

Stiff Person Syndrome with Good Treatment Response to Intrathecal Baclofen

Dinesh Mohan Chaudhari* and Pushendra Nath Renjen

Indraprastha Apollo Hospital, New Delhi, India

Abstract

Stiff person syndrome is a rare disorder affecting the musculoskeletal system due to an underlying autoimmune process. Our case describes a 36 year old female who presented with painful, distressing, intermittent muscular rigidity and a possible associated seizure disorder. The key highlight of our case is the misdiagnosis of her disease in the early stage and the successful management of stiff person syndrome with intrathecal baclofen.

Keywords: Stiff person syndrome; Musculoskeletal; Autoimmune; Seizure disorder

Background

Stiff person syndrome (SPS) is an autoimmune disease characterised by intermittent muscular rigidity and painful muscle spasms. It begins in the axial and proximal muscles, progressively involving the distal muscles resulting in profound disability [1]. Being a rare disease, it is often under-diagnosed and the treatment of cases are challenging. Our case report describes a patient who was initially misdiagnosed before a confirmed diagnosis of stiff person syndrome was made. She had been receiving oral doses of baclofen but showed no improvement. However, upon receiving intrathecal baclofen as a symptomatic treatment for SPS, a good clinical outcome was observed.

We report this case to emphasize the importance of maintaining a high clinical suspicion for SPS in patients with a similar presentation and confident use of intrathecal baclofen which improves the functional status significantly.

Case Presentation

A 36 year old female presented to our hospital with stiffness of the lower back and right lower limb of three years duration. She had been receiving oral baclofen as a symptomatic treatment for a suspected HLA B27 negative Ankylosing Spondylitis, but did not have any relief. She also gave a history of generalized tonic clonic seizures (GTCS) followed by loss of consciousness, so she was receiving oral carbamazepine as a treatment for suspected lumbo-sacral intervertebral disc prolapse with an isolated seizure disorder. She suffered four GTCS episodes in the duration of three years. Following this, during an isolated generalized painful spasm episode, she sustained a right-sided neck of femur fracture.

On physical examination she was conscious, co-operative and alert. No pallor, icterus or lymphadenopathy. Neurological evaluation revealed muscular rigidity of lower limbs. Her Modified Ashworth scores for spasticity (Table 1) were 3 to 4 in lower extremities and 0 to 1 in upper extremities. Sensory examination was normal. Deep tendon reflexes were normal. Gait was antalgic due to fracture of the neck of femur. Local examination of right lower limb revealed externally rotated limb, oedema around the hip and tenderness on palpation around the hip joint. Other systemic examination revealed no abnormalities.

Investigations

Blood tests including blood count, electrolytes, liver function test, thyroid function tests, fasting glucose, creatine kinase, erythrocyte sedimentation rate, C reactive protein, serum B12, folate, treponemal agglutination, rheumatoid factor were normal. Anti GAD antibodies

Modified Ashworth Scale for grading Spasticity Grade	Description
0	No increase in muscle tone
1	Slight increase in muscle tone, manifested by a catch and release, or by minimal resistance at the end of the range of motion when the affected part(s) is moved in flexion or extension
2	Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the range of movement (ROM)
3	More marked increase in muscle tone through most of ROM, but affected part(s) easily moved
4	Considerable increase in muscle tone, passive movement difficult
5	Affected part(s) rigid in flexion and extension

Table 1: Modified ashworth scale for grading spasticity grade.

in the CSF and serum were significantly high, suggestive of Stiff person syndrome. EMG revealed continuous low frequency motor unit activity, simultaneously occurring in agonist and antagonist muscles, confirming SPS. Imaging MRI brain and cervical spine were normal. X-ray right hip and leg showed fracture of neck of the femur.

Differential Diagnosis

Diseases presenting with similar symptoms and a positive Anti-GAD antibody titre in CSF or serum such as Cerebellar ataxia, Limbic encephalitis, Myasthenia gravis.

Treatment

She was initiated on infusion Midazolam, at the rate of 2-5 mg per hour, for the spasms. However, her condition failed to improve. So the decision was made to insert an intrathecal baclofen pump at 50 to 100 µg per day.

Outcome and Follow-Up

Following the placement of the intrathecal baclofen pump, she

*Corresponding author: Dinesh Mohan Chaudhari, Indraprastha Apollo Hospital, New Delhi, India, Tel: 040 2316 0039; E-mail: meet2dinum@gmail.com

Received July 06, 2015; Accepted August 10, 2015; Published August 17, 2015

Citation: Chaudhari DM, Renjen PN (2015) Stiff Person Syndrome with Good Treatment Response to Intrathecal Baclofen. J Clin Case Rep 5: 573. doi:10.4172/2165-7920.1000573

Copyright: © 2015 Chaudhari DM, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

showed good improvement in performing her daily activities and reported significantly diminished muscular spasms and muscular pain. Her Modified Ashworth Scores were now 0 to 1 in both upper and lower extremities.

Discussion

Stiff person syndrome is a rare disabling autoimmune disorder typically affecting the axial and proximal limb muscles. The age of onset is at an average age of 41.2 years (range 29–59 years) and women are affected more commonly than men [2]. Onset is insidious and SPS presents as progressive rigidity of truncal muscles and painful localized or generalized muscular spasms. It is exaggerated by external stimuli such as stress, concurrent infection or cold weather. The symptoms are alleviated by sleep in the early stages of the disease.

