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Case Report

Stiff Person Syndrome

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Abstract

Stiff Person Syndrome is a rare neurologic disorder characterized by progressive rigidity and stiffness and linked with features of an autoimmune disease. Stiffness, which primarily influences the truncal muscles, eventually leads to postural deformities. Here, I report a case of Stiff Person Syndrome in association with thyroiditis, epilepsy and vitiligo.

Introduction

Stiff Person Syndrome (SPS) is an extremely rare neurological disorder, with an expected prevalence of less than 1 per million [1]. The first described case of SPS in the literature was reported in 1959 by Moersch and Woltman [2]. SPS is featured by progressive muscle stiffness, rigidity, and spasm involving the axial muscles, which may result in severely impaired ambulation. The most likely mechanism implicated in the pathogenesis of SPS is an autoimmune process, which is being supported by the association with other autoimmune diseases as well as the increased concentration of oligoclonal IgG antibody in the cerebrospinal fluid of most SPS patients. These antibodies were found to target GABAergic (gamma amino butyric acid) neurons and their nerve terminals [3].

Here, a case report of Stiff Person Syndrome in association with thyroiditis, epilepsy, and vitiligo, is presented for the first time from Saudi Arabia.

Case

A 52 years old female known to have hyperthyroidism and epilepsy presented with a history of paroxysmal intense spasm of the upper and lower extremities and the back. Upon presentation, the patient suffered spasms on daily basis for the past 6 months, with each attack lasting 1-2 hours, during which the patient was unable to walk. The attacks were aggravated by stress and improved with sleep. There were no jerky movements or loss of consciousness. Physical examination revealed generalized rigidity in the axial muscles. Cranial nerve examination was normal. Motor and sensory functions were intact. Reflexes were exaggerated. Skin examination showed vitiligo (Figure 1) and

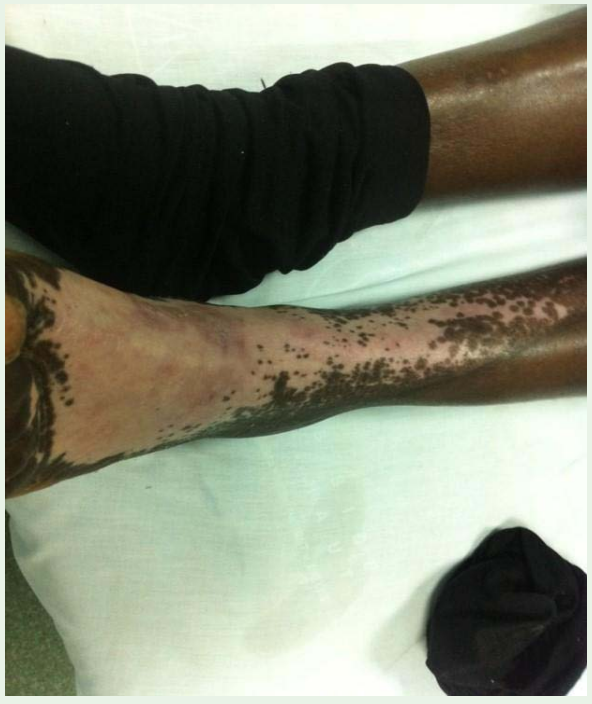

Figure 1: Physical examination of the skin showing vitiligo.

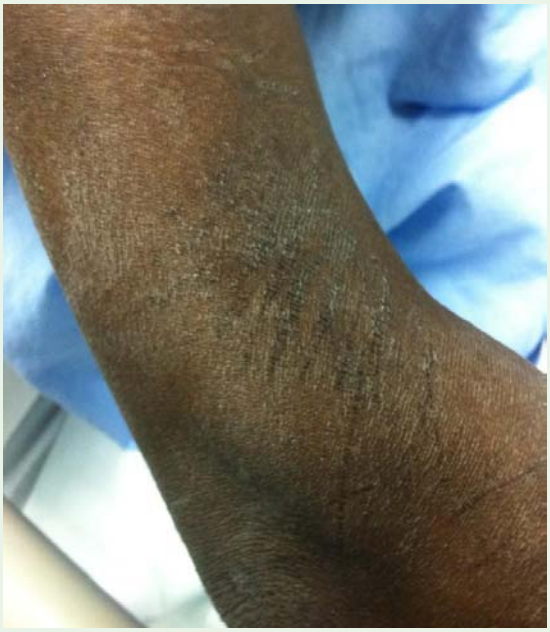

Figure 2: Physical examination of the skin showing eczema.

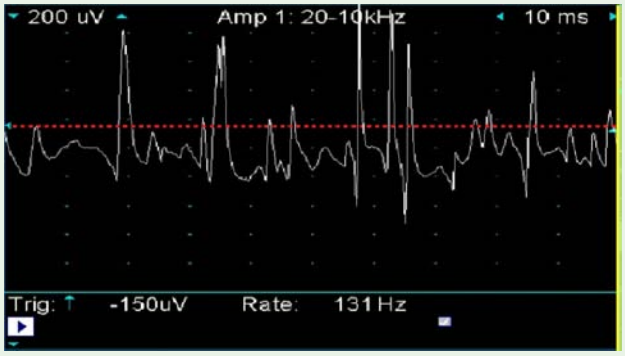

Figure 3: EMG showing continuous motor-unit activity in agonist and antagonist muscles.

eczema (Figure 2). Laboratory analysis revealed that serum TSH was 0.005 U/mL, and T4 was 24 ug/dL. Thyroid antibodies showed thyroid peroxidase activity of 600 IU/mL and positive thyroid antibody. The CT of the head, the chest, and the abdomen were normal and MRI of the head and spinal cord were also normal. Thyroid Nuclear Image showed a high level of Iodine concentration near the thyroid in addition to cold nodules in the left lobe. Anti-Hu, Anti-Ri and Anti-Yo were not detected. Glutamic acid decarboxylase antibodies were 2000 nmol/L. Electromyography (EMG) studies showed continuous motor-unit activity in agonist and antagonist muscles (Figure 3).

