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CASE REPORT

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Stiff person syndrome: avoiding misdiagnosis

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Abstract Stiff person syndrome (SPS) is a rare neurological disorder characterised by muscular rigidity and superimposed spasms of the trunk and limbs that may be precipitated by voluntary movements and unexpected tactile, auditory or emotional stimulation. The high prevalence of autoantibodies against glutamic acid decarboxylase (antiGAD) in both serum and cerebrospinal fluid, as well as the frequent association of SPS with other autoimmune disorders, suggest an autoimmune pathogenesis. SPS is frequently misdiagnosed as axial dystonia or psychogenic movement disorder. We report a patient with SPS in order to emphasise the reasons for this common misdiagnosis.

Key words Movement disorders • Stiff person syndrome • Anti-GAD antibodies

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Stiff person syndrome (SPS) is a rare neurological disorder characterised by fluctuating muscular rigidity, superimposed episodic spasms of the trunk and limbs and heightened sensitivity to external stimuli [1, 2]. The high prevalence of autoantibodies against glutamic acid decarboxylase (antiGAD), the presynaptic enzyme responsible for the synthesis of γ-aminobutyric acid (GABA) in both serum and cerebrospinal fluid [3, 4] the frequent association of SPS with other autoimmune disorders such as type I diabetes mellitus or thyroiditis and the response to immunotherapies strongly suggest an autoimmune pathogenesis [2, 4, 5]. Specific malignancies are associated with SPS in about 5% of patients. Most of these patients are positive for antibodies directed against amphiphysin. Paraneoplastic SPS has been reported in association with breast cancer, small cell lung carcinoma, thymoma and Hodgkin lymphoma, although no antibodies have been isolated in the latter two instances [6]. We report a patient with SPS in which there was a delay of three years in reaching diagnosis.

Case report

A 41-year-old female patient was referred because of episodes of spasms and intense painless clonic jerks of the trunk and limbs, of long duration (30 min to 2 h), without impairment of consciousness. The episodic spasms were spontaneous or reflex, varied in severity and were provoked by unexpected tactile stimuli, sudden noises and emotional upset. Generalised myoclonic jerks began with an abrupt jerk followed by prolonged tonic–clonic activity and were accompanied by profuse sweating and tachycardia. Their onset was two years before her first visit but in the last 6 months she had experienced an increase in severity, duration and incidence of these episodes, for which she had to visit an emergency room for IV therapy with diazepam. The patient also complained of lower back stiff-

ness and difficulty in walking over the last three years. Initial diagnosis was axial dystonia and she had been treated with botulinum toxin with partial response. As gait disturbance deteriorated, she developed phobia associated with unaccompanied walking in open space and the question of a psychogenic movement disorder was addressed. The precipitation of the clonic jerks by emotional stimuli and their resolution with the administration of diazepam strengthened this belief. Eventually, she could not walk unaided in open space, cross a street or descend stairs. She underwent psychiatric evaluation and fulfilled the diagnostic criteria in the Diagnostic and Statistical Manual (DSM-IV) for panic disorder with agoraphobia. Thereafter she followed a few sessions of cognitive-behavioural therapy, with minimal results.

Careful neurological examination revealed muscle rigidity of the trunk and limbs with lumbar hyperlordosis, protuberant abdomen and stiff-legged gait (Fig. 1). Clinical evaluation of stiffness was performed using the distribution of stiffness index, which reflects the number of stiff areas and of spasms using the heightened sensitivity score, which reflects the number of factors triggering spasms [3]. Stiffness index was 4 (upper and lower trunk, both legs and abdomen) and heightened sensitivity score was 5 (unexpected noises, somatosensory stimuli, voluntary activities, emotional upset and nocturnal spasms).

Spontaneous involuntary normal motor unit potentials were demonstrated on EMG in lumbar paraspinal and abdominal muscles and in lower limbs in agonist and antagonist muscles simultaneously. The diagnosis of SPS was established by the presence of anti-GAD-65 antibodies in the serum, at high titre (>300 U/ml, normal values <50 U/ml). The assay used for anti-GAD antibody detection was immunoprecipitation.

