anterior cingulate cortex; which is related to the affective components of pain, such as catastrophism, attention, and vigilance. These effects are maintained for a certain amount of time after stopping stimulation (10), which may allow for cyclic administration of therapy in ON/OFF periods.

We present the case of a patient who developed neuropathic pain after total resection of a thoracic ependymoma and was managed with tonic and burst stimulation for approximately 10 years. To our knowledge, this is the first study to report the use of SCS for the treatment of neuropathic pain secondary to thoracic ependymomas.

CASE

A 27-year-old female patient was operated upon for spinal ependymoma in 2007, leaving pain in the lower extremities and the left rib region as sequelae. In her initial evaluation, she reported burning pain in both legs and feet, as well as in the left costal region, and painful paresthesias in both feet.

Pharmacological treatment with anticonvulsants and antidepressants was initiated with a partial response and the appearance of side effects that limited dose escalation. Intercostal nerve blocks were performed with local anesthetics and corticosteroids with no response.

In November 2012, a 16-pole/5-column surgical lead was implanted at the T9 level with adequate coverage of the painful area in the lower extremities, in which the Visual Analog Scale (VAS) score decreased from 8 of 10 to 2 of 5 without modifying the pain perception in the costal region. After a 19-day trial period, a subcutaneous electrode in the left subcostal region, with adequate coverage of the painful area, was added to the stimulation system. Because stimulation of the lower extremities could be achieved with 8 consecutive contacts of the surgical epidural lead, the other 8 could be canceled. The new subcutaneous electrode was connected to the free channel of the permanent rechargeable generator (Eon mini, St. Jude Medical Neuromodulation Division, Plano, TX), with adequate coverage of the costal area, reducing the VAS from 6 to 8 of 10 to 1 to 3 of 10, which allowed a decrease in analgesic medication.

In May 2013, the subcutaneous electrode became inefficacious and was replaced by another epidurally implanted at the T5 level. This combination improved pain relief, which remained for 3 and a half years, until the beginning of 2017, when symptomatic worsening and a decrease in the analgesic effect were observed. Throughout this period from 2012 to 2017 the patient was always treated with regular paresthesia-based tonic stimulation at frequencies ranging from 50 to 110 Hz, pulse widths of 200 to 350 μs, and pulse amplitudes around 4 to 5 mA in 2 independent areas (stim sets) for both pain regions.

In February 2017, the patient underwent a 2-week trial phase with burst stimulation. The leads were temporarily disconnected from the implanted generator and connected through percutaneous extensions to an external generator capable of administering this type of stimulation. After the test phase, the patient reported higher relief (VAS = 2) equal to the maximum obtained previously with conventional stimulation, and it was decided to connect the electrodes to a nonrechargeable permanent generator, programmed for burst stimulation (40-Hz bursts of 5 1000-μs /500-Hz pulses) in the continuous mode at 2.9 mA, which was later reduced to 0.5 to 1.0 mA in cycles of 30 seconds ON/90 seconds OFF. The patient has maintained stable pain relief and has not required programming adjustments to date (March, 2022).

Discussion

The surgical resection of ependymomas has been shown to achieve high survival and low recurrence rates, with 4 out of 5 cases following incomplete resection (11) and significantly positive results, even with partial resection being subsequently treated with radiotherapy (12). In general, the painful condition does not seem to improve after surgery or in the long term; on the contrary, the appearance of painful neuropathic syndromes is relatively frequent and does not seem to be related to

the achievement of total tumor resection, but rather to surgical manipulation, especially in large tumors. In the case described here, 2 very different and distant painful areas were established, with burning and intense pain in both feet and costal area.

SCS has proven to be a successful treatment for neuropathic pain, the most common being postlaminectomy syndrome, complex regional pain syndromes, radiculopathies, and peripheral neuropathies, with or without a diabetic component. In the context of the inflammatory response that occurs in any chronic pain condition, an interaction occurs between the release of proinflammatory agents and the molecular patterns of response to the damage that they cause. In this context, the recognition of pathogens, cytokines, and adhesion factors that remain elevated for weeks or months in several chronic pain conditions is the determining factor that leads to the development of chronic pain mediated by an inflammatory process (13). In studies on inflammatory mediators using burst stimulation, an increase in interleukin 10 (a key anti-inflammatory cytokine in the resolution of the inflammatory phase) has been found in patients with low back pain, maintaining stable levels of the proinflammatory substance HMGB-1 (high mobility group box 1) (14).

In our patient, the pain was located in 2 well-differentiated areas that were difficult to cover with paresthesia using a conventional stimulation system. The initial attempt to cover the entire painful area with a surgical 16-contact/5-column electrode was unsuccessful; therefore, an additional subcutaneous lead in the costal area was added to stimulate this area. In relation to the variation of inflammatory markers in peripheral nerve stimulation, since 2004, it has been known that this modality can modify the local concentration of biological mediators (15) and can have a direct effect on decreasing the concentration of inflammatory mediators, blood flow, and pain transmission (16).

