Stiff Person Syndrome Masquerading as Acute Coronary Syndrome

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Abstract: Stiff person syndrome (SPS) is a rare neuroimmunological disorder characterized by severe progressive muscle stiffness in axial and lower extremity musculature with superimposed painful muscle spasms. Although chest pain is a common reason for SPS patients presenting to the emergency room, this disorder is overlooked and not part of the differential diagnosis of chest pain. Herein, we report on a middle age male presenting with classic symptoms of SPS; however, due to the rarity of this disease, he was initially thought to have acute coronary syndrome. Clinicians should consider the diagnosis of SPS in patients with fluctuating muscle spasms in the torso and/or extremities in the setting of repeated hospitalizations without subsequent symptom relief.

Abbreviations: SPS, Stiff Person Syndrome; GABA, Gamma Amino Butyric Acid; ACS, Acute Coronary Syndrome; GAD, Glutamic Acid Decarboxylase; IVIG, Intravenous Immunoglobulins

Keywords: Stiff-person syndrome■Glutamic acid decarboxylase antibody■Autoimmune disease

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BACKGROUND

Stiff person syndrome (SPS) is a rare neuroimmunological disorder characterized by severe progressive muscle stiffness in axial and lower extremity musculature with superimposed painful muscle spasms. SPS prevalence is estimated to be one per million and occurs more commonly in women between ages 30 and 50.[1,2] Although chest pain is a common reason for SPS patients presenting to the emergency room (ER), this disorder is overlooked and not part of the differential diagnosis of chest pain. Herein, we report on a middle age male presenting with classic symptoms of SPS; however, due to the rarity of this disease, he was initially, thought to have acute coronary syndrome (ACS) with the correct diagnosis uncovered 3 years after initial symptoms onset.

CASE REPORT

A 41-year-old African American man with vitamin B12 deficiency and chronic eczema presented to the ER with worsening painful muscle spasms in his chest and back. He was in his usual state of health until 3 years ago when he started having these symptoms. The muscle spasms frequently involved his chest, lower back/legs, were sudden in onset, cramping in nature, and aggravated by voluntary movement, emotional stress and unexpected loud auditory stimuli. The patient had undergone multiple hospitalizations for chest pain and underwent evaluation for suspected ACS. During a previous hospitalization he was found to have a mildly elevated creatinine kinase (CK-MB) which prompted a cardiac catheterization; however, that did not demonstrate any coronary obstruction. Subsequently, he began treatment for non-obstructive ACS without improvement of his symptoms.

During his most recent admission, the patient had presented with chest pain and diaphoresis. His vital signs were normal and his general examination revealed mild pallor and lower extremity rigidity. His lungs were clear to auscultation and he had no murmurs/gallops or abnormal rhythm. Neurological examination revealed dysarthria, spasticity in all extremities, hyper-reflexia, and impaired ambulation. Initial laboratory testing was significant for a CK of 612 U/L. EKG was normal and chest CTA ruled out pulmonary embolus. Head CT was unremarkable. Due to his progressive neurological decline, he was ultimately transferred to a tertiary care center for subspecialty evaluation. On repeated physical exam, he was noted to have hyperlordosis, paravertebral muscle spasms and torso rigidity. His diagnostic work-up was expanded to include an extensive search for autoimmune disorders, which revealed an anti-Glutamic acid decarboxylase-65 (GAD65) antibody of 53,650 U/mL (normal $\leq$1.0 U/mL). All other serum autoantibody testing were negative including paraneoplastic and rheumatic panel. EMG demonstrated continuous motor unit activity in the vastus medialis and T10 paraspinal muscles. Neuraxial imaging and PET-CT scan ruled out anatomical pathology. Given the clinical presentation and paraclinical findings above,

