Interventional Pain Management Reports
ISSN 2575-9841 Volume 3, Number 2, pp 41-48

Case Report

Spinal Cord Stimulation in Buerger's Disease – A Case Report

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Buerger's disease (BD) or thromboangeitis obliterants is a nonatherosclerotic segmental inflammation of the medium- and small-size arteries and vessels of the extremities. The pathogenesis of this process remains unclear. This disease is typically seen in male smokers under 45 years of age, and successful therapy is possible only with abstinence from tobacco. Methods to control ischemic pain include nonpharmacological and pharmacological options, such as prostanoids, or surgical intervention (sympathectomy or revascularization). This case report describes an unusual case of Buerger's disease in a 60-year-old woman with a moderate smoking habit. Despite apparent tobacco abstinence and therapeutic optimization, there was no clinical improvement in this patient with pharmacological treatment. Attending to the imminent risk of amputation of her fingers, spinal cord stimulation (SCS) system implantation was the chosen therapeutic option. Transcutaneous oxygen pressure (TcPO2) was measured at different points in time after implantation and there was a significant increment of TcPO2 in both hands. In fact, the patient reported no pain after the first month of spinal stimulation; analgesics were progressively reduced and complete healing of ulcers was achieved. Furthermore, the patient reported a substantial improvement in her quality of life and total functional recovery in her hands mobilization after 6 months of treatment. The Brief Pain Inventory Scale and EuroQol-5D scale were used to evaluate disease progression and its impact on quality of life. SCS system implantation is considered a safe procedure and cost-effective in the long term. The mechanisms behind these effects are still unknown, but SCS is a promising treatment option. More studies that include larger numbers of patients are needed.

Key words: Buerger, tobacco, ischemia, amputation, electrical spinal cord stimulation, transcutaneous oxygen pressure

Buerger's disease (BD) or thromboangiitis obliterans is a nonatherosclerotic segmental inflammation of the medium- and small-size arteries and vessels of the extremities. Although this disease often affects young adult men, the incidence in young women is also increasing (1-5).

The pathogenesis of this inflammatory process remains unclear, but there is a strong association with cigarette smoking or environmental tobacco smoke exposure (6). Moreover, some studies highlight that genetic and autoimmune factors may be other possible causal factors. However, more studies are needed in order to clarify BD pathogenesis and identify its risk factors (7,8).

Onset of BD often occurs between 40 and 45 years of age. Clinically, BD begins with ischemia of the distal small vessels of extremities (arms, hands, legs, and feet). Patients may present with limb claudication (9), vasospasm (Raynaud's phenomenon), functional impairment, and severe pain. Other signs and symptoms of the disease may include numbness

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and tingling in the limbs. In the most severe cases, patients may present ulcerations and gangrene in their digits. There is almost always more than one limb affected and progression of the disease may lead to involvement of more proximal arteries. The literature also reports the involvement of cerebral, coronary, lung, renal, and mesenteric arterial systems (9-12).

A clear diagnosis of thromboangiitis obliterans is difficult to establish and several different criteria have been proposed for its diagnosis (13). In 1990, Kumar et al (14) asserted that the following criteria must be met for the diagnosis to be made: age under 45 years; history of tobacco use; presence of distal-extremity ischemia indicated by claudication, pain at rest, ischemic ulcers or gangrenes and non-invasive vascular testing; exclusion of autoimmune diseases, hypercoagulable states, and diabetes mellitus; exclusion of a proximal source of emboli by echocardiography or arteriography; and consistent artheriographic findings in the clinically involved and noninvolved limbs (14-17).

Complete smoking cessation is the best treatment approach to stop disease progression. Even using methods of nicotine replacement may keep the disease active (6).

Some nonpharmacological measures like physical exercise and care to avoid thermal, chemical, or mechanical injury should always be present.

Several pharmacological and surgical therapies have been proposed. The former include the use of prostanoids, anticoagulants, platelet antiaggregants, nonsteroidal anti-inflammatory drugs, fibrinolytics, calcium agonists, and hemorheologic agents (13). Prostanoids, such as Iloprost and PGE1, are widely used and data show a better outcome with Iloprost versus aspirin (6,18).Surgical revascularization is not an option in most cases because of the diffuse segmental involvement (19).

