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CASE REPORT

Spinal cord stimulation in patients suffering from chronic pain after surgery for spinal intradural tumors: A case report and literature summary

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Abstract

Background: The prevalence of pain after treatment of a spinal intradural tumor is remarkably high, approximately up to 40% of the patients suffer from central neuropathic pain. Publications on spinal cord stimulation (SCS) and its effect on pain caused by intradural spinal tumors are rare. We discuss the case of a patient suffering from chronic pain after removal of a Th7 level meningioma who was successfully treated with SCS and give an overview of the literature.

Methods: MEDLINE database was searched for neuropathic pain and intradural tumors.

Results: The initial search identified 35 articles, including hand-searched manuscripts. Six articles were included for analysis.

Case Report: A 57-year-old female suffers from neuropathic pain in both legs after surgical removal of a Th7 level intradural meningioma. Postoperative magnetic resonance imaging shows no gross abnormalities, although she developed chronic pain in both legs. Pain in combination with side effects of analgesic intake are too disabling to have decent quality of life. A successful implantation of SCS is achieved at Th5 level as a treatment for the central neuropathic pain, and, at 36 months follow-up, there is significant pain relief and almost complete discontinuation of analgesics.

Discussion: Central pain from spinal intradural tumors may have a different mechanism of origin than pain seen after an acute spinal cord injury (SCI). However, the basic principles of neuromodulation are the same in both etiologies, as for successful stimulation intact pathways in the spinal cord are necessary. The efficacy of SCS as treatment in intradural spinal tumors is rarely described as only a handful of case reports are published. Interestingly, the case reports show that stimulation both above and below the lesion can be effective. In patients with incomplete SCI or intradural tumor resection stimulation below the lesion could be considered and tried in a trial setting before definitive implantation.

KEYWORDS
chronic pain, spinal cord injury, spinal cord stimulation, spinal intradural tumor

INTRODUCTION

Spinal cord stimulation (SCS) is an effective advanced therapy for patients refractory to therapy and medications used for the management of chronic, intractable pain. The use of SCS widely varies as it is used for chronic benign and malignant pain.[1,2] However, the effect of SCS on central pain caused by surgical removal of intradural spinal tumors, is limited as only a handful case reports are published.[3–5]

The authors present a case of successful implantation of SCS at Th5 level as a treatment for central neuropathic pain after Th7 meningioma removal and summarize the available evidence regarding the prevalence of central pain after surgical removal of intradural tumors and the efficacy of SCS as treatment for this origin of pain.

MATERIALS AND METHODS

Case report

History

A 57-year-old female with no important medical history presented in January 2018 with neuropathicpain in both legs after complete microsurgical removal of an intradural meningioma (WHO grade 1). The meningioma was located at level Th7 and resected through hemilaminectomy in July 2015 (Figure 1). Preoperatively, she experienced numbness in her legs and back pain. There was no paralysis of the legs, although she experienced limitations with balance and coordination. Postoperatively, within some weeks, she developed chronic pain in both legs. She described the pain as electrical shocks, tingling, stinging, and numbness. Postoperative magnetic resonance imaging showed no signs of stenosis or disk problems, no tumor recurrence or other abnormal findings.

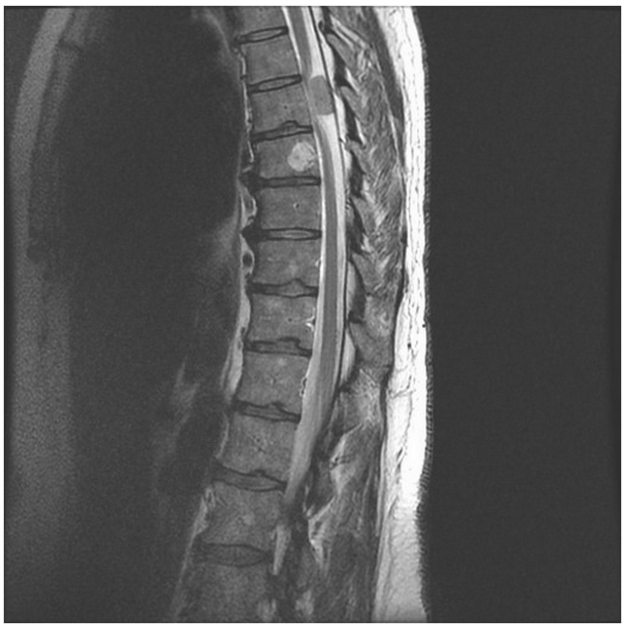

FIGURE 1 Preoperative sagittal T2W MRI showing the tumor and its relation to the spinal cord.

