

Two Stiff Person Cases Misdiagnosed as Conversion Disorder

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Abstract

Modern psychiatric diagnostic systems classify neurological symptoms that cannot be explained by a physical disease or another psychiatric disorder as conversion disorder (CD) or dissociative motor disorder. It is a well-known fact that the overall rate of misdiagnosis of conversion symptoms is high. The most common presenting symptoms of misdiagnosed patients are gait and movement disturbances.

Stiff-person syndrome (SPS) is a rare progressive autoimmune neurological disorder. The identification of antibodies against glutamic acid decarboxylase (GAD) in association with SPS provided an important contribution to the understanding of the pathophysiology of this syndrome. Patients may present with severe muscle rigidity and sudden contractions. Simultaneous contraction of agonist and antagonist muscles produces gait disturbance. SPS can be exacerbated by emotional stressors, and sudden auditory, visual, and tactile stimuli.

Herein we present 2 patients that were referred for psychiatric assessment, because their neurological symptoms initially could not be explained by a neurological disease, and subsequently diagnosed as SPS. The aim of this case report is to draw attention to the psychiatric presentations of SPS and to emphasize the importance of complete psychiatric and neurological examination, including brain imaging and electrophysiological studies, in the differential diagnosis of CD.

Key Words: Conversion Disorder, Stiff-Person Syndrome, Differential Diagnosis

INTRODUCTION

Motor or sensory signs that cannot be explained by a neurological disorder are common in neurological practice. In all, 20% of neurological outpatients and 5% of inpatients present with psychological signs that cannot be explained by a physical disorder (Lempert et al., 1990; Mace and Trimble, 1991; Akagi et al., 2001; Fink et al., 2003). The most common psychological findings in neurology practice are paralysis, impaired vision, gait disturbances, pseudoseizures, and movement disturbances.

Modern psychiatric diagnostic systems classify neurological symptoms that cannot be explained by physical illness or another psychiatric disorder as conversion disorders (CD) (APA) or dissociative motor disorders

(WHO). Research shows that misdiagnosis in CD is quite common. In a recent review it was reported that the overall proportion of misdiagnosed cases is 8.4%, and that the most common presenting symptoms of misdiagnosed patients are gait and movement disorders (Stone et al., 2005). Comorbidity of CD and neurological disorder is common (Marsden, 1986). Among neurological inpatients, 1%-30% are diagnosed as CD, either as a primary or comorbid diagnosis.

Stiff-Person Syndrome (SPS) is a rare autoimmune neurological disorder, which was first described by Mersching and Woltman (1956). The most important contribution to understanding the pathophysiological and immunological basis of SPS was the identification of antibodies against glutamic acid decarboxylase (GAD) in association with SPS (Solimena et al., 1988). GAD

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is an enzyme localized in the presynaptic terminals of GABAergic inhibitory synapses and is involved in gamma aminobutyric acid (GABA) synthesis. GAD antibodies can be detected in 70% of patients with SPS. Two additional antibodies anti-amphiphysin and anti-gephyrin are implicated in paraneoplastic variants of SPS. Like GAD, amphiphysin and gephyrin are also involved in neurotransmission. It has been suggested that the pathogenic mechanism is either a reduced level of GABA in the cerebrospinal fluid and the brain, or the toxic effects of anti-GAD antibodies on GABAergic neurons.

