CASE REPORT

EFFECTIVENESS OF INTRATHECAL BACLOFEN FOR INTRACTABLE STIFF-PERSON SYNDROME: A CASE REPORT

Bruce ZHANG, MD1, Richard LAU, MD1, David VAN WHY, MD2,3 and Michael SAULINO, MD, PhD2,3

1Department of Physical Medicine and Rehabilitation, Temple University Hospital, Philadelphia, PA, USA
2MossRehab, Elkins Park, PA, USA
3Department of Rehabilitation Medicine, Sidney Kimmel Medical College, Philadelphia, PA, USA

Background: Intrathecal baclofen is considered an adjuvant therapy for patients with intractable spasms due to stiff-person syndrome. There is increasing evidence to support the use of intrathecal baclofen in the management of symptomatic stiff-person syndrome, with improvement in function.

Case report: A 38-year-old woman with stiff-person syndrome initially presented to inpatient rehabilitation for intractable muscle spasms. The symptoms made her non-ambulatory and limited her tolerance to wheelchair use for mobility. The patient underwent up-titration of oral baclofen and diazepam, with concurrent intravenous immunoglobulin cycles, leading to transient symptom relief. She agreed to explore intrathecal baclofen therapy. An initial trial of a single bolus of 50 μg intrathecal baclofen resulted in a significant decrease in spontaneous spasms, enabling modified independence in transfers and ambulation. The patient was subsequently implanted with a permanent intrathecal delivery system. To date, the intrathecal baclofen had been titrated to 186 μg per day with simple continuous delivery. The patient was weaned off oral baclofen. She attained complete functional independence with ambulation without the need for assistive devices, and has had no lasting post-procedural complications to date.

Conclusion: This case report adds to the increasing evidence of cases of refractory stiff-person syndrome managed successfully using intrathecal baclofen therapy.

Key words: stiff-person syndrome; intrathecal baclofen; intrathecal therapy.

Accepted Feb 4, 2021; Published Mar 3, 2021
JRM-CC 2021; 4: jrmcc00052

This case describes a woman with refractory stiff-person syndrome (SPS) who derived marked clinical improvement with intrathecal baclofen (ITB) therapy after failing up-titration of oral diazepam and baclofen with concurrent intravenous immunoglobulin (IVIG) cycles. Oral baclofen and diazepam are considered first-line therapies for symptomatic treatment of SPS, but often require aggressive up-titration, with at times, intolerable side-effects. IVIG is considered next-line therapy, with
the potential for symptom management and alteration of disease progression (1, 2). Case reports and series have demonstrated the viability of ITB therapy as an effective option for patients with intractable spasms due to SPS (3–7). This case report serves to add to the literature suggesting the efficacy of ITB as a successful adjuvant therapy. The notable aspect of this particular case is the significant functional improvement associated with ITB therapy.

**CASE REPORT**

A 38-year-old woman with a medical history of type I diabetes mellitus and SPS initially presented to inpatient rehabilitation with intractable and painful muscle spasms due to SPS. The diagnosis of SPS was confirmed by elevated anti-glutamic acid decarboxylase antibody levels (>250 IU/mL). Her symptoms were episodic in nature and triggered by light palpation along the lower limbs. Emotional distress also worsened symptoms. Episodes would last up to 8 h per day. Examination was notable for severe and painful muscle flexor spasms, which were clonic and diffuse. The spasms were particularly notable in her left lower limb with corresponding left ankle inversion, and right upper limb with elbow flexion and forearm supination. The patient underwent serial up-titration of oral baclofen up to 15 mg 3 times a day and diazepam up to 20 mg every 6 h, with concurrent IVIG cycles, with only transient symptom control. Her symptoms made her non-ambulatory and limited her tolerance to using a wheelchair for mobility. She also required moderate-to-maximum assistance for bed mobility, transfers and lower limb dressing. The patient was subsequently referred to the spasticity clinic to be assessed for ITB therapy. She underwent a trial of a single bolus of 50 μg baclofen via a lumbar puncture at the L3–L4 interspace (Fig. 1A and Fig. 1B), resulting in a significant decrease in spontaneous spasms, which lasted for hours. She demonstrated modified independence on transfers and ambulation following the test dose procedure, without requiring an assistive device. The patient was then referred to neurosurgery and ultimately implanted with a SynchroMed II intrathecal delivery system (Medtronic, Inc. Minneapolis, Minnesota, USA), with the catheter tip placed at the T8 spinal level. Her post-procedural course was complicated only by a transient post-dural puncture headache. To date, her ITB has been titrated to 186 μg per day with simple continuous delivery. The patient was weaned off oral baclofen and required only intermittent oral diazepam, with 5 mg once or twice daily. To date, she has mild allodynia in the left lower limb. She attained complete functional independence with ambulation and continues ambulating without needing an assistive device. She remains independent in bed mobility, lower limb dressing, and transfers. She continues ITB therapy with occasional IVIG cycles, directed by neurology. Her baclofen dose has been stable for 36 months following the titration phase of therapy. She has experienced no lasting adverse effects from ITB therapy.