Sympathetic block has been shown to provide short-term pain relief and to promote superficial ischemic ulceration healing, but does not decrease the limb amputation rate (6,10); the same applies to sympathetic pharmacologic blockade (20-22).

Electrical spinal cord stimulation (23) is an accepted therapeutic method because of its analgesic effects, the improvement of skin microcirculation in the treated area (13), and the healing of ulcers in severe peripheral atherosclerotic arterial disease (24). The mechanisms behind these effects are still unknown (6,19,23,25-28).

This disease significantly impairs patients' quality of life and is associated with elevated health care costs. In spite of the available therapeutic options, about 20% of patients undergo limb amputation (12).

CASE REPORT

A 60-year-old white woman, whose background history included a moderate smoking habit (10 to 15 cigarettes per day for 30 years), dyslipidemia, and psoriasis, was admitted to the hospital with ungueal ulceration and severe pain in the right thumb.

Further investigation revealed episodes of Raynaud's phenomenon with 10 years of evolution. Blood test markers ruled out collagenopathies or other autoimmune diseases. Angiography of the upper limbs showed patency of the arterial tree to handle, and then only collateral branches made up the blood supply. A Doppler ultrasound study revealed a triphasic humeral waveform and a monophasic radial and cubital waveform.

On the basis of these findings, antiaggregant treatment was initiated using 150 mg of acetylsalicylic acid; analgesic therapy with paracetamol, 375 mg, and tramadol, 37.5 mg, twice a day; and vasodilator therapy with prostaglandin perfusion (iloprost).

After 4 months, the patient was referred to the chronic pain unit for treatment. She reported persistent pain in both hands with frequent periods of pain intensity exacerbation and recurrent ulcer infections. Pain was characterized as burning, tingling, cold pain and pinprick sensation. Maximum pain intensity on the 0 to 10 Numeric Rate Scale (NRS-11) was 9, with a mean NRS-11 score of 6 in the previous week. No relief factors were identified, and pain worsened with cold and movement. Objective examination revealed worsening ulcerative lesions distally in the second,

third, and fourth fingers of the right hand and third finger of the left hand. Both hands were cyanotic and presented no sensory changes (such as allodynia, hypoesthesia to touch or prick) at physical examination.

At this point, the patient had quit smoking 15 months prior and analgesic therapy was optimized, starting with 25 mg of oral pregabalin (titrated to 50 mg) twice a day and 17.5 mcg/h of transdermal buprenorphine (titrated up to 35 mcg/h) Once a day. After 8 months of follow-up by the chronic pain unit, her symptoms persisted despite optimal analgesic treatment and tobacco cessation. Attending to an eminent risk of finger amputation, treatment with SCS was decided upon after multidisciplinary discussion. This therapy was explained to our patient and informed consent was obtained. A psychological evaluation was also performed to assess the patient´s psychological conditions in order to proceed with SCS implantation.

The procedure was carried out in a single stage. An octapolar electrode catheter (Medtronic Neurological Inc., Minneapolis, MN) was inserted at the C4 intervertebral space level. The epidural space was approached at the T10-T11 level and electrodes were advanced under fluoroscopic guidance. Paresthesias were elicited in both hands for correct positioning confirmation and a generator (Medtronic Neurological Inc., Minneapolis, MN) was placed in the left flank pouch. The patient was discharged the day after the procedure uneventfully.

After SCS system placement, ulcers on both hands gradually began to recover. The patient reported no pain after the first month of spinal stimulation and analgesics were progressively reduced until total cessation. Ulcerations on her hands completely healed after 3 months. Eight months after SCS, the patient remained asymptomatic without any analgesic therapy. The patient reported substantial improvement in her quality of life (EuroQol-5 D scale) (29,30) and total functional recovery in her hands mobilization (Brief Pain Inventory Scale; Fig. 1) (31-33).

Transcutaneous oxygen pressure (TcPO2) (34,35) was measured at different points in time: before implantation of the SCS and 1, 3, 4, 6, and 8 months after implantation (Fig. 2). During this follow-up, there was a significant increment of TcPO2 in both hands, except in the period between the first and third month of follow-up in the patient´s right hand due to inadequate device utilization by the patient (low amplitude stimulation parameters). After receiving appropriate patient education about the device´s utilization, this situation was completely reverted (Fig. 2).