The syndrome is characterized by progressive, severe muscle rigidity and sudden contractions. Spine and leg involvement, with painful contractions, is present in almost all patients. The stiffness may either be persistent, or waxing and waning. Patients may exhibit autonomic dysfunction, including increased heart rate, hyperhidrosis, fluctuation in blood pressure, or gastrointestinal (constipation) and urinary system (urinary retention) symptoms. The female to male ratio is 2:1 and onset is typically in middle age. The association with autoimmune diseases and neoplasms is critical. It often co-occurs with breast cancer, diabetes mellitus, thyroiditis, vitiligo, and pernicious anemia. It is typical that the legs will be held in extension because of contraction of the antagonist muscles. Painful spasms in the abdominal and lumbar muscles may occur. Upper extremities are rarely involved. Simultaneous contraction of agonist and antagonist muscles are relieved by administration of benzodiazepines, and can be detected with electromyography (EMG). Emotional stressors, and sudden auditory, visual, and tactile stimuli can exacerbate symptoms. This stress-associated exacerbation of symptoms may be misperceived as muscles contracting under voluntary control. Patients may avoid open spaces, particularly crossing roads, because of abrupt motor reactions to triggers. As the symptoms exacerbate in response to emotional stressors, patients are usually referred for psychiatric assessment. Psychiatric symptoms are common in SPS. A retrospective study reported that 12 of 24 patients with SPS had such psychiatric manifestations as anxiety, depression, and substance abuse. It has been hypothesized that the GABA system is involved in both the neurological and psychiatric symptoms observed in these patients (Tinsley et al., 1997). In another study, 8 of 13 patients had at least 1 additional psychiatric diagnosis (depression, substance use disorder). It is hypothesized that GABA deficiency or GABAergic neuron dysfunction leads to psychiatric symptoms in SPS patients (Black et al., 1998).

Herein we present 2 patients that were referred for psychiatric assessment, because of unexplained neuro-

logical signs, and subsequently diagnosed as SPS. The aim of this case presentation is to draw attention to psychiatric presentations of SPS and to emphasize the importance of complete psychiatric and neurological examination, including brain imaging or electrophysiological studies, in the differential diagnosis of CD.

CASE 1

Ms. A. was a 43-year-old, single clerk. She was admitted to the neurology department of a university hospital in 1997 with impaired speech, difficulty climbing stairs, clumsiness, and weakness in her left hand. Cerebral and cerebellar atrophy, and a millimetric lesion in left frontoparietal region were detected with MRI and CT. Brain magnetic resonance angiography was normal. Brain biopsy from the parietal lesion was reported as chronic subdural hematoma in 1998. The symptoms improved for 3 months after the brain biopsy; however, unsteadiness, staggering gait, difficulty climbing stairs, and impaired handwriting subsequently emerged. As the severity of her unsteadiness increased, she was virtually unable to walk outdoors without help. In August 2002 she presented to the neurology department of our university hospital. With the diagnosis of cerebellar ataxia, underlying causes were searched. Blood tests (including vitamin B12, folic acid, vitamin E, anti-gliadin IgA and IgG levels, tumor markers, serum), EMG, electroencephalography (EEG), somatosensory-evoked potentials (SEP), echocardiography, cerebrospinal fluid investigations, and urine electrophoresis were normal. DNA sample analysis conducted to rule out Friedrich ataxia and peroxisomal storage diseases was negative. The patient was followed-up annually by the neurology department. Follow-up neurological examinations were stable; however, her functioning deteriorated.

In January 2003 she was transferred to a different department at her workplace. She could not adapt herself to her new job and her complaints worsened. She was unable to learn the new work procedures demanded by her boss and became unwilling to go to work. By the end of 2004 she was creeping on her hip and unable to work; her sister who works at the same office was carrying out her responsibilities. In April 2005 she could no longer go to work. In September 2005, even though she was neurologically stable, she was unable to stand up. When she stood up with assistance she could hardly take a step because of excessive contractions of the adductor and extensor muscles. Due to her inconsistent neurological exam findings she was referred to the psychiatry department.

She was fully incapacitated and reported that something was impeding her ability to walk. She talked about her symptoms continually, complaining about stiffness, and stretching sensations in her hands and her legs. She had involuntary leg movements and sometimes felt abrupt warming and cooling sensations. All her needs were met by her family members and anything that was out of order easily frustrated her. From time to time she burst into tears without any apparent reason and slept only 2-3 hours a day. Her appetite was diminished.

