STIFF PERSON SYNDROME: A DIAGNOSTIC AND MANAGEMENT CHALLENGE

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Date of submission: *October 5, 2014,* ***Date of revision:*** *October 22, 2014,* ***Date of acceptance:*** *November 1, 2014*

ABSTRACT

Stiff person syndrome (SPS) is a rare neurological disorder characterized by progressive muscle stiffness and rigidity, mostly involving axial muscles, resulting in functional disability. It is associated with elevated anti- Glutamic acid decarboxylase (GAD) antibody levels. Electromyography findings are often diagnostic. We present a case of a 48 years old male, who presented with progressive stiffness and rigidity of axial muscles and limbs. His EMG was consistent with SPS. Anti GAD antibodies were markedly elevated. He was treated with rituximab and has improved significantly. SPS is a difficult diagnosis, usually under diagnosed due to lack of awareness among medical community. There is a dire need to further study the disease and invent better treatment options for patients suffering from SPS.

CASE REPORT

A 48 year old male, known case of Type I Diabetes Mellitus and depression, presented to Neurology Outpatient department with complaints of progressive pain and stiffness of neck, shoulder and abdominal muscles for the past six months. The pain and spasm aggravated with stress and movement and was temporarily relieved on taking Non steroidal anti-inflammatory drugs and muscle relaxants. Initially he did not have any disability and despite stiffness he was able to carry out his daily life activity. However, the stiffness worsened over time, resulting in difficulty in walking and performing daily tasks. Physical examination revealed stiffness over muscles of neck, shoulder and abdominal regions. He had a robot like gait. Rest of the neurological examination, including cranial nerves, motor and sensory examination, was unremarkable. Based on the history and physical examination he appeared to be suffering from stiff person syndrome. The pertinent baseline investigations were normal (Table 1).

Table 1: Pertinent baseline investigations

Laboratory Investigation	Results
CRP	2.35 U/L
ESR	2 mm 1st hr
Calcium	9.4 mg/dL
25 Hydroxy Vitamin D	36.2 ng/mL
TSH	2.18 micro IU/L
CPK	199 U/L
Aldolase	7.0 U/L
X-Ray Lumbo-sacral spine	Unremarkable
MRI brain with contrast	Normal

Anti-GAD antibodies were sent which were found to be markedly elevated to a level of > 2000IU/mL. To further confirm our diagnosis, Electromyography (EMG) was done, which showed continuous motor activity in agonist and antagonists muscles, subsiding on the administration of Intravenous diazepam 5 mg (Figure 1).

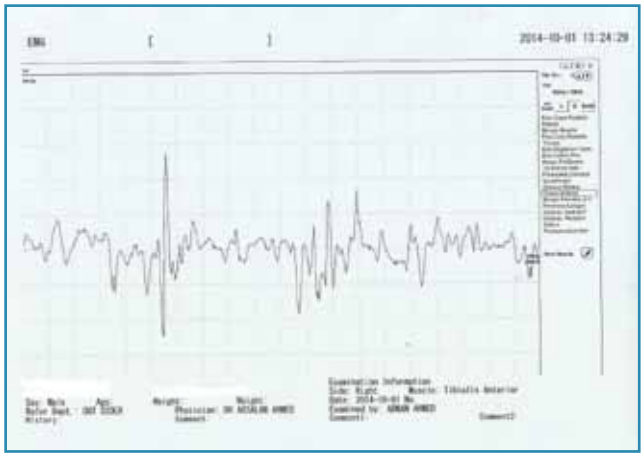

Figure1a

Figure 1: EMG showing a) continuous motor activity which b) subsided on giving 5 mg IV diazepam.

The patient was treated with Diazepam 2.5mg PO qHS and Baclofen 5mg three times daily. On a two week follow up visit, the patient showed improvement in pain, stiffness and functional status. A Rheumatology consult

was sought regarding the disease modifying treatment options, and Rituximab infusion was advised after screening for Hepatitis B and C.