DISCUSSION

Buerger's Disease

As described above, Buerger's disease more commonly affects young men and usually lower limbs. We present the unusual case of a middle-aged woman whose disease affected both hands. Diagnosis is based on clinical, angiographic, and histologic criteria. The presence of distal arterial lesions in smokers in whom other entities have been ruled out supports a diagnostic suspicion. Autoimmune diseases, connective tissue diseases, and hypercoagulable states were excluded with appropriate blood tests. Angiography supports the diagnosis, showing the typical patterns of bilateral segmental stenosis in the distal vasculature ("cork-screw" appearance) (36), with the absence of other vascular pathologies, such as calcifications or atheroma plaques (4,10).

Even though the main strategy in the prevention of disease progression is complete cessation of tobacco consumption, some patients are still noncompliant with this recommendation. Despite apparent tobacco abstinence and therapeutic optimization, there was no clinical improvement in this patient with pharmacological treatment (10).

Attending to the imminent risk of finger amputation, SCS implantation was the chosen therapeutic option.

SCS should be considered a therapeutic option to be used when all other treatments have failed. However, some studies argue that SCS should be considered earlier as a therapeutic option, given the significant improvement it provides to these patients (13,37). Indeed, SCS provides reduction in length of hospital stay and health care resource utilization, prevention of amputation, functional recovery, quality of life improvement, and effective pain control. Therefore, SCS is cost-effective in the long term (38). However, more studies that include larger numbers of patients still remain necessary (13,19).

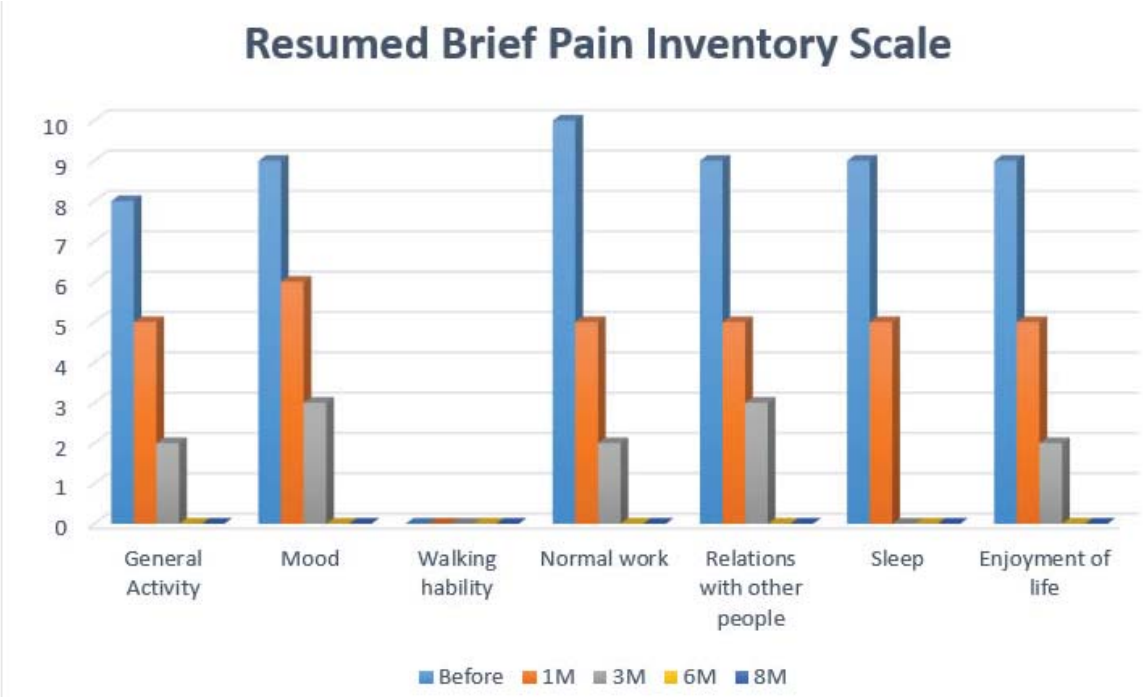

Fig. 1. Resumed Brief Pain Inventory Scale evaluates before SCS treatment and 1,3,6, and 8 months after SCS system implantation. 0- does not interfere; 10- completely interferes. “Normal work” includes housework and outside work.