Table 1. Classic and Variants of Stiff Person Syndrome

A. Adapted Dalakas Criteria[1] for diagnosis of classic stiff person syndrome

1. Stiffness and rigidity in the axial musculature that can result in hyperlordosis over time
2. Painful spasms in torso and/or extremities that are often provoked by abrupt load noises, tactile stimuli, and exposure to cold or emotional stress
3. Electromyography demonstrating co-contraction of agonist and antagonist muscles and/or continuous involuntary firing of motor units at rest
4. Stiffness not explained by other neurological disease
5. Positive serology for anti-GAD65 (or amphiphysin) antibodies
6. Response to benzodiazepines (most commonly valium)[2]

B. Variants[8] of Stiff Person Syndrome presenting with atypical signs and symptoms

1. Stiff Limb Syndrome: focal onset of stiffness and rigidity in one leg followed by more widespread involvement later on in some patients. The majority of patients are anti-GAD65 Ab negative.
2. Progressive Encephalomyelitis with Rigidity and Myoclonus (PERM): Presents with more rapid neurological decline with features of brainstem dysfunction (nystagmus, opsoclonus, ophthalmoparesis, deafness, dysarthria, and dysphagia) and profound autonomic dysfunction. A portion of patients with PERM will have anti-GAD65 antibodies, although in anti-GAD65 negative cases glycine receptor antibodies may be present.
3. Paraneoplastic Stiff Person Syndrome (SPS): Represents approximately 5% of SPS cases. Breast, ovarian and lung cancer are most commonly associated with this variant. Patients will often present stiffness and rigidity in their neck, upper torso, and arms. Some patients will have anti-GAD65 antibodies present, although this variant is also associated with the synaptic proteins amphiphysin and gephyrin antibodies.
4. Other variants of SPS: There can be an admixture of other signs and symptoms superimposed on classic features of SPS including cerebellar dysfunction, gait instability, oculomotor dysfunction, dysarthria, peripheral neuropathy, vertigo, parkinsonism, and seizures.

[1]*Table adapted with the permission of the author of related manuscript.*
[2]*Not part of Dalakas criteria, but helpful in diagnosis.*

the patient was diagnosed with SPS. He was started on diazepam, baclofen, and IVIG with notable clinical improvement; decreased spasms/pain/rigidity, resolution of dysarthria, and regained ability to walk. He was ultimately discharged to a rehabilitation facility and currently remains on monthly IVIG and daily GABAergic agonist medications.

DISCUSSION

The uniqueness of our case resides in its presentation: an extremely rare disease (SPS) masquerading as a very common disease − ACS. The estimated incidence of SPS is 1 case per million.[1] It affects women 2−3 times more often than men, and most patients present between the ages of 20 and 50.[1,2] The disease is commonly classified as classic SPS which comprises the majority of cases or variant SPS (Table 1). In patients with variant SPS, stiffness and spasms are usually anatomically limited to one or both lower extremities (stiff limb) while patients with progressive encephalomyelitis with rigidity and myoclonus (PERM), present with rapidly progressive and widespread stiffness and spasms.[3,4] The characteristic clinical features of classic SPS are stiffness and rigidity in axial and proximal limb muscles with superimposed stimulus-sensitive axial and appendicular spasms that lead to functional impairments with inability to walk and/or care for oneself over time (Table 2). This physical impairment results in excessive falls with increased anxiety/phobia about leaving the home. At onset, the spasms and rigidity may be sporadic, but as the disease progresses symptoms become more persistent, leading to loss of independence and severe disability.

The rigidity and continuous motor unit activity disappear during sleep and with anesthesia which indicates a central origin for SPS symptoms. The sporadic stiffening and painful spasms usually result from loss of GABA inhibitory transmission which inhibits spontaneous discharge from spinal motor neurons, resulting in involuntary continuous firing of muscle motor units. Muscle spasms occur spontaneously or by triggered events such as emotional stress, a startle, cold environments and certain movements and involve co-contraction of antagonist muscles.[5] The loss or reduced presynaptic synthesis of GABA is thought to be secondary to autoantibodies against GAD-65, which is present in about 60−80% of SPS cases. SPS can also occur as a paraneoplastic syndrome associated with autoantibodies to