



근육 강직 증후군: 진단적 어려움

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Stiff-Person Syndrome: Diagnostic Difficulty

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Stiff-person syndrome is a rare disorder, and the natural history of the syndrome has not been completely ascertained. The symptoms range from mild to severe and can progress over time: the final result can be significant disability. However, this syndrome is often misdiagnosed due to a lack of understanding of the clinical manifestations. We report the case of a patient who presented with slowly progressing gait disturbance and lower extremity pain and was later diagnosed as suffering from stiff-person syndrome. The patient experienced symptomatic improvement after the administration of benzodiazepines. No recurrence of symptoms has been reported. If the characteristic clinical features and electromyography findings of the syndrome are accurately interpreted, diagnosis of patients with abnormal muscle tension can be effectively done.

Key Words: Stiff-person syndrome, Leg, Spasm, Autoimmune disease, Autoantibodies

Stiff-person syndrome (SPS) is rare neurological disorder. The prevalence isn't clearly defined, but according to one study, it is estimated to be very rare disease of 1:1,250,000.¹⁾ SPS is typically characterized by progressive muscle stiffness and spasms of the axial and proximal lower limb muscles and the spine. However, it can be manifested by various clinical symptoms. The symptoms range from mild to severe and can progress over time, resulting in significant disability. Diagnosis is established by clinical characteristics and confirmed by electromyography (EMG) or antibody testing. Almost all cases have an autoimmune basis; most involve the glutamic acid decarboxylase (GAD) autoantibody, but paraneoplastic varieties also exist. Moersch and Woltman²⁾ first described SPS in 1956 in 14 patients who presented with tightness of the

back, abdominal, and thigh muscles. They described progressive, fluctuating rigidity, and painful spasms in the patients, resulting in the characteristic "wooden man" appearance, with postural instability and falls. SPS is a rare disease but may be underdiagnosed due to a lack of understanding of the clinical manifestations. We report the case of a patient with the clinical features of SPS and consider the accuracy of SPS diagnosis in cases of unexplained stiffness and spasms.

The study has been reviewed and approved by our institutional review board.

CASE REPORT

A 28-year-old male patient was referred to our clinic due to a slowly progressing gait disturbance and lower extremity pain. Two months prior to his visit, stiffness and unnatural symptoms first developed during voluntary movement of the right ankle joint. The symptoms improved and worsened repeatedly. Recently, similar symptoms occurred in the left ankle joint and subsequently pro-

Received May 7, 2019 Revised July 17, 2019 Accepted August 2, 2019

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Financial support: None.

Conflict of interest: None.

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gressed to both knees. At presentation, he complained of gait disturbance due to bilateral lower limb contracture and toe hyperflexion. In addition, he suffered from intermittent paroxysmal bilateral leg pain and spasms. He was prescribed anti-inflammatory and pain control medication, which was administered for approximately two weeks. The treatment was ineffective, and consequently, the patient was hospitalized.

The patient's medical history revealed back and hip pain approximately three months prior to presentation at our clinic. He visited several orthopedic hospitals and received conservative treatment without obvious diagnosis. Lumbar spine magnetic resonance imaging (MRI) was performed at the hospital, but there were no specific findings. No history of diabetes or thyroid disease was reported, and there were no unusual findings in his family history.

A physical examination revealed that the ankle and toe contracture worsened during standing, with the muscle tone of the ankles and hyperflexion of the toes decreasing slightly when sitting or lying down. The resistance to flexion in the knees was slightly increased, simultaneous firing of the extension and flexion muscles of the lower leg was detected, and claw toe was observed due to

the action of the flexion muscle (Fig. 1). There was no atrophy of the muscles of the bilateral lower extremity. Sensory tests showed normal tactile, tenderness, temperature, and vibration senses in both lower extremities and no tenderness point. There were no abnormalities in the pathological reflexes.

MRI revealed no specific findings while examining discs from the cervical vertebra to the lumbosacral spine. Additionally, no specific findings were observed throughout the spinal cord (Fig. 2). Ultrasonography revealed no abnormal findings in the sciatic, tibial, and peroneal nerves from the thigh to the ankle. A hematological exam revealed that blood count, erythrocyte sedimentation rate, C reactive protein, chemistry, rheumatoid factor, antinuclear antibody test, and serum protein electrophoresis were all normal.

We found no association between the patient's symptoms and any orthopedic disorder; hence, we referred him to a neurologist for EMG and further examination. Nerve conduction study (sensory nerve conduction test, motor nerve conduction test, and H-reflex) demonstrated normal findings. But, the complete interference pattern was observed at rest in the right tibialis anterior muscle; no abnormal findings were observed in other leg muscles. EMG revealed abnormal finding and the patient had clinical feature, so the

