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Case Report

Stiff Person syndrome: a case report

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ABSTRACT

Stiff person syndrome (SPS) is rather unique among neurologic diagnoses. At relaxation, motor- unit activation, continuous agonist and antagonist muscular contractions, as well as contractions triggered by tactile triggers, quiescent stretch, and involuntary movement of affected or unaffected musculature, startled sounds and emotional stimuli are the clinical signs of SPS. Sleep, general anesthesia, myoneural, and peripheral nerve blockage all help to reduce rigidity and spasms. The syndrome may be a sporadic autoimmune syndrome (associated with anti–glutamic acid decarboxylase (GAD) antibodies and often accompanied by other autoimmune diseases such as type 1 diabetes) or paraneoplastic (associated with anti–amphiphysin antibodies). People with SPS respond to high doses of diazepam and several anti-convulsants, gabapentin and tiagabine. Immunomodulatory drugs including steroids, plasmapheresis, and intravenous immunoglobulin appear to help significantly. The symptoms of our patient progressed slowly over time. Neuroimaging and electrophysiological studies ruled out other possible causes of comparable symptoms such as neuromyotonia. Raised anti-GAD autoantibodies titer in serum found by immunocytochemistry assays, our patient's history, clinical examination findings, and reaction to benzodiazepines all pointed to SPS.

Keywords: SPS, Paraneoplastic, Spasms, Stiff-Person syndrome

INTRODUCTION

The stiff man syndrome must be distinguished from tetanus, Isaacs syndrome, and the rare syndrome of subacute myoclonic spinal neuronitis. In both the stiff man syndrome and myoclonic spinal neuronitis, the intense spasms and stiffness of muscles are a result of disinhibition of interneurons in the gray matter of the spinal cord.[12]

The syndromes of continuous muscle activity are usually distinguishable clinically and electromyographically from extrapyramidal and corticospinal abnormalities such as dystonia, dyskinesia, and rigidity, although early phases of axial dystonic disorders and stiff man syndrome have similarities.[13]

We report a patient who was identified with stiff person syndrome due to neurological symptoms and had a favorable outcome after therapy, as well as a review of the literature.

CASE REPORT

A 26-year-old male patient was admitted to the general medical ward with progressive fatigue, stiffness and painful spasms of his legs, resulting in difficulty of standing up and walking for 3 days. No history of animal bite or infected wound. He admits working in hot weather for a long time. His muscle cramps were worsening and become generalized with mainly axial rigidity. The patient was admitted by the assumed diagnosis of heat stroke and rhabdomyolysis. His renal functions and electrolytes were normal. The patient developed severe axial and extremity

muscle rigidity, disappear during sleep, aggravated with light and touch. His CK on arrival was >2000 IU/l. On assessment, he was vitally stable, afebrile, fully conscious, alert and oriented, looks rigid and resisting movement. He can move limbs with pain, but he has severe rigidity of the neck and back muscles. Cranial nerves were intact, limb power, sensation and reflexes were normal.

Initially, intravenous (IV) fluids, diazepam and baclofen were given with monitoring of patient's general and biochemical status showed a progressive increase in creatinine kinase (after initial decline). The patient became in a state of severe generalized muscle stiffness. Because of that patient shifted to intensive care unit (ICU) to control muscle stiffness and to monitor his hemodynamic status.

Few days later, he developed severe lactic acidosis, acute kidney injury, desaturation, tachycardia, profuse sweating and generalized severe muscle spasms (including abdomen, limbs, neck and back muscles). The urine output in 24 hours was 400 ml and elective intubation was done.

The symptoms of our patient began slowly and progressed over time. Movement-induced contractions and other triggers were a major source of impairment. Muscle strength appeared normal unless disrupted by twitches or impaired by acute stiffness, and brainstem and pyramidal signals were absent.

A thorough diagnostic research that included brain imaging and investigation for indications of an infectious, neoplastic, or inflammatory origin yielded no results. Neuroimaging and electrophysiological studies ruled out other possible causes of comparable symptoms, such as neuromyotonia. Raised anti-GAD autoantibodies titer in serum found by immunocytochemistry assays, our patient's history, clinical examination findings, and reaction to benzodiazepines all pointed to SPS.

