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Stiff Person Syndrome: A Rare Presentation of a Rare Disorder

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Stiff Person Syndrome: A Rare Presentation of a Rare Disorder

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Abstract

Stiff Person Syndrome (SPS) is a rare autoimmune disease that is caused by the lack of inhibition to excitatory neurotransmitters in the central nervous system (CNS) which then leads to inappropriate and excessive motor unit firing causing stiffness, a characteristic feature of the disease. SPS has an incidence of one case in a million and occurs in the middle-aged population with a female predominance. SPS mostly occurs in the background of autoimmune disorders like type 1 diabetes, thyroid disorders, pernicious anemia, and less often, vitiligo. The pathophysiology is not completely understood; however, there is a strong correlation between high titers of anti-glutamic acid decarboxylase antibody (anti-GAD Ab) and the disease. We present an 82 years old man who complained of stiffness and weakness, mostly on the right side, with multiple negative workups. He was then eventually diagnosed with SPS based on the characteristic history and physical examination findings and being positive for anti-GAD Ab. He was treated with a combination of baclofen, gabapentin, intravenous immunoglobulins (IVIG), and physical therapy. We review the case presentation which was unusual in terms of age and sex, and treatment options in the context of a severe presentation of this disabling disease.

Keywords

Stiff Person Syndrome, autoimmune, intravenous immunoglobulins, anti-glutamic acid decarboxylase antibody

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Conflict of Interest Statement

There is no conflict of interest.

CASE REPORT

Stiff Person Syndrome: A Rare Presentation of a Rare Disorder

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Abstract

Stiff Person Syndrome (SPS) is a rare autoimmune disease that is caused by the lack of inhibition to excitatory neurotransmitters in the central nervous system (CNS) which then leads to inappropriate and excessive motor unit firing causing stiffness, a characteristic feature of the disease. SPS has an incidence of one case in a million and occurs in the middle-aged population with a female predominance. SPS mostly occurs in the background of autoimmune disorders like type 1 diabetes, thyroid disorders, pernicious anemia, and less often, vitiligo. The pathophysiology is not completely understood; however, there is a strong correlation between high titers of anti-glutamic acid decarboxylase antibody (anti-GAD Ab) and the disease. We present an 82 years old man who complained of stiffness and weakness, mostly on the right side, with multiple negative workups. He was then eventually diagnosed with SPS based on the characteristic history and physical examination findings and being positive for anti-GAD Ab. He was treated with a combination of baclofen, gabapentin, intravenous immunoglobulins (IVIG), and physical therapy. We review the case presentation which was unusual in terms of age and sex, and treatment options in the context of a severe presentation of this disabling disease.

Keywords: Stiff person syndrome, Autoimmune, Intravenous immunoglobulins, Anti-glutamic acid decarboxylase antibody

1. Introduction

SPS is a rare autoimmune disorder that is caused by the lack of inhibition to the excitatory neurotransmitters in the CNS which then manifests as an involuntary contraction of muscles leading to the characteristic feature of rigidity.¹ SPS is an extremely rare disorder, and although the exact incidence of the disease is unknown, according to one estimate the average incidence of the disease is 1 in a million among the general population.² It mostly occurs in females and the most common age of occurrence is between 30 and 60 years of age.² However, it can also occur in the elderly male population.³ It has a varied spectrum of presentation ranging from stiffness in one limb (known as stiff limb syndrome) to generalized stiffness with encephalomyelitis, brainstem dysfunction, and dysautonomia (known as progressive encephalomyelitis with rigidity and myoclonus,

PERM).¹ The course of SPS is varied among patients with some having slow progressive disease while others have acute exacerbations.⁴ We report a case of an elderly male who presented with stiffness and weakness in his upper and lower limbs, more on the right side, since the last year.

