Stiff Person Syndrome Masquerading as Multiple Sclerosis

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Introduction

- Stiff person syndrome (SPS) is a rare autoimmune or paraneoplastic disorder that classically causes rigidity and spasms of the proximal and axial muscles and gait dysfunction
- It is typically associated with auto-antibodies against glutamic acid decarboxylase (GAD)65 and with EMG findings revealing co-contraction of agonist and antagonist musdes and/or continuous motor unit activity[1,2].
- Despite these 'classic' features, SPS is an enigmatic disease that can present with a wide variety of signs and symptoms, such as ataxia and encephalomyelitis[3,4] that can mimic various neuro-inflammatory diseases.

Objective

- We describe a case series of patients with a diagnosis of SPS who were previously diagnosed with multiple sclerosis (MS).

Methods

- We performed a retrospective chart review of over 100 patients with SPS who were treated at Johns Hopkins Hospital from 1996 to 2015 and identified five patients previously diagnosed with MS.
- All review was done in accordance with the IRB-approved protocol. Detailed pertinent demographic and medical findings are outlined in Tables 1 and 2.

Results

- Patients were female with an average age of 53 years old (range; 43-64). Average time to SPS diagnosis was 5.5 years for this cohort.
- Patients presented with typical SPS symptoms (axial/leg spasms, torso rigidity, gait instability) as well as atypical symptoms (hemiparesis, hemi-sensory dysfunction, and fine motor impairment) and were all initially given a diagnosis of MS.
- Exam findings typical of SPS included axial rigidity, lumbar hyperlordosis (figure 1), spasticity, and slow unsteady gait.
- SPS diagnosis was supported by GAD65 antibodies in each patient at 8 months to 15 years after initial symptom onset.
- Two patients were previously treated with disease-modifying therapies for MS, including one treated with three different therapies, before being diagnosed with SPS.

Results

Table 1. Background information of patients included in study

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Gender	Female	Female	Female	Female	Female
Ethnicity	African-American	Caucasian	African-American	Caucasian	Caucasian
Medical history	HTN, OSA, degenerative spine disease	Migraine	HTN, HLD	DM, HTN, HLD, ulcerative colitis, neuropathy	HTN, HLD, intracranial stenosis, psoriasis, melanoma
Symptoms	Gait instability, axial and leg spasms and rigidity, dysphagia, dysarthria	Poor memory recall, hemiparesis, hemi-sensory deficits, axial rigidity and spasms, leg and arm cramps, anxiety attacks	Foot tingling, leg stiffness, gait instability, gait dysfunction, limb and axial rigidity, urinary urgency	Atypical leg sensory symptoms, leg spasms, fine motor impairment, abdominal/back spasms, urinary urgency, headache	Gait instability, balance impairment, dysarthria, fine motor impairment, intermittent diplopia

Abbreviations: HTN = hypertension, HLD = hyperlipidemia, DM= diabetes mellitus, OSA= obstructive sleep apnea.

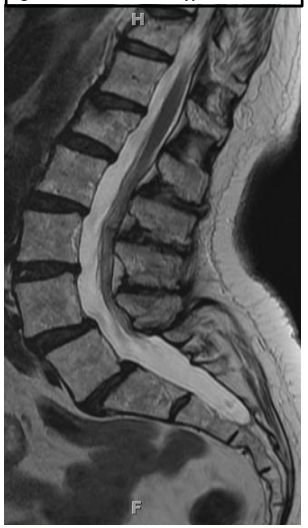
Table 2. Patient exam findings, results, and treatment history

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Exam findings	Hypomimia, dysarthria, axial rigidity, bradykinesia, mild proximal left-sided weakness and dysmetria, slow unsteady gait	Lumbar hyperlordosis, T11-12 sensory level, positive Romberg sign, spastic gait	Hypometric horizontal saccades, lumbar hyperlordosis, axial rigidity, lower extremity hyperreflexia, left hemi-sensory deficits, dysdiadochokinesia, impaired tandem walking	Bilateral upper extremity hyperreflexia, reduced vibration sensation hands and feet, antalgic gait without ataxia or instability	Lumbar hyperlordosis, left-sided dysmetria, bilateral upper extremity hyperreflexia, bilateral lower extremity spasticity, slow wide-based unsteady gait
MRI findings	Non-specific non-enhancing subcortical T2+ lesions, normal spinal cord	Non-specific non-enhancing subcortical and periventricular T2+ lesions, questionable T2+ lesion at C6	Non-specific non-enhancing subcortical and periventricular T2+ lesions, normal spinal cord	Numerous non-enhancing subcortical and periventricular T2+ lesions, normal spinal cord	Minimal non-specific non-enhancing subcortical T2+ lesions, normal spinal cord
CSF Results	Not tested	Normal	Normal	Normal	Normal
EMG Results	Normal	Normal	Not tested	Normal	Normal
Anti-GAD65 (U/ml)	>40,000	130.7	18,420	2.4	19,580
Age at Diagnosis	49	43	61	47	64
Time until SPS Diagnosis	8 months	6 years	3 years	3 years	15 years
Prior MS Therapy	None	Avonex, Copaxone, Tysabri	None	None	Avonex
SPS Treatment	BZD, anti-spasmodics, PLEX, CellCept, Rituximab,	IVIG, BZD, anti-spasmodics,	IVIG, BZD, anti-spasmodics,	BZD, anti-spasmodics,	BZD, anti-spasmodics, IVIG, PLEX, CellCept, RItuximab
Treatment Response	Worsening gait instability	Improved	Stabilized	Improved	Stabilized

BZD = benzodiazepine, IVIG = intravenous immunoglobulin, PLEX = plasma exchange. *Normal < 1.0 U/ml.

Results

Figure 1. Severe lumbar hyperlordosis.



Conclusions

- SPS is a rare disease that is difficult to diagnose in its early presentation and it is often misdiagnosed.
- Each of the patients possessed a number of features that shared similarities between MS and SPS: strong female predominance, white matter abnormalities on MRI, as well as certain signs/symptoms including gait and balance instability, progressive myelopathy, and bladder issues. More importantly, each patient had features that were atypical of MS, including axial rigidity, prominent leg spasms, lack of MRI lesion formation over time, lack of spine lesions, and negative CSF oligoclonal bands.
- These cases demonstrate the need to consider less common neuroimmunological disorders, such as SPS, especially in patients with atypical features for MS.

References

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