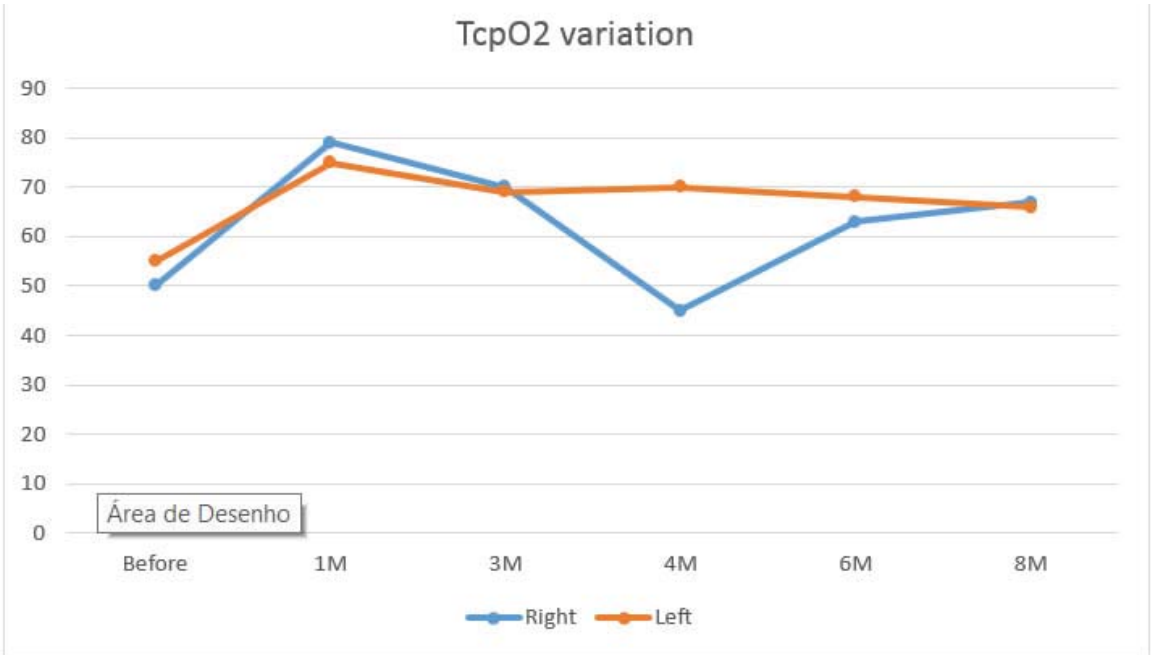

Fig. 2. Evolution of the TcpO2 of the right and left hands before SCS treatment and 1, 3, 6, and 8 months after SCS system implantation.

The patient described in this case report obtained significant relief from ischemic pain, ulcer healing, and significant improvement in quality of life and functionality. In order to monitor and evaluate the therapeutic response, transcutaneous oxygen pressure (TcPO2) was measured in affected extremities. This is a simple, noninvasive and effective method of assessing distal microcirculation. Numerous reports have evaluated TcPO2 in staging peripheral arterial occlusive disease and predicting therapeutic response (6,34). Values below 40 mm Hg indicate suboptimal perfusion, while values below 30 mm Hg are associated with critical ischemia in the lower limbs (35,39,40). In this patient, the initial value was 50 mm Hg in the right hand and 55 mm Hg in the left.

Five days after the SCS system placement, the patient described improvements in color, temperature, and fine motor skills of both hands. She reported a maximum pain intensity of 4 on the NRS-11. One month later, the clinical improvement was accompanied by an increase in TcPO2 (Fig. 2), an NRS-11 score of 0, and a reduction in analgesic requirement. The patient stopped all analgesic medications within 2 months of SCS. In the period between the first and third month of follow-up, we observed a reduction in TcPO2 in the patient´s right hand due to inadequate device utilization by the patient. Despite the obtained values, the positive influence of SCS has been proven by the absence of pain or new trophic lesions, and by ulcers healing. As indicated by the Brief Pain Inventory Scale (Fig. 1), the patient reported at 6 months that BD no longer affected her daily life, specifically her relationships with others, mood, quality of sleep, work, and general activity. Maximum satisfaction was achieved at the sixth month.