Diagnosis

The diagnosis of stiff-person syndrome was suspected after poor response to initial treatment and constellation of clinical signs with normal brain imaging and cerebrospinal fluid (CSF) studies. SPS was confirmed after a high titer of GAD antibodies detected in serum and electromyography (EMG) findings of simultaneous continuous motor unit activity in agonist and antagonist muscles.

Nerve conduction procedure

EMG of selected muscles in upper and lower limbs showed continuous firing from all muscles tested, normal motor unit potentials with normal recruitment and interference pattern. There was continuous activity from antagonizing muscles. No myotonic discharges identified. Findings were consistent with the diagnosis of stiff-person syndrome. CK on discharge was 205 IU/l.

Differential diagnosis

Differential diagnosis included: tetanus, neuroleptic malignant syndrome, serotonin syndrome, meningitis, and dystonia.

Treatment and management

Initial treatment with IV fluids, diazepam 5 mg BID and baclofen 10 mg TID failed to entirely control his symptoms. Diazepam was further increased to 10 mg QID which was moderately effective. We started intravenous immunoglobulin 2 gram/kg over 5 days followed by five sessions of therapeutic plasma exchange then he started to show good improvement. During his stay he received physical and rehabilitation care.

Progress

On discharge, the patient was conscious, alert and oriented. Markedly improved, ambulating with residual ankle and calf muscle rigidity and les tightness in upper arms and axial muscles.

Table 1: Laboratory and imaging results.

Parameter	Range
CSF cytology, protein, glucose and culture	Normal
CSF meningoencephalitis PCR panel	Negative
CT brain	Normal
MRI brain	Normal
Anti-GAD antibody	Positive (93 IU/ml)
Tumor markers	Negative
CK	(2198) IU/l - CK rising to (5000) IU/l

DISCUSSION

SPS a rare autoimmune neurological disorder, it has an estimated prevalence of one to two cases per million, with an incidence of one case per million per year. Most patients present between the ages of 20 to 50, and women are affected two to three times more often than men.[6] Patients with SPS usually present with a subacute onset of painful muscle spasm involving mainly the paraspinal musculature and the lower extremities. The spasms, initially fluctuating and fairly localized, tend to increase in frequency and severity and occasionally lead to abnormal postures, incapacity, and bone fractures. Trigger factors for the spasms include tactile, auditory, or emotional stimuli. Clinical manifestations range from diffuse involvement of the trunk and four limbs to localized spasms in one limb (stiff limb syndrome). Typically, the spasms disappear with sleep and anesthesia. Patients with SPS may also develop paraneoplastic encephalitis, and there is growing evidence relating to co-occurrence with autoimmune epilepsy syndrome.[11]

Antibodies against amphiphysin are associated with breast cancer and SPS. Anti-GAD antibodies, which are also anti–pancreatic island cells, are found in patients with nonparaneoplastic SPS. The majority of these patients also have other autoimmune diseases such as type 1 diabetes mellitus. GAD and amphiphysin are enriched in the presynaptic terminals of spinal cord interneurons that secrete the inhibitory neurotransmitters γ-aminobutyric acid and glycine. Some patients with the paraneoplastic SPS have both antiamphiphysin and anti-GAD antibodies. Other antibodies associated with SPS are anti-Ri and antigephyrin antibodies.[12]

Characteristic electrophysiologic features include continuous activity of motor units in the stiffened muscles, which typically improves with diazepam or other anesthesia.[2,3]

A normally segmented EMG activity is recorded during spasms in addition to the electrophysiological findings of SPS; anti-GAD antibodies and autoimmune disorders are less frequent. The gamma-aminobutyric acid (GABA) neuromodulator diazepam has been the usual treatment for patients. Initial outcomes are usually positive, but adaptation and illness progression necessitate increasing the dose to 200 mg daily. The potential for addiction and consequent negative effects limits the use of high dose oral treatment.[7]

The improvement of SPS symptoms with immunotherapy adds to the evidence for the disease's autoimmune concept. IV immunoglobulin treatment has had a better track record.[8,9] Physical treatment improves quality of life significantly.[10]

CONCLUSION

In this report, we describe a case of severe SPS, no association with other autoimmune disorder or malignant process was found. Intense medical therapy with high doses of diazepam, baclofen, IVIG and plasma exchange together with focused physical and rehabilitation treatment resulted in significant clinical improvement in his functional status.

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