**DISCUSSION**

SPS is a rare disorder, consisting of muscle rigidity and rhythmic spasms, which can cause severe disability with impaired ambulation. The symptoms of SPS are thought to be secondary to decreased inhibition within the central nervous system (CNS) due to antibody-derived inhibition of glutamic acid decarboxylase (GAD), a crucial enzyme within the gamma amino butyric acid (GABA) formation pathway (1, 2). Patients have serum anti-GAD antibodies and, subsequently, have decreased GABA within the CNS. It is unclear whether titre levels correspond with clinical severity or presentation (8). The disease process is
Intrathecal baclofen therapy for stiff-person syndrome

CONCLUSION

Although it is considered an adjuvant therapy, case reports and series have demonstrated the viability of ITB therapy as an effective option for patients with intractable spasms due to SPS (3–7). This case report adds to the growing evidence of successfully managed cases via ITB therapy.

ACKNOWLEDGEMENT

This case report was presented as a poster at the 2019 Annual Assembly of the American Academy of Physical Medicine and Rehabilitation.

Dr. Saulino has served on speakers boards and has received funds for research from Medtronic, Inc.

The authors have no conflicts of interest to declare.

REFERENCES

1. Dalakas MC. Stiff Person syndrome: advances in pathogenesis and therapeutic interventions. Curr Treat Options Neurol 2009; 11: 102–110.
2. Baizabal-Carvallo JF, Jankovic J. Stiff-person syndrome: insights into a complex autoimmune disorder. J Neurol Neurosurg Psychiatry 2015; 86: 840–848.
3. Abbatemarco JR, Willis MA, Wilson RG, Nagel SJ, Machado AG, Bethoux FA. Case series: intrathecal baclofen therapy in stiff-person syndrome. Neuromodulation 2018; 21: 655–659.
4. Maramattom B. Intrathecal baclofen pump implantation in a case of stiff person syndrome. Neurol India 2010; 58: 115.
5. Ho BL, Shih PY. Successful intrathecal baclofen therapy for seronegative stiff-person syndrome: a case report. Acta Neurol Taiwan 2008; 17: 172–176.
6. Stayer C, Tronnier V, Dressnandt J, Mauch E, Marquardt G, Rieke K, et al. Intrathecal baclofen therapy for stiff-man syndrome and progressive encephalomyelopathy with rigidity and myoclonus. Neurology 1997; 49: 1591–1597.
7. Seitz RJ, Blank B, Kiwit JCW, Benecke R. Stiff-person syndrome with anti-glutamic acid decarboxylase autoantibodies: complete remission of symptoms after intrathecal baclofen administration. J Neurol 1995; 242: 618–622.
8. Nakajima H, Nakamura Y, Inaba Y, Tsutsui C, Unoda K, Hosokawa T, et al. Neurologic disorders associated with anti-glutamic acid decarboxylase antibodies: a comparison of anti-GAD antibody titers and time-dependent changes between neurologic disease and type 1 diabetes mellitus. J Neuroimmunol 2018; 317: 84–89.
9. Awaad Y, Rizk T, Siddique I, Roosen N, McIntosh K, Waines GM. Complications of intrathecal baclofen pump: prevention and cure. Int Sch Res Notices 2012; 2012: 1–6.
10. Meineck HM, Tronnier V, Rieke K, Wirtz CR, Flügel D, Schwab S. Intrathecal baclofen treatment for stiff-man syndrome: pump failure may be fatal. Neurology 1994; 44: 2209–2210.
11. Bardutzky J, Tronnier V, Schwab S, Meineck HM. Intrathecal baclofen for stiff-person syndrome: life-threatening intermittent catheter leakage. Neurology 2003; 60: 1976–1978.