2. Case description

An 80 years old male had ongoing bilateral weakness and stiffness in his upper and lower limbs, which was more on the right side since the last 1 year. His stiffness, which was more prominent in the right upper and lower limbs, had progressed to the degree that he had trouble with ambulation and holding onto objects. He had mechanical falls due to his leg stiffness. He also had a 10 pounds unintentional weight loss. Due to his debilitating symptoms and lack of social support at home, he was unable to take care of and feed himself. Initially,

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he didn't seek medical care but when the symptoms worsened, he was referred to an outpatient neurologist by his primary care physician. His neurologist found very significant neurologic findings with weakness, exaggerated reflexes and clonus on the right side. He was sent to ED for an emergent MRI to rule out spinal cord compression. His past medical history was significant for hypertension, hyperlipidemia, and depression. He did not have any personal or family history of malignancy or autoimmune conditions. He was a former smoker with a pack per day (PPD) for 18 years and quit smoking 12 years ago, he drank only socially and denied drug abuse. He never had a colonoscopy done. On examination, vital signs showed BP 115/82 mm Hg, Pulse 78 bpm and regular, O2 saturation of 98% at room air, and a temperature of 98.6 F. His neurological examination showed intact cranial nerve I to XII, bilateral upper and lower extremity weakness which was more pronounced on the right side with a power of 3/5 as compared to the left side with a power of 4+/5, diffuse hyperreflexia with reflexes 3+ in the right upper and lower extremity, right ankle and right knee clonus, fasciculation in the right arm and right leg and sensory loss of crude touch in the right lower extremity. He was oriented to time, place, and person. The rest of his examination was unremarkable.

His blood work results are shown in Table 1.

CSF studies are as follows in Table 2.

MRI brain, cervical spine, thoracic spine, and lumbar spine were negative for demyelinating pathology or space-occupying lesions and only showed mild degenerative changes. He had a malignancy workup with CT chest/abdomen/pelvis which were unremarkable.

Mayo Clinic ENC2 Panel was also sent and it came back positive for *Glutamic Acid Decarboxylase antibodies (GAD Ab)*.

Table 1. Complete Blood Count (CBC) and Basic Metabolic Panel (BMP).

Lab Work	Value	Lab Work	Value
White Cell Count	7.7 10 ³ /uL	Urea	18 mg/dL
Hemoglobin	12.6 g/dL	Creatinine	0.9 mg/dL
Platelets	306 10 ³ /uL	Thyroid Stimulating Hormone	1.16 uIU/mL
Erythrocyte Sedimentation Rate	4 mm/h	CRP	<4 mg/L
Sodium	137 mEq/L	Vitamin B12	252 pg/mL
Potassium	4.1 mEq/L	Creatinine Kinase (CK)	166 U/L
Calcium	9.1 mg/dL	Lyme antibodies	Negative
Magnesium	1.8 mg/dL	Anti-Nuclear Antibody (ANA)	Negative

Table 2. Cerebrospinal Fluid (CSF) analysis.

Lab	Value	Lab	Value
Protein	84 mg/dL	RBC	1/uL
Glucose	62 mg/dL	Nucleated Cells	2/uL
Color	Colorless	IgG Index	Negative
Appearance	Clear	Oligoclonal Bands	Negative

He was started on Baclofen 10 mg every 8 h and Gabapentin 100 mg every 8 h initially before the results of the ENC2 panel were available to help with his stiffness but it had little improvement in his symptoms. Then he was given intravenous immunoglobulins IVIG (0.4 mg/kg/day for 5 days) and the patient responded well to the treatment with his stiffness and ambulation improved. His power in the right upper and lower limb improved to 4+/5 and his reflexes were 1+ in comparison to 3+ on admission. He was then able to walk without assistance. He was discharged on baclofen and gabapentin and has been following up as an outpatient with neurology. On his outpatient follow-up appointments with neurology, he has reported improvement in his symptoms and has been working closely with physical therapy for rehabilitation.