The EuroQol-5D scale (EQ-5D) is a standardized instrument developed by the EuroQol Group as a measure of health-related quality of life (29,41-44). In comparison with the initial value of 30 out of 100 on the EQ-5D scale, at the sixth month of treatment, the value was 95 out of 100, reinforcing the finding that SCS had a very significant impact on the patient's quality of life.

Spinal Cord Stimulation

Cook et al (8) first proposed SCS for the treatment of Peripheral Vascular Disease (PVD) in 1976. Since then, many studies have been done to access its efficacy, and it has become an accepted therapy for specific patients with vascular diseases (9). The mechanisms by which SCS provides its benefits are not completely understood, but it may have several actions. Electrodes for SCS are implanted along the posterior epidural space, thus preferentially stimulating the dorsal columns of the spinal cord (45).

Current knowledge supports the antidromic hypothesis, in which SCS activates the sensory fibers; the neural information is transmitted from the site of stimulation in the spinal segments to the nerve endings in peripheral tissues, leading to the release of vasodilators such as nitric oxide, prostaglandins, and calcitonin (46). Another proposed mechanism is that SCS decreases sympathetic outflow and attenuates the constriction of arterial vessels (47). In addition to these 2 classic hypotheses, other mechanisms are also potentially involved in SCS effects. One is that the release of vasodilators may improve endothelial function and suppress the formation of new atherosclerotic plaques; second, that SCS may not only increase local blood flow in the ischemic area in the short term, but also promote angiogenesis, increasing blood flow to the ischemic area over a long period (6,47-50).

Reduction of pain in these patients is probably associated with improvement in limb perfusion, antidromic stimulation of TRPV1-sensitive fibers, and the increment of endorphin release at the spinal level (47,50,51).

Currently SCS is one therapeutic option for ischemic pain treatment; the overall beneficial effects last for at least one year in 80% of patients, and for up to 5 years in 60% of patients (27,52-55).

SCS system implantation is considered a safe procedure. The most common complications are hardware-related, such as lead migration or fracture. Biological complications such as infection or pain over the device are less common, and neurological injury is rare. In a recent study on complications related to SCS, the most feared neurological complications (hematoma or abscess) had an overall incidence of 1.1% (56,57).

There are currently no controlled trials published on

the efficacy of SCS in the treatment of Buerger's disease. Its efficacy in this specific population has been supported in a retrospective observational study. In this study, 29 patients underwent SCS for Buerger's disease and only 2 patients had major amputations after SCS, while the other 27 patients reported some benefit from SCS (4 were submitted to minor amputations) (6). Several case reports have also been published that invariably show excellent efficacy of SCS in Buerger's disease (Table I) (13,19,24,48,58-60).The results of these reports support the use of SCS therapy in refractory cases of Buerger's disease, not only for pain control but also to improve perfusion of limbs and reduce amputation ratio (58).

Table 1. Case reports about SCS in Buerger's disease.

Study	n	Affected limb	Improvement	Amputation	Follow-up
Talis 1983	1	LL	Yes	No	9 mo
		UL	No	No	
Augustinsson 1985	1	*	Yes	No	4 mo
Swigris 1999	1	UL	Yes	No	1 mo
Chierichetti 2002	3	LL	Yes	No	*
Pace 2002	3	LL	Yes	No	4 mo
Vaquer Quiles 2009	2	LL	Yes	No	4 & 15 mo
De Andres 2013	3	LL	Yes	1	6 mo
Ryu 2013	1	UL	Yes	No	6 mo

LL = lower limb; UL = upper limb; *Not reported

Fig. 3. a) Hands before SCS implantation; b) 1 month after SCS implantation.

In the case reported here, not only were complete pain relief and functional recovery achieved, but complete remission of the patient's digital ulcers was also obtained with SCS (Fig. 3).

CONCLUSION

Buerger's disease is a peculiar form of nonatherosclerotic segmental inflammation of vessels that can seriously affect patients' quality of life. SCS is a highly useful therapy for pain control and healing of ulcers, even in severe peripheral atherosclerotic arterial disease. This treatment should be considered for patients who do not respond to standard therapy and to minimize amputation risk. The absence of severe complications, the minor surgical procedure, and the good outcomes across several studies should encourage more use of this therapy.

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