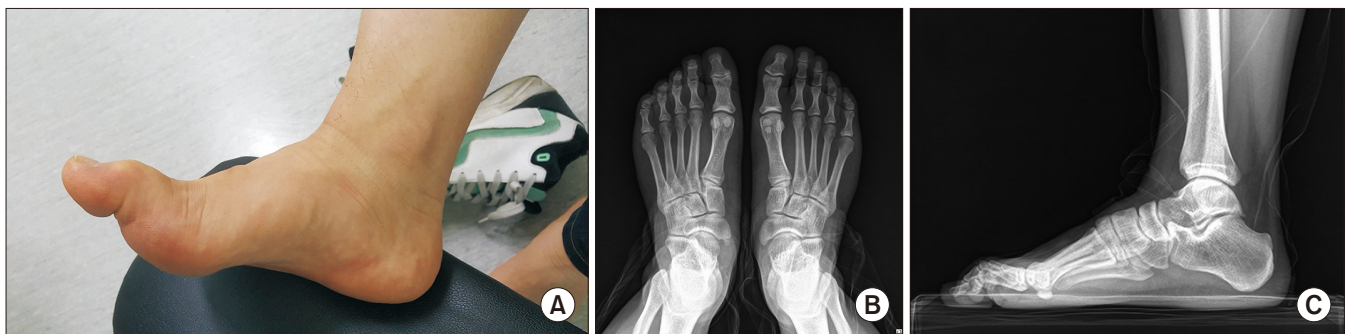


Figure 1. Clinical image (A), standing anteroposterior and lateral foot X-ray images (B, C) showing hyperextension of the metatarsophalangeal joint and flexion of the interphalangeal joint, respectively.

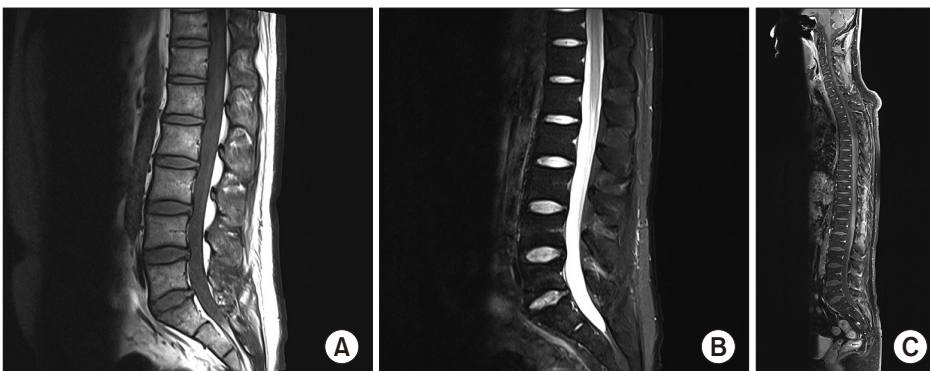


Figure 2. Spine magnetic resonance image. No specific findings other than mild bulging of the disc were observed. (A, B) Lumbar spine T1-weighted, T2-weighted and (C) cervical-thoracic-lumbar sagittal image.

expert neurologist conducted a blood test to differentiate the SPS. A special blood test was performed, revealing that the serum level of anti-GAD antibody was increased to 28,99 U/mL (normal: 0~1.0 U/mL). In neuromuscular disease, anti-GAD antibodies could also be elevated in cerebellar ataxia, but this could be ruled out because of different clinical features with the patient. Additionally, paraneoplastic antibody test was performed for assessing about paraneoplastic SPS. Because paraneoplastic syndrome can cause clinical features such as SPS and elevated anti-GAD antibodies. Blood test revealed that the CA-125 marker level was increased to 74.48 U/mL (normal: 0~35 U/mL). But, no specific findings were found using an abdominal computed tomography. Finally, SPS was diagnosed with clinical features, detection of abnormality on EMG, and elevated GAD antibodies on serum.

Following the diagnosis of SPS, oral administration of diazepam (5 mg) and baclofen (5 mg) three times daily for two weeks resulted in the disappearance of paroxysmal spasms. Additionally, voluntary movement, gait function, and walking speed of both lower limbs were increased. Prednisolone (10 mg) was administered for three months, and the patient showed symptomatic improvement and was instructed to stretch by themselves during the recovery phase. Following medication, he showed normal appearance in legs, with no specific findings on EMG. And his anti-GAD antibodies and CA-125 levels were reduced to normal levels. The patient has been doing well, with no recurrence of symptoms till date.

DISCUSSION

The rarity of SPS and its elusive clinical findings make an accurate diagnosis difficult. SPS (or stiff-man syndrome) is characterized by progressive muscle stiffness and spasms of the legs and spine, often in association with an autoimmune disease. Patients are frequently misdiagnosed as having dystonic syndromes or psychogenic disorders, especially during the early stages of the disease when motor disturbances are intermittent and neurological examination findings are normal.³⁾ Beginning insidiously in middle age, diagnosis is often delayed, and the disease may remain unconfirmed by antibody test results for several years.⁴⁾ A typical patient has palpable, disabling muscle stiffness, pain, and spasms triggered by noise, touch, or emotional stress.⁵⁾ Clinical diagnosis is supported by characteristic continuous motor unit activity on an EMG and the presence of autoantibodies (GAD or amphiphysin). Stiffness, spasm, pain, falls, and startle can all be related to failure of spinal cord inhibition. The symptoms alleviate in response to

treatment with benzodiazepines and other γ -aminobutyric acid agonists. Baclofen is a mechanism similar to benzodiazepine and can be administered orally or