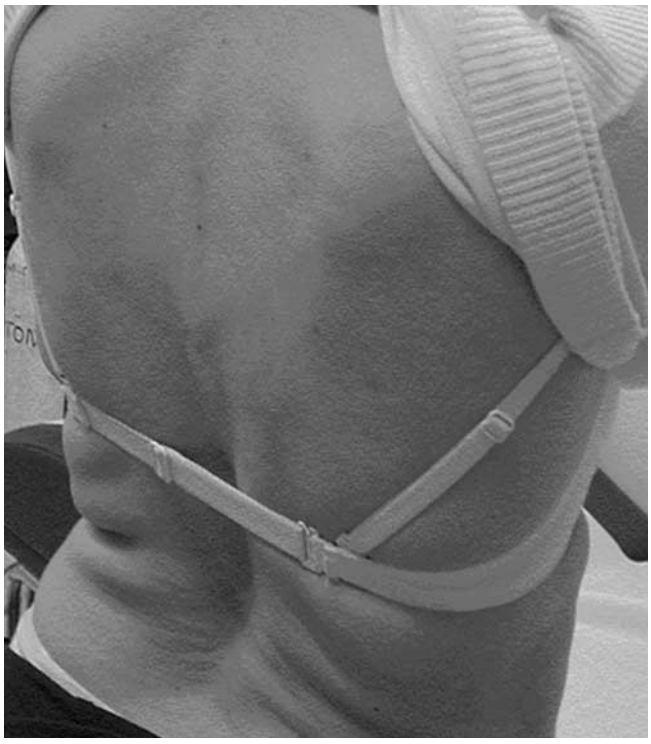

Fig. 1 Patient with SPS. Note the rigidity of the paraspinal muscles and the lumbar hyperlordosis

The patient was accordingly treated with oral diazepam 45 mg t.i.d. and she responded satisfactorily: clonic jerks abated and mobility improved. The number of stiff areas dropped to 3 and the heightened sensitivity score to 0. Improvement of psychiatric symptoms quickly followed the response of neurological signs to therapy. During the patient's initial psychiatric assessment three Cognitive-Behavioural Therapy questionnaires were administered: a 15-item questionnaire of agoraphobic cognitions, a 13-item panic appraisal inventory and a 10-item questionnaire of avoidance behaviours (for all items the patient had to rate from 0 to 100 the presence of symptoms or thoughts). The patient completed the same inventories for evaluation of improvement of psychiatric symptoms, 6 months after remission of spasms. The improvement was confirmed as the inventory results showed a 78% decrease of agoraphobic cognitions, 88% decrease on panic attacks inventory and 90% decrease in avoidance behaviours. The percentile difference was estimated as the difference between the total initial and total final scoring of the items of each inventory divided by the total initial scoring multiplied by 100:

((initial scoring – final scoring)/initial scoring)#100.

The response was sustained during the two-year follow-up.

Discussion

The rarity of SPS and the elusive clinical signs make its accurate diagnosis difficult. Disease variants [6–8] further complicate diagnostic uncertainty, although it is controversial whether they represent different entities or variable manifestations of the same disease process. Patients are frequently misdiagnosed as having dystonic syndromes or psychogenic disorders [3, 9, 10], especially during the early stages of the disease, when motor disturbances are intermittent and neurological examination is entirely normal, as happened in our case. The widely held belief that marked anxiety is a particular feature of psychogenic movement disorders further increases the risk of misdiagnosis [10]. Moreover, patients with phobia are more likely to present with exaggerated startle responses and consequently to be misdiagnosed [3, 10].

In our case, the presence of episodes of severe spasms that responded to therapy with diazepam delayed correct diagnosis by three years. The severity and high frequency of episodic spasms predominated and overshadowed muscular rigidity. Delay in reaching diagnosis has been previously reported, especially when anxiety and phobias are prominent [3]. The improvement of agoraphobia and panic attacks following the

satisfactory response of neurological signs strongly favours the secondary nature of psychiatric symptoms in our case. SPS can be serious or disabling if untreated and can lead to total body rigidity [3, 8]. Because treatment response and prognosis are good [1, 8], early recognition of the disorder and initiation of therapy are important. It should be mentioned however, that benzodiazepine therapy may be problematic for long-term treatment due to tolerance. Immune therapies (immunosuppressants, plasmapheresis or intravenous immunoglobulin) have been shown to be effective in anti-GAD-positive patients with SPS [11].

In conclusion, the presence of phobia in patients with fluctuating stiffness should raise suspicion of SPS syndrome and response to oral diazepam should not lead to misdiagnosis of a psychogenic movement disorder. Screening for high titres of anti-GAD antibodies could help to confirm diagnosis, although their absence does not exclude it.

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