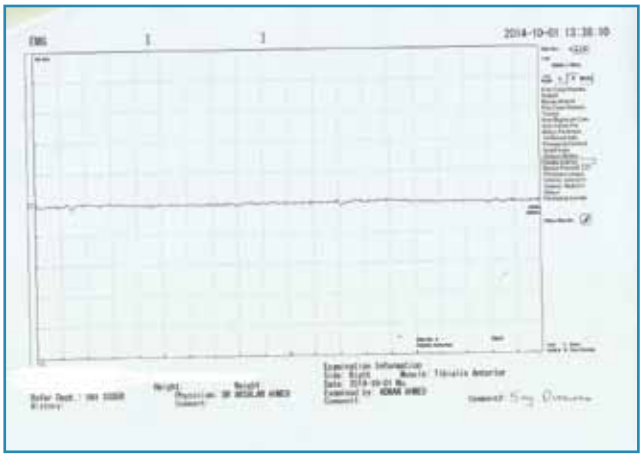

Figure1b

He was given a total of three doses of Rituximab infusion 500mg in 500ml of normal saline over 2 to 3 hours, each one week apart. He was pre-medicated with Injection Methylprednisolone 100mg diluted in 500mL of Normal saline given intravenously along with two tablets of acetaminophen 500mg per orally and Injection chlorphenamine 10mg Intravenously. Complete blood count, Liver function tests, Blood urea nitrogen and creatinine were checked after the administration of first and third dose and were normal. Anti GAD antibodies will be re-checked after two months.

DISCUSSION

Stiff person syndrome (SPS) is a rare neurological disorder characterized by fluctuating muscle rigidity of trunk and limbs resulting in abnormal postures (1). Muscle rigidity and episodic spasms result in functional disability of the patients. This rare neurological disorder was first described by Moersch and Woltman in 1956 (2). A Dalakas criterion, as given below (Table 2) is the most widely used scale for establishing the diagnosis of SPS (3).

Table 2. Dalakas Criteria

Dalakas criteria for diagnosis stiff person syndrome
Episodic stiffness of the muscles, mostly involving the axial
muscles, leading fixed deformity
Superimposed painful spasms elicited by triggers such as noises,
emotional stress and tactile stimuli
Absence of neurological or cognitive impairment
Confirmation of continuous motor activity by electro-myographic
findings (EMG). (subsides with diazepam*)
Positive serology for GAD65 or amphiphysin autoantibodies
*not a part of Dalakas criteria, but commonly included in the
diagnostic criteria

The exact cause of the disease is yet unknown. Most patients with classical SPS have antibody against Glutamic acid decarboxylase (GAD), an enzyme that plays a vital role in the regulation of an important inhibitory neurotransmitter of Central nervous system, gamma amino butyric acid (GABA) .Destruction of the GAD enzyme results in less availability of GABA neurotransmitter and hence, leads to excessive stimulation of the muscles by motor neurons causing muscle stiffness [4]. SPS is a clinical diagnosis, confirmed using Electromyography (EMG). EMG of patients with SPS shows continuous motor activity which can be suppressed by diazepam. This is a confirmatory test [5]. Anti GAD antibodies are also checked in patients suspected for SPS. In approximately 85% of patients with SPS have high titers of anti GAD antibodies [6]. There is a strong suspicion of an association between SPS and other autoimmune diseases. SPS is more commonly seen in patients with insulin dependent diabetes mellitus, thryoiditis, paraneoplastic syndromes and epilepsy [7]. SPS has no permanent cure. However two therapeutic strategies have been tried for patients with SPS. First includes the use of GABA enhancing medications for symptomatic relief by decreasing muscle stiffness. Baclofen and benzodiazepines are most commonly used drugs for this purpose. These drugs increase GABA activity and hence alleviate muscle stiffness [8].The second approach is to use disease modifying agents like rituximab and intravenous immunoglobulin to decrease the progression of the disease [9]. Both treatment approaches along with physical and occupations therapy should be used in patients for ultimate favorable results. The role of steroids and plasma exchange is still questionable. New trials are being conducted to study the role of rituximab in patients with stiff person syndrome. According to the studies conducted so far, clinical improvement has been seen in patients using rituximab especially in those who did not respond well to traditional therapy [10]. Further studies are needed before it could become an established drug of choice for SPS.

CONCLUSION

SPS is an under diagnosed neurological disorder. This is due to lack of awareness of the disease among medical community. In order to avoid delay in the treatment and improve prognosis, early diagnosis is necessary. A multi-disciplinary approach can help in diagnosing and managing such patients.

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Conflict of interest: Author declares no conflict of interest.

Funding disclosure: Nil

Author's contribution:
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Dr. Anam Abrar: Data collection, data analysis, manuscript writing, manuscript review
Dr.Zafarullah: Manuscript writing, manuscript review
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Dr. Wasim Tariq: Manuscript writing, manuscript review
Dr.Arsalan Ahmed: Data analysis, manuscript writing, manuscript review