3. Discussion

SPS is a rare medical disorder and has a prevalence of around 1–2 cases per million.¹ The pathophysiology of the disease is incompletely understood but there is a strong association between the disease process and the presence of GAD antibodies.⁴ The characteristic rigidity and painful muscle spasms can be explained by the loss of central inhibition of inhibitory signals and as a result, there is an inability of opposing muscles to relax when the contralateral muscles contract.⁵ SPS can manifest in various forms including classic SPS, partial SPS, jerking SPS, progressive encephalomyelitis with rigidity and myoclonus (PERM), and paraneoplastic SPS, and all of them have the common characteristic of muscle stiffness. Classic SPS is described as diffuse stiffness, truncal rigidity, and muscle spasms. Partial SPS mostly involves a single limb e.g leg and thus is commonly known as “stiff limb syndrome”. Jerking SPS comprises of myoclonic jerks in addition to the characteristic stiffness. Progressive encephalomyelitis with rigidity and myoclonus consists of rigidity as well as brainstem and autonomic dysfunction. Paraneoplastic SPS comprises 5% of the total cases⁶ and it occurs in the background of malignancy most commonly breast and lung malignancies.

SPS is difficult to diagnose as the disease is rare and the symptoms develop over time. In one cohort

it was found that on average it takes 3.5 years from the onset of symptoms to the diagnosis and almost 5 years till the initiation of immunomodulatory treatment.⁷ Most common differential diagnosis for similar symptoms are myelopathies, Parkinson disease, myopathies, autoimmune encephalitis and primary lateral sclerosis. The diagnosis of SPS is based on a combination of clinical findings, antibody testing, CSF analysis, and imaging to rule out structural lesions. Malignancy workup can also be included to rule out paraneoplastic causes of SPS.⁴ Most patients have truncal rigidity, positive GAD Ab, and electromyography (EMG) findings of continuous motor unit firing in the absence of any other cause. The pathognomonic antibody is GAD Ab but some patients also have glycine- α 1 receptor Ab (anti-GlyR).⁵ Our patient had the characteristic limb rigidity with positive GAD Ab. He did not undergo EMG but based on his clinical presentation, positive GAD Ab, and otherwise negative workup, we were able to diagnose and treat him as SPS. Although he never had a colonoscopy, he denied any symptoms concerning for a colon malignancy.

Unfortunately, there is no permanent cure for the disease and the mainstay of treatment is to reduce the severity of symptoms and improve the quality of life. The treatment strategy is divided into three tiers, 1) Symptomatic treatment like muscle relaxants e.g baclofen and diazepam, and therapies affecting GABA transmission e.g gabapentin and pregabalin. 2) Immunomodulatory treatment in the form of first-line immunosuppressants e.g intravenous immunoglobulins (IVIG), plasma exchange, steroids, and second-line immunosuppressants e.g rituximab, azathioprine, and mycophenolate mofetil. 3) Non-medical therapies e.g physical therapy, heating pads, stretching, and acupuncture. IVIG is an effective therapy in patients with SPS, especially in those who have not responded well to other forms of therapy.⁸ Treatment with IVIG has shown to be more effective as compared to plasma exchange and has better outcomes.⁹ In comparison to IVIG, steroids lead to more side effects and are especially difficult to use in diabetics due to hyperglycemia.¹⁰ Our patient was initially started on baclofen and gabapentin which resulted in only mild improvement in his stiffness. The use of baclofen and gabapentin has been validated by the literature and can be used to provide symptomatic relief to the patient.¹¹ He was then started on IVIG which markedly improved his symptoms and functional status. He had an increase in his power

on the right side of the body and a reduction in stiffness.

4. Conclusion

In conclusion, SPS is a rare disorder that can have a variable clinical presentation. It can present in an older age population without an underlying autoimmune disorder or malignancy. Although it is rare, it has to be considered in the differential of a patient presenting with muscle stiffness as the correct treatment can halt the course of the disease. Symptomatic therapy with muscle relaxants and immunomodulatory agents remains the mainstay of therapy in SPS and helps to reduce symptoms and improve quality of life.

Conflicts of interest

There is no conflict of interest.

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