Based up on physical, immunological, and other clinical data, we could able to diagnose this case reported here as a SPS.

Patient was treated with oral diazepam at 10 mg BID and Intravenous Immunoglobulin (IVIG) at 2 g/kg, after which she started to improve gradually; however, repeated IVIG doses were required.

Discussion

Stiff Person Syndrome is arare neurological disorder with age of onset varies between 30 to 60 years; most frequently affects people in their 40s with females being affected more than males.

It has been postulated andaccepted that SPS is underlined by an autoimmune process. SPSoccurs in association with a variety of autoimmune diseases including type 1 diabetes mellitus, thyroiditis, myasthenia gravis, pernicious anemia, epilepsies, cerebellar ataxia, vitiligo and adrenal insufficiency.

Although up till now the underlying mechanism of SPS has not been elucidated, the "symptom complex" of SPS proposes a "derangement of physiology mediated by spinal cord reflexes". Glutamic Acid Decarboxylase (GAD), which is a presynaptic autoantigen, is believed to play a central role in the pathogenesis, however, the precise mechanism of which SPS patients are affected by those auto antibodies is still also unknown [3].

On the other hand, most SPS patients with high-titer GAD antibodies also have other antibodies that inhibit GABA-Receptor-Associated Protein (GABARAP). The antibodies appear to interact with antigens in the brain neurons and the spinal cord synapses, causing a functional blockade with gamma-aminobutyric acid synthesis. This leads to GABA impairment, which causes the spasms and stiffness. Amphiphysin and gephyrin are also sometimes found in the serum and CSF of SPS patients. Further autoantibodies have been defined in alliance with anti-GAD antibodies. Theseautoantibodies were found to bind to the surface of GABAergic neurons rather than being targeted to GAD [3].

The clinical hallmark of SPS is an insidious and progressive muscle rigidity and stiffness, which involve mainly the axial muscles (lumbar or cervical) and progresses slowly to involve proximal limb muscles.Additionally, there may be a considerable pain in a symmetric fashion, and voluntary movements become difficult. Ankylosis of lower extremity may develop owing to the prolonged immobility and stiffness of the lower extremities.Activities of daily living is severely limited. The most sensitive and specific feature of SPS is the occurrence of episodic muscle spasms which are triggered by noise, abrupt movement or emotional distress. Moreover, both focal and grand mal seizures have been reported in patients with SPS.

Neurologic dysfunction of SPS can be severe enough to cause death due to the paroxysmal autonomic instability, which is characterized by transient hyperpyrexia, diaphoresis, tachypnea, tachycardia, pupillary dilatation, and arterial hypertension [4].

In the early stage of disease, the stiffness of the back and sometimes the neck are the typical symptoms. Patients may walk and sit with an exaggerated upright posture (classic "tin-soldier" appearance). Later in the disease, response to stimuli becomes more obvious and startle may lead to prolonged spasms. These symptoms typically worsen with anxiety and stress. At the end stages of the disease, few muscles in the body are spared. Joint deformities, skeletal fractures and muscle ruptures were reported. Moreover, anxiety, panic attacks, specific phobias and depression have been reported [5].

Workup for a patient with SPS includes complete blood count, thyroid function test, thyroid antibodies, Hemoglobin A1c and CT of the of chest looking for thymoma. Special tests include Anti-

GAD antibodies, Anti-pancreatic islet cell antibodies and Anti-amphiphysin antibodies.

Anti-glutamic acid decarboxylase antibodies are found in 60% of patients and are strongly supportive of SPS. Antiamphiphysin antibodies are detected when SPS is associated with malignancy. The absence of anti-glutamic acid decarboxylase antibodies does not rule out a diagnosis of SPS [6]. Electromyography studies have shown a characteristic continuous motor unitactivity with normal morphology, especially in the paraspinal muscles. Myotonic potentials are absent. The activity breaks down by sleep and benzodiazepines. Furthermore, the opposing muscles have been noticed to have synchronous constant motor activity [5].

Benzodiazepines (20 to 60 mg/day of diazepam) are considered the core treatment of SPS through their modulating effects on GABA [7]. Another GABA-modulating drug is Baclofen. Baclofen, which is administered orally or intrathecally, can be added to benzodiazepines or used as monotherapy if thereare contraindications or side effects to the use of benzodiazepines. The second-best line of treatment is intravenous immunoglobulin (IVIG). Intravenous immunoglobulin is infused over 2-5 days with a usual does of 2 g/kg [5]. Furthermore, physical therapy and occupational therapy are important to the recovery of the patient.

Conclusion

In this report, we describe a patient with SPS associated with hyperthyroidism, epilepsy and vitiligo, treated with diazepam and IVIG, resulted in significant clinical improvement in her functional status.

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