After she was admitted to the psychiatric ward, she was using a wheelchair and needed assistance. Neurological examination revealed dysarthric speech and ataxic gait; however, all extremity muscle groups had normal strength. Although she was not able to flex her knee joints in an upright position, she could while lying down. The mental examination revealed anxious and depressed mood, and impaired attention. A physiotherapy rehabilitation program was established and an antidepressant was prescribed. As she had experienced adverse effects with serotonin re-uptake inhibitors, mirtazapine 15 mg/day was initiated. At first she complied with the exercises and was able to walk with assistance. She could get up from a lying or sitting position and could stand for 10-15 seconds. She could not read because her eyes burned. She had limited contact with other patients in the ward because she considered them boring or offending. No change was reported in the repeat MRI. The Bender Gestalt Visual Motor Coordination Test, Benton Short Term Visual Memory Test, and Wechsler Adult Intelligence Test revealed impaired verbal memory performance, visual motor coordination, and organization.

After 1 week she was unable to continue physiotherapy treatment because of severe exhaustion and pain in her left foot. She declined the offer of antidepressant medication. She felt better and her movements became faster after stopping the medication.

As her contractions worsened while initiating any movement, we consulted the neurology department in order to rule out a neurological disorder. Because of the simultaneous contraction of agonist and antagonist muscles EMG was planned. EMG showed continuous motor unit activity in accordance with muscle stiffness in SPS. Diazepam 2 mg/day was prescribed. With this treatment her contractions and pain diminished, and she was transferred to the neurology department.

Diazepam was increased to 25 mg/day, but because of sedation and nausea it was discontinued. As intravenous (IV) IG did not work, 5 sessions of plasmapher-

esis was performed. She partially benefitted from plasmapheresis and was discharged with levetiracetam 1000 mg/day. Her previous cerebellar system symptoms were attributed to SPS. Currently, she cannot stand or walk without assistance.

CASE 2

Mr. B is a 41-year-old engineer working as the director of a private company. In November 2006 he presented to a hospital because of itching at the abdominal area, elbow, and backside of the knees; he was disgusted by the smell of food, had difficulty tasting food, and had mild ankle swelling. He was prescribed an antihistaminic medication. Three days later his feet began to tremble, and he could only walk slowly and unsteadily. As he fainted once he was referred to a neurologist. Neurological examination, brain MRI, and EEG were normal, and he was subsequently referred to a psychiatrist. The psychiatrist prescribed citalopram 20 mg/day, clonazepam 2 mg/day, and vitamin supplements. After a few days his complaints gradually subsided and he could even go shopping. He took a couple of days off from work and rested at home. After his return to work his complaints returned following an upsetting incident. The following day he had difficulty urinating, and he lost his balance and fell down. The same day myoclonic jerks began in his legs. He was evaluated by a physical therapist and his EMG results were in the normal range, but he was told that he might have multiple sclerosis. Again, he was referred to a neurologist and sensorial-evoked potentials (SEP) were run. The findings were normal and he was advised to consult a psychiatrist. After a psychiatric examination he was admitted to the psychiatric inpatient unit of our university hospital.

At the time he was admitted to the inpatient unit he was using a wheelchair and myoclonic movements were observed in his legs. He had difficulty speaking because of contractions in his lower jaw. He had a labile affect with pathological expressions of smiling or crying. His thought process and content were normal. He reported that whether his disorder was neurological or psychological was unimportant; his aim was to regain his health. There was an intentional tremor in his left hand. Bilateral rigidity in the lower extremities was observed. Deep tendon reflexes were lost due to muscle rigidity. Suspecting a neurological disease, EMG was ordered. EMG results showed overfiring motor units; his jerks were triggered by unexpected stimuli. After a 10-mg diazepam injection his EMG normalized and within 1 minute he was able to stand still and walk with some help. With the diagnosis

of SPS he was transferred to the neurology department and was administered 1 mg/day IV pulsed steroid. Later, deflazacort 30 mg/day, diazepam 30 mg/day, gabapentin 1200 mg/day, baclophen 20 mg/day were initiated. During this time ptosis in his left eye occurred. Within a few days his gait improved and involuntary contractions diminished. Autoimmune markers anti-glutamic acid decarboxylase (antiGAD) and anti-topoisomerase (antiTPO) and cancer markers prostate specific antigen (PSA), Ca 19-9, and Ca 125 were negative. Because of the pain in his hip an X-ray examination was performed and bilateral fractures were observed. Rest was advised. IV IG treatment three times weekly was started. During the follow-up his symptoms remitted and currently he has regained most of his functionality.