The pain failed to respond to an epidural injection, intravenous lidocaine 24 h, tramadol (150 mg/day), pregabalin (450 mg/day), amitriptyline (40 mg/day), and physical and psychological therapy. Furthermore, she used sertraline (200 mg/day) for depression.

Examination

Examination revealed hypesthesia in dermatome T6-8 with decreased sharp-blunt differentiation. All motor functions and reflexes were normal. No further abnormal findings were found in neurological examination. There were no signs of pyramidal tract dysfunction.

Preoperative questionnaires were conducted to assess the patient's quality of life (QoL), mental health and dealing with pain. These questionnaires showed a significant decrease in all dimensions.

Treatment

In December 2018, a trial SCS was performed by implanting a surgical paddle lead (Penta lead, Abbott) at Th5-6 level which was connected to an external stimulator (Figure 2). The Penta lead was chosen based on the fact that this lead is the shortest surgical paddle lead available and therefore requires preparation of maximal 2 interlaminar spaces to have the lead placed exactly in the midline. Deliberately we did not choose to implant a cylindrical lead via a percutaneous technique since we expected that this would cause problems due to the hemilaminectomy that was performed before and the occurrence of scar tissue in the epidural space. No complications were reported during the surgery and stay in the hospital. The trial stimulation lasted 16 days and showed significant pain relief, that is, >50% pain reduction in Numeric Rating Scale (NRS), in burstDR stimulation setting, although in the beginning the patient preferred the tonic–clonic stimulation. However, after 2 months the patient finally chose for burst stimulation, since she experienced a restless feeling in both legs when stimulated with tonic–clonic setting. After this successful trial a permanent implantable pulse generator was implanted (Proclaim 7 Elite, Abbott). The Abbott system was chosen due to the possibility of switching between tonic–clonic and burst stimulation. One month after permanent implantation the pain in both legs decreased from 8 to 1.5 measured with the NRS. At 4 months, the patient reported a 80% reduction in pain in comparison with before the implantation (NRS 2). Furthermore, the patient could reduce her analgesic daily intake to

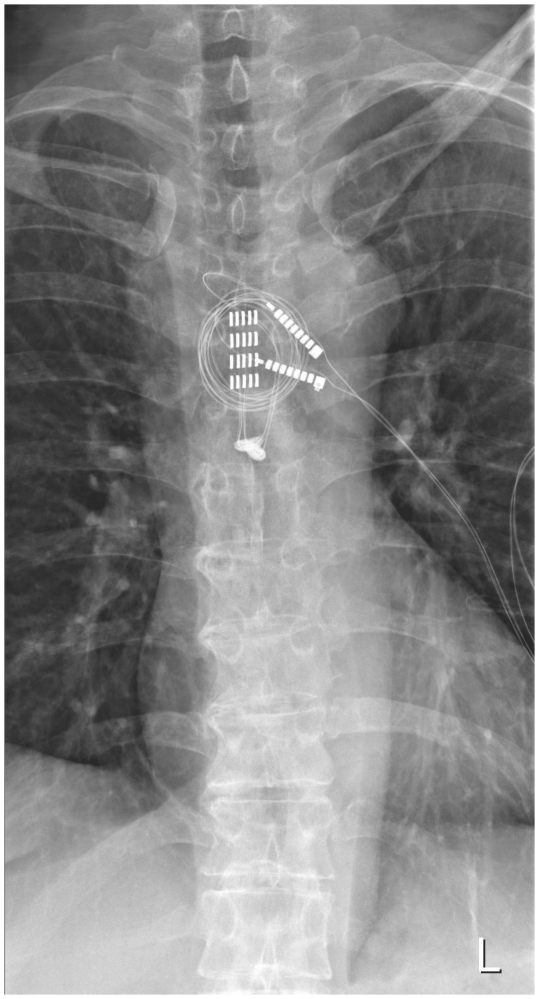

FIGURE 2 Postoperative X-ray in AP direction showing the lead at level Th5.

amitriptyline 40 mg, pregabalin 150 mg, and tramadol 100 mg. At 12 months follow-up, there was an increase of daily activities and her QoL improved significantly, and she could reduce the analgesic intake. At 24 months follow-up, amitriptyline and tramadol were stopped and the pregabalin was reduced to 75 mg. Daily functioning remained good to excellent. At 36 months follow-up, the patient was very satisfied with the effect of the neurostimulation (programming setting: program 1 = 4+5–6-8+9–10-; perception 1.4; target 0.6). The pain in her back and legs was minimally present. She only used amitriptyline 40 mg for the night because it made her feel more "comfortable."