The pathogenesis of SPS is linked to auto-antibodies against synaptic proteins involved in the inhibitory synaptic transmission. These auto-antibodies are primarily targeted against enzyme Glutamic Acid Decarboxylase (GAD) which is responsible for the catalysis of Glutamic Acid to γ -Aminobutyric acid (GABA). GABA is an inhibitory neurotransmitter in brain and spinal inter neurons [3,4]. GAD is also an auto antigen involved in the pathogenesis of insulin dependent diabetes mellitus which is often associated with SPS [5]. SPS can be a potential component of paraneoplastic syndrome in patients with lung cancer or breast cancer associated with antibodies against amphiphysin [6] and gephyrin [7-9].

Our patient's diagnosis of SPS was made primarily based on Dalaka's criteria [2,10] which includes: Stiffness in the axial muscles leading to a fixed deformity; superimposed painful spasms precipitated by unexpected noises or stress or tactile stimuli; confirmation of continuous motor activity in agonist and antagonist muscles by EMG; absence of neurological or cognitive impairment; positive serology for GAD65 or Amphiphysin antibodies and response to diazepam.

The EMG reveals continuous motor unit activity in the resting state in SPS. The firing rates and recruitment of MUPs are maintained. There is co-contractions of the agonist and antagonist muscle groups, which occurs spontaneously or by a triggering event [4].

Past literature has described a relationship of SPS with epilepsy; about 10% patients with SPS also have associated epilepsy [11], which leads us to believe that this patient may have associated epilepsy with SPS.

The multidisciplinary treatment of SPS is aimed at relief of the painful muscular spasms and extreme rigidity. Several pharmacological agents used such as benzodiazepines, antispasmodics like baclofen or dantrolene, immunosuppressive agents such as steroids, rituximab, and plasma exchange or intravenous immunoglobulins. Other treatment modalities are physiotherapy and occupational rehabilitation [1].

First line treatment is benzodiazepines such as midazolam or diazepam. Failure to improve on benzodiazepines, are treated with oral baclofen, where some patients show good clinical outcome while others fail to improve. As the disease progresses intrathecal Baclofen can be initiated with good results [1] Intrathecal baclofen results in higher CSF bioavailability, as CSF penetration of baclofen is limited for oral baclofen. 50 times higher CSF levels of drug are achieved at much lesser fraction of intrathecal baclofen versus oral administration [12].

Silber et al in a double blinded placebo controlled trial of intrathecal baclofen proved a significant improvement in the electrophysiological activity of SPS patients. Baclofen is a GABA-B agonist and can be used

in combination with benzodiazepines. Patients are started on an oral maintenance dose at 5-60 mg in divided doses. Intrathecal baclofen at 50-100 μ g/day is used for severe spasticity. However, the clinician has to be cautious about the drug delivery rate as a drop in intrathecal baclofen drug delivery rate can cause severe withdrawal and also prove fatal [8,9].

Learning Points

- SPS is a rare and frequently misdiagnosed disease. Hence, stiff person should be considered in the differential of a patient with painful, intermittent progressively worsening, muscular spasms. Especially in females, due to higher female predilection.
- When oral treatment fails, intrathecal baclofen should be next treatment option and initiated early in the disease for better results.

References

1. Hadavi S, Noyce AJ, Leslie RD (2011) Stiff person syndrome. *Prac Neurol* 11: 272-282.
2. Dalakas MC, Fujii M, Li M (2000) The clinical spectrum of anti-GAD antibody-positive patients with stiff-person syndrome. *Neurology* 55: 1531-1535.
3. Dinkel K, Meinck HM, Jury KM (1998) Inhibition of gamma-aminobutyric acid synthesis by glutamic acid decarboxylase autoantibodies in stiff-man syndrome. *Ann Neurol* 44: 194-201.
4. Rakocevic G, Floeter MK (2012) Autoimmune stiff person syndrome and related myelopathies: understanding of electrophysiological and immunological processes. *Muscle Nerve* 45: 623-34.
5. Baekkeskov S, Aanstoot HJ, Christgau S (1990) Identification of the 64K autoantigen in insulin-dependent diabetes as the GABA-synthesizing enzyme glutamic acid decarboxylase. *Nature* 347: 151-156.
6. Nguyen-Huu BK, Urban PP, Schreckenberger M (2006) Anti-amphiphysin-positive stiff-person syndrome associated with small cell lung cancer. *Mov Disord* 21: 1285-1287.
7. Butler MH, Hayashi A, Ohkoshi N (2000) Autoimmunity to gephyrin in Stiff-Man syndrome. *Neuron* 26: 307-312.
8. Silbert PL, Matsumoto JY, McManis PG (1995) Intrathecal baclofen therapy in stiff-man syndrome: a double-blind, placebo-controlled trial. *Neurology* 45: 1893-1897.
9. Meinck HM, Tronnier V, Rieke K (1994) Intrathecal baclofen treatment for stiff-man syndrome: pump failure may be fatal. *Neurology*, 44: 2209-2210.
10. Dalakas MC (2009) Stiff person syndrome: advances in pathogenesis and therapeutic interventions. *Curr Treat Options Neurol* 11: 102-110.
11. Martinelli P, Pazzaglia P, Montagna P (1978) Stiff-man syndrome associated with nocturnal myoclonus and epilepsy. *J Neurol Neurosurg Psychiatry* 4: 458-462.
12. Knutsson E, Lindblom U, Martensson A (1974) Plasma and cerebrospinal fluid levels of baclofen at optimal therapeutic responses in spastic paresis. *J Neurol Sci* 23: 473-484