DISCUSSION

We presented 2 SPS patients with dissimilar clinical presentations that were misdiagnosed as CD. The peculiar presentation of clinical symptoms (variation of examination findings in different positions) and manifestation of psychiatric symptoms misled the physicians, and they diagnosed psychiatric rather than neurological disorders. In SPS contractions can be induced or exacerbated by stress, and lead to psychiatric consultation. Motor symptoms during the initial phase of SPS are frequently misdiagnosed as psychogenic movement disorder, particularly in patients with phobic anxiety. Neither pharmacological nor behavioral therapies help psychiatric symptoms, but with the improvement in motor symptoms that follow treatment of SPS, phobic symptoms are relieved (Henningsen and Meinck, 2003).

In patients that have been diagnosed with a neurological disorder (as with cerebellar syndrome in the first case) meticulous differential diagnosis of newly emerging symptoms is essential. It is, however, a well-known fact that neurological and psychiatric disorders frequently co-occur (Marsden, 1986). In the evaluation of such cases psychiatrists and neurologists should carefully collaborate.

In the absence of clear symptoms and MRI findings, and variations in examination findings, Ms. A.'s subjective complaints led to the diagnosis of CD. Ms. A.'s symptoms worsened after her involuntary work transfer. Exacerbation of symptoms due to psychological distress was misinterpreted as avoidance of responsibilities by deliberately exaggerating neurological symptoms and her family's compensatory efforts were mistook as overprotection that reinforced the symptoms. Her avoidant,

easily offended personality traits and non-verbal communicative pattern were read as a vulnerability factor for CD.

During her clinical follow-up she presented with depressive symptoms, such as depressed mood, loss of interest, sleep disturbance, and loss of appetite. Physical therapy didn't help her motor symptoms and had detrimental effects on her daily activities. Anxiety provoked her avoidant behavior and resistance to treatment. Because the diagnosis of SPS was made after detecting permanent motor unit activation in EMG, it could be considered that not only her motor symptoms, but also some of her psychiatric symptoms were caused by the neurological disease.

Mr. B did not have a history of neurological or psychiatric disorder. In his mental examination the only pathological sign was a labile affect. He was referred to the department of psychiatry with the diagnosis of CD because his complaints appeared to be triggered by psychological stressors and the severity of his gait disturbance fluctuated throughout the day. He was, however, a well-educated middle-aged man without a history of psychiatric disorder, his personality was well-adjusted, and no secondary gain but detrimental effects of the symptoms were observed. His suffering led us to reevaluate the diagnosis. Repeat EMG showed involuntarily overfiring of motor units and symptom relief after benzodiazepine injection led us to the diagnosis of SPS. Bilateral hip fractures were the result of his falling down.

Benzodiazepine, baclophen, and GABAergic drugs for increasing cortical and spinal inhibition, and steroids, plasmapheresis, or IV IG for immunomodulation can be used to treat SPS. SPS has a progressive course if not treated. It was reported that symptoms are exacerbated by the use of tricyclic antidepressants (Lockman and Burns, 2007).

In the case of Ms. A., symptoms worsened following mirtazapine treatment and improved after it was stopped. In a recent study increased cortical excitability was reported both in healthy controls and in depressed epileptic patients (Munchau et al., 2005). Change in cortical excitability and inhibition balance could have exacerbated her symptoms. Her symptoms partially remitted in response to benzodiazepine, plasmapheresis, and IV IG; she was discharged with a prescription for levetiracetam. In the case of Mr. B., clonazepam, which was prescribed before the diagnosis of SPS, helped in diminishing his symptoms. Eventually, he benefited from GABAergic drugs and IV IG.

CD was ruled out by the diagnosis of SPS, but it should be kept in mind that psychiatric symptoms may emerge during the course of the disease. These case reports highlight the difficulty in diagnosing CD in the presence of a neurological disorder. On the other hand, SPS can

be easily misdiagnosed, particularly due to a labile affect. Misdiagnosis leads to delay in treatment, which could negatively affect the disease course. In cases with painful muscle contractions and gait disturbances SPS should be considered and EMG can aid early diagnosis.

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