Literature review

To evaluate the available evidence regarding the prevalence of central neuropathic pain and its treatment with SCS after surgical removal of spinal intradural tumors, a search strategy was implemented in PubMed on 5th of July 2021. The search strategy consisted of the following terms:

(Neuralgia[Mesh] OR neuropathic pain[tiab]) AND (Spinal Cord Neoplasms[Mesh] OR Spinal Cord Neoplasms[tiab] OR intramedullary spinal cord tumor[tiab] OR IMSCT[tiab] OR intramedullary[tiab] OR extramedullary spinal cord tumor[tiab] OR EMSCT[tiab] OR extramedullary[tiab]) AND (Surgical removal[tiab] OR surgery[tiab] OR surgical resection[tiab] OR Spinal Cord Stimulation[Mesh] OR Spinal Cord Stimulation[tiab] OR SCS[tiab])

This resulted in 28 original articles available for screening. Seven additional manuscripts were hand-searched bringing the total at 35 original studies. Evaluation of the full text resulted in inclusion of six papers which presented original prevalence numbers. Other papers were not relevant, did not differentiate in the results, or had no numbers available. The prevalence of central neuropathic pain after surgical removal of spinal intradural tumors is drawn from these six studies and are added to Table 1. If the central pain was treated with SCS, then the location of the lead(s), and the effect of SCS on pain was also noted.

RESULTS

Table 1 provides an overview of newly developed neuropathic pain after surgical removal of spinal intradural tumors. A distinction is made between intradural extramedullary and intradural intramedullary tumors. The group of intramedullary tumors are notorious for their high complication rates as approximately 40% (21.9%–56%) of the operated patients developed central pain.[6–8] Extramedullary tumors are generally of a compressing nature and are therefore easier to remove, resulting in fewer complication rates as only a handful cases presented with central neuropathic pain after removal of extramedullary tumors. Only three case reports were found, describing SCS as a treatment for the newly developed neuropathic pain: two patients underwent prior surgery for extramedullary meningioma, and one patient for intradural ependymoma. In these patients, with a relatively short follow-up, an excellent pain relief and discontinuation or reduction in analgesics is reported.

DISCUSSION

Spinal intradural tumors regardless being intramedullary or extramedullary are rarely described as being a cause for developing chronic pain. Even after surgery of these intradural tumors chronic pain is not a well-described entity, although the prevalence seems to be more or less up to 40%.[6–9] The pathophysiology is not known, the underlying mechanisms may be similar when compared to chronic pain after spinal cord injury (SCI), which is

TABLE 1 Overview of the literature: Clinical course of spinal intradural tumors, related neuropathic pain, and use of SCS

Study	Total of patients, *N*	Intramedullary	Extramedullary	Postoperative neuropathic pain, *N* (%)	SCS?	Placement of electrodes	Effect
Nakamura et al. (2012)[6]	85	43 ependymoma 17 astrocytoma 13 hemangioblastoma 8 cavernous angioma 2 neurilemmoma 1 lipoma 1 fibroma	None	48 (56%) moderate-to-severe pain (NPSI >10) 37 (44%) mild pain (NPSI <10)	None	N/A	N/A
Klekamp (2013)[7]	225	99 ependymoma 76 astrocytoma 28 hemangioblastoma 13 cavernous angioma 15 hamartoma 8 lipoma 7 dermoid cyst 6 metastasis 5 melanocytoma 4 ganglioglioma 2 neuroma	2 meningioma	21.9%	None	N/A	N/A
Babu et al. (2013)[8]	13	8 cavernous hemangioma	4 capillary hemangioma 1 cavernous hemangioma	23.1%	None	N/A	N/A
Eisenberg and Brecker (2002)[5]	1		C1 meningioma	1	Yes	Below the lesion (Th12)	9 months FU: nearly complete pain relief Analgesic intake reduced
Lee et al. (2009)[3]	1		Th5 meningioma	1	Yes	Above the lesion (Th1-2)	8 months FU: VAS greatly improved. Functional status improved
Benedetti (2013)[4]	1	C6 ependymoma		1	Yes	Below the lesion (Th8)	3 months FU: improvement of symptoms. Multiple drugs were discontinued
Present study	1		Th7 meningioma	1	Yes	Above the lesion (Th5-6)	36 months FU: nearly complete pain relief. Multiple drugs were discontinued or reduced

