Case report

A patient presenting with a panic attack and lower back pain diagnosed as stiff person syndrome: A case report

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Abstract

We present a case of a 43-year-old man diagnosed with hypothyroidism, autoimmune hepatitis and steroid-induced diabetes, presenting with a panic attack and backache for three months duration. He had a stiff back with right lower limb stiffness and hyperreflexia. He was confirmed to have stiff person syndrome with positive electromyography and the presence of a high titre of glutamic acid decarboxylase (GAD) antibodies. With a background history of autoimmune diseases and stiffness of limbs, it is important to have a high index of suspicion of stiff person syndrome (SPS), not to miss a treatable organic disorder.

Keywords: Stiff person syndrome, Glutamic acid decarboxylase antibodies, Panic attacks, Diabetes mellitus

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Funding: None
Competing interest: None
Received: 07.09.2023 Accepted revised version: 02.07.2024 Published: 06.08.2024

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Introduction

Stiff persons syndrome is a disabling disorder that was first explained in 1956 by Moersch and Woltman, following a review of 14 cases [1]. Its incidence is around one per million with female preponderance affecting in their mid-fifth decade. The characteristic features are rigidity and episodic spasms of muscles involving thoracolumbar, paraspinal, abdominal and proximal thigh muscles [2].

Case presentation

A 43-year-old male patient who had a history of hypothyroidism, autoimmune hepatitis and long-term steroid therapy-related diabetes presented with lower back pain associated with right lower limb pain for 3 months. Upon examination, he was found to have a stiff back with a stiff right leg and mild hyperreflexia.

magnetic resonance imaging (MRI) of the entire spine was unremarkable, and the initial electromyography (EMG) was negative for features of lumbar radiculopathy or SPS. He had fluctuating symptoms, and it was attributed to a functional neurological disorder initially.

Three months after the initial presentation, he was admitted to the emergency treatment unit with a panic attack where he was restless and sweating. He had painful cramps involving his lower limbs with severe back pain. He was unable to walk alone and had scoliosis. On examination, the tone was difficult to assess due to stiffness in bilateral lower limbs and the lower half of the trunk. Increased tone of lower half of the trunk showed increased lumbar lordosis (figure 1). The muscle power was normal, along with brisk knee
reflexes and flexor plantar response. The sensory examination was normal.

He was treated with benzodiazepines for his stiffness and muscle spasms. He made a marked improvement the following day. His complete blood count, serum electrolytes, serum calcium, inflammatory markers and creatine phosphokinase levels were normal. Cerebrospinal fluid (CSF) analysis was unremarkable. On strong suspicion of stiff person syndrome, Antibodies against glutamic acid decarboxylase (anti-GAD) was tested and found to be positive with a high titre of >10000IU/mL (normal<5IU/mL). Follow-up EMG showed continuous motor unit activity in agonist and antagonist muscles.

Figure 1: A, Skin creases at the lumbar region of back, indicating hyperlordosis; B, hyperlordosis

He was started treatment with oral diazepam and intravenous methylprednisolone pulses daily for five days. Afterwards, he was commenced on intravenous immunoglobulin 0.4/kg/day for five days along with oral prednisolone 1mg/kg daily and added tizanidine (2mg bd). With that, he achieved a good recovery of stiffness and was able to engage in his usual activities of daily living.

Discussion

This case report highlights a common presentation of an extremely rare disorder which may go undiagnosed and mismanaged if not suspected as one of the differential diagnoses.

The current diagnostic criteria of classic stiff person syndrome (SPS) include: 1. Stiffness of the axial muscles, prominent in thoracolumbar paraspinal and abdominal region; 2. Painful spasms triggered by unexpected tactile or auditory stimuli; 3. Electromyographic evidence of continuous motor unit activity of agonist and antagonist muscles; 4. Absence of other neurological impairments that could support an alternating diagnosis; 5. Positive serology for anti-GAD65 or amphiphysin autoantibodies; 6. Clinical response to therapy with benzodiazepines [3].

Since the original description of classic SPS which involves the torso and lower than upper extremities, additional phenotypes have been described as partial SPS, SPS-plus, pure cerebellar ataxia, progressive encephalomyelitis with rigidity and myoclonus (PERM). In partial SPS, symptoms are limited to one limb which is known as the stiff limb syndrome. When classic SPS is associated with brainstem or cerebellar symptoms or signs, this condition is known as SPS plus. Musculoskeletal symptoms are lacking in the pure cerebellar ataxia form. The spectrum is now known as stiff person spectrum.

Several antibodies have been described as associated with SPS. The comment is GAD-65, while the other associations are glycine receptor, Amphiphysin, Zic4, DPPX, Gephyrin, GABAA receptor and GABARAP antibodies [4]. GAD antibodies represent nearly 80% of SPS patients, which is the rate-limiting enzyme for GABA synthesis [5]. The pathogenic mechanism behind SPS is due to the affected GABAergic synapse pathway, which leads to the loss of inhibitory signals on spinal motor neurons, which subsequently results in muscle stiffness and spasms [6].

GAD is also expressed in pancreatic cells. Type 1 Diabetes (DM-1) has a low-titre anti-GAD antibodies. 35% of SPS patients also have associated DM-1 along with other autoimmune diseases, such as vitiligo, pernicious anaemia, celiac disease or thyroiditis [5].

A significant number of patients present with psychiatric manifestations, including panic attacks, generalised anxiety disorder or phobia. It is estimated that there is a high risk of co-existent psychiatric diseases in patients with SPS compared to the general population. Considering the rarity and associated neuropsychiatric symptoms, clinicians tend to misdiagnose patients as having a functional neurological disorder [7]. Further, SPS is known to associate with uncontrollable autonomic dysfunction [6]. The diagnosis is challenging and relies on clinical criteria and EMG findings, and it is supported by
positive anti-GAD antibody test and associated autoimmune disorders, [8] like in our patient who had hypothyroidism and autoimmune hepatitis and later developed diabetes which is not improving even after stopping steroids. So, there may have been a propensity for him to develop autoimmune diabetes also, in this background of other autoimmune illnesses.

Less than 5% of SPS are paraneoplastic and commonly associated with breast cancer, small-cell lung cancer, lymphoma and thymoma. It is, therefore, important to consider a para neoplastic process in the elderly and individuals that present within five years from symptom onset [4]. Paraneoplastic SPS cases are almost always associated with amphiphysin antibodies and a single case against gephyrin [5].

Treatment of SPS is based on symptomatic treatment and immunosuppression. Benzodiazepines are used as an initial strategy and when patients are not well responding or intolerant to them, immunosuppressives including glucocorticoids and IV immunoglobulins have a place [9]. In refractory patients, plasma exchange, rituximab, azathioprine, mycophenolate mofetil, cyclophosphamide and stem cell therapies have been used with variable success [4].

Conclusion

Stiff person syndrome is a rare condition which is difficult to diagnose due to its various clinical presentations, including neuro-psychiatric manifestations. Therefore, SPS has to be in the list of differentials when a patient with chronic backache is evaluated. Early diagnosis helps commence early treatment which can prevent the progression of the disease and disability.

Consent

Written informed consent was obtained from the patient to publish the clinical details and images.

References