A notable aspect of long-term electrical nerve stimulation is the appearance of tolerance. In a retrospective review of 234 patients, Hayek (17) estimated that 13% of patients experienced a complete loss of relief in the first 8 years of therapy after successful initiation. In a multicenter analysis of 954 patients published in 2017 (18), 101 units (10.6%) were explanted for insufficient pain relief. Burst stimulation has shown efficacy as a rescue therapy in patients who, despite adequate coverage of the painful area with tonic stimulation, failed or lost efficacy over time (19).

Our patient experienced loss of efficacy with tonic stimulation after 4 years of treatment, which was apparently due to the loss of coverage or significant variations in the stimulation parameters. The application of burst stimulation restored and even improved the previous relief, and these results have been sustained for the past 5 years, especially after decreasing the energy expenditure by means of amplitude reduction and cycled administration of the therapy.

CONCLUSION

Our experience suggests that SCS, among its various modalities, can be an adequate and long-lasting therapy for patients with pain secondary to the resection of spinal cord tumors.

REFERENCES

1. Rashad S, Elwany A, Farhoud A. Surgery for spinal intramedullary tumors: Technique, outcome and factors affecting resectability. *Neurosurg Rev* 2018; 41:503-511.
2. McGirt MJ, Chaichana KL, Atiba A, Attenello F, Yao KC, Jallo GI. Resection of intramedullary spinal cord tumors in children: Assessment of long-term motor and sensory deficits. *J Neurosurg Pediatr* 2008; 1:63-67.
3. Nakamura M, Tsuji O, Iwanami A, et al. Central neuropathic pain after surgical resection in patients with spinal intramedullary tumor. *J Orthop Sci* 2012; 17:352-357.
4. Cui J-G, O'Connor WT, Ungerstedt U, Linderoth B, Meyerson BA. Spinal cord stimulation attenuates augmented dorsal horn release of excitatory amino acids in mononeuropathy via a GABAergic mechanism. *Pain* 1997; 73:87-95.
5. De Ridder D, Vanneste S, Plazier M, van der Loo E, Menovsky T. Burst spinal cord stimulation: Toward paresthesia-free pain suppression. *Neurosurg Online* 2010; 66:986-990.
6. Crosby ND, Goodman Keiser MD, Smith JR, Zeeman ME, Winkelstein BA. Stimulation parameters define the effectiveness of burst spinal cord stimulation in a rat model of neuropathic pain. *Neuromodulation* 2015; 18:1-8.
7. De Ridder D, Vanneste S. Burst and tonic spinal cord stimulation: Different and common brain mechanisms. *Neuromodulation* 2016; 19:47-59.
8. Yearwood T, De Ridder D, Yoo HB, et al. Comparison of neural activity in chronic pain patients during tonic and burst spinal cord stimulation using fluorodeoxyglucose positron emission tomography. *Neuromodulation* 2020; 23:56-63.
9. Saber M, Schwabe D, Park HJ, et al. Tonic, burst, and burst-cycle spinal cord stimulation lead to differential brain activation patterns

as detected by functional magnetic resonance imaging. *Neuromodulation* 2022; 25:53-63.

10. Deer T, Wilson D, Schultz D, et al. Ultra-low energy cycled burst spinal cord stimulation yields robust outcomes in pain, function, and affective domains: A subanalysis from two prospective, multicenter, international clinical trials. *Neuromodulation* 2022; 25:137-144.
11. Savoor R, Sita TL, Dahdaleh S, et al. Long-term outcomes of spinal ependymomas: An institutional experience of more than 60 cases. *J Neurooncol* 2021; 151:241-247.
12. Oh MC, Ivan ME, Sun MZ, et al. Adjuvant radiotherapy delays recurrence following subtotal resection of spinal cord ependymomas. *Neuro Oncol* 2013; 15:208-215.
13. Chakravarthy KV, Xing F, Bruno K, et al. A review of spinal and peripheral neuromodulation and neuroinflammation: Lessons learned thus far and future prospects of biotype development. *Neuromodulation* 2019; 22:235-243.
14. Kinfe TM, Muhammad S, Link C, et al. Burst spinal cord stimulation increases peripheral antineuroinflammatory interleukin 10 levels in failed back surgery syndrome patients with predominant back pain. *Neuromodulation* 2017; 20:322-330.
15. Chae J, Yu DT, Walker ME, et al. Intramuscular electric stimulation for hemiplegic shoulder pain: A 12-month follow-up of a multiple-center, randomized clinical trial. *Am J Phys* 2005; 84:832-842.
16. Papuc E. The role of neurostimulation in the treatment of neuropathic pain. *Ann Agric Environ Med* 2013; 1:14-17.
17. 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; 18:603-608; discussion 608-609.
18. Van Buyten JP, Wille F, Smet I, et al. Therapy-related explants after spinal cord stimulation: Results of an international retrospective chart review study. *Neuromodulation* 2017; 20:642-649.
19. Reddy RD, Moheimani R, Yu GG, Chakravarthy KV. A review of clinical data on salvage therapy in spinal cord stimulation. *Neuromodulation* 2020; 23:562-571.