Abbreviations: FU, follow-up; N/A, not available; NPSI, Neuropathic Pain Symptom Inventory; SCS, spinal cord stimulation.

present in 60%–69% of the SCI population.[10] The main difference is that SCI is commonly seen in sudden, traumatic injury of the spine with impact on the spinal cord. The ascending and descending pathways within the spinal cord are severed with brute force, resulting in anatomic changes (gray and white matter may be damaged followed by Wallerian degeneration), which may lead to imbalance between excitatory and inhibitory pathways, and structural changes including intraspinal sprouting and remapping of central neurons. Additionally, secondary pathologic changes may follow due to an increase in excitatory amino acids (glutamate) and a decrease in inhibitory neurons (loss of normal tonic inhibitory processes). Neuroinflammatory changes (involvement of glial cells) promote regeneration and degeneration may also contribute to the development of central pain.[11,12] Animal studies suggest that different pathophysiologic mechanisms may be responsible for the development of chronic pain following spinal cord injury.[13] In patients with spinal intradural tumors, there is no acute impact. When the tumor is intradural extramedullary there is a gradual compression of the spinal cord, but in theory no destruction and changes in anatomical pathways, except the case that the patient is presented too late when having already developed a myelopathy. On the other hand, intradural intramedullary lesions can lead to destruction and anatomical changes within the spinal cord, but still different when compared with the situation as in acute SCI.

The pain that results from SCI can theoretically be divided into nociceptive and neuropathic pain with neuropathic pain further divided into above-level, at-level, and below-level pain, where level refers to the level of the spinal cord that was injured.[12–14] Below-level pain is localized to dermatomes distal to the injury site. It develops gradually and is spontaneous and stimulus-independent. At-level pain refers to pain in dermatomes near the injury site and develops shortly after the actual injury. This pain is often accompanied by thermal sensory deficits in the painful area.[15] Pain above the level of the injury site also occurs. Such a distinction is not described in patients suffering pain from spinal intradural tumors but is likely to be present.

In our case, the patient suffered from neuropathic pain in both legs, diagnosed as pain from failed back surgery syndrome. After discussing the patient in our multidisciplinary team, we chose to try neuromodulation as a last-resort therapy since all other treatments failed thus far with no other feasible treatment options left. With regard to the basic principles of neuromodulation, we choose to stimulate above the lesion, so cranial of the tumor location. These basic principles are based on the theory that modulation of the central nervous system is possible if intact ascending and descending pathways are present in the spinal cord. We were not sure whether there was no damage in the spinal cord at the level of Th7, although the postoperative MRI did not show gross abnormalities like myelopathy. Another uncertainty was that we were not sure whether we could stimulate both legs closely above Th7, since in a normal situation to stimulate the legs we routinely prefer to stimulate between the Th8 and Th12.[16] Furthermore, we choose to implant a surgical paddle lead and not a percutaneously implanted cylindrical lead since we expected that epidural fibrosis and spinal adhesions due to surgical removal of the tumor would make it difficult to guide the percutaneous lead to the preferred location above the level of the tumor location. Dorsal root ganglion and peripheral nerve stimulation were not considered to be reasonable options in this patient since the pain was located diffuse in both legs, and not specific bound to 1 or 2 dermatomes, which would best be achieved by central stimulation. Furthermore, intrathecal drug delivery therapy was discussed, however, not seen as best available option due to the higher risk of complications such as overdoses, underdoses, and unwanted side effects.

Two case reports in the literature overview in Table 1 show that SCS placement below the lesion can also have an effect on neuropathic pain. Eisenberg and Brecker[5] placed an electrode with success at Th12 level while the surgical removal of the meningioma was at C1 level. In addition, Benedetti[4] also described improvement of symptoms and discontinuation of drugs at the electrode level of Th8 while the ependymoma was removed at C6 level. The evidence is however limited and possibly biased as below-level stimulation is rarely performed since pain anesthesiologists hesitate to guide the lead above an operated level, afraid that the lead will get stuck due to anatomical abnormalities. Trial stimulation below the level of tumor location is not performed as far as we could find in our search, or perhaps the outcomes were not worth publishing. As described, pain doctors are taught to implant the lead above the level where the pain is generated in order to have intact anatomical pathways up to the brain. The question is whether it is possible to modulate everywhere within the spinal cord, regardless the level where the pain is generated.

The correct placement of the lead(s) with regard to the lesion site remains unclear as studies reported different placement levels with still significant pain relief. Conventional SCS implanted proximal to the lesion which may attenuate above-level and at-level pain generates activation of supraspinal mechanisms resulting in inhibition of pain perception, affection, and descending facilitation in the brain. Implantation distal to the lesion which may attenuate below-level and at-level pain generates activation of spinal segmental mechanisms resulting in inhibition of central sensitization and disinhibition in the dorsal horn.[17] The spinal mechanisms of tonic SCS can be further explained due to the release of GABA into the extracellular space in the spinal dorsal horn while intracellular GABA is reduced.[18] The supraspinal mechanisms are the result of activation of supraspinal areas and modulation of incoming nociceptive signaling at the

spinal levels through their descending projections. In SCI pain, it is possible that supraspinal mechanisms, hyperexcitability of wide dynamic range neurons near and proximal to the lesion, and sensitization of nociceptive-specific and low-threshold dorsal horn neurons may play an important role.[19] Activation of thermosensory nociceptive neurons in clinically complete SCI patients mimics chronic pain sensations implying that activity in residual spinothalamic pathways plays a crucial role in maintaining central pain.[20] In addition, the SCI can interrupt descending inhibitory pathways arising from the brainstem which play an important role in modulation of dorsal horn neurons. The hyperexcitability of these neurons can take place far below the level of injury and pathological activity of intact dorsal horn neurons may arise due to inflammatory processes associated with degeneration of neighboring axon terminals and neurons in the dorsal horn.[20]

Cioni et al.[21] concluded that in their series of 25 subjects suffering from intractable pain due to a chronic spinal cord lesion ranging from traumatic to postsurgical, there was no relation between the electrode level and analgesic effect. Unfortunately, the results were not distinct for the postsurgical group, resulting in exclusion of the results in our literature overview. Based on further analysis of the results of Cioni et al. by dividing the spinal cord injuries according to their location, one might conclude that placement of the electrode is only likely to be successful proximal to the site of injury within the spinal cord. However, percutaneously inserted stimulation above or proximal to the lesion cannot always be performed due to excessive scar tissue around the lesion. The preferred option of SCS placement is above the lesion due to the intact tracts that are needed for stimulation. However, stimulation below the lesion also shows promising results which could be explained due to the presence of residual tracts.

Interestingly, Onishi-Kato et al.[22] found in univariate analyses regarding resection of intramedullary tumors that intraoperative hypotension, postoperative corticosteroids, and decrease in Japanese Orthopedic Association scores were found to be independently associated with postoperative chronic central pain. The patient in our case suffered from an extramedullary tumor which may have a different pathophysiology with regard to the origin of the chronic pain. Nevertheless, it is remarkable that administration of corticosteroids and intraoperative hypotension, which could be avoided or modified during perioperative management, have a significant correlation with central pain and intramedullary tumor resection.

Finally, a last but important point is the awareness that in this group of patients with spinal intradural tumors follow-up scans are necessary. Not all neuromodulation systems are MRI compatible, especially not when separate extension cables are used. Best is to connect the lead direct into the IPG, without using extension cables. In these patients, the whole system is MRI conditional for 1.5T MRI scans like in our patient. An alternative may be to do the follow-up using CT scans with and without contrast.

CONCLUSION

Central neuropathic pain after surgical removal of spinal intradural tumors seems to be more prevalent than generally reported in the literature, with intramedullary tumors being the most prevalent cause. The evidence of a positive effect of SCS for the treatment of pain in these patients is limited. However, a number of case reports including the present study report significant pain relief and reduction of analgesics in patients who underwent removal of an intradural tumor. The best location for the SCS electrode, above or below the lesion, remains unknown. In complete SCI, the preferred option seems to be above the lesion, while in patients with incomplete SCI or intradural tumor resection stimulation below the lesion could be considered and tried in a trial setting before definitive implantation. More research is needed to confirm the efficacy of SCS for central pain and the best electrode location with regard to the lesion.

AUTHOR CONTRIBUTIONS

Robin K. Noordhof undertook the description of the case report, review of the literature and discussion. Saman Vinke provided feedback regarding grammar, vocabulary, and structure including use of figures. Erkan Kurt acted as the independent reviewer of the literature and manuscript. All authors participated and acted as an author as required in the authorship and contributorship guidelines and gave their input and feedback.

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CONFLICT OF INTEREST

The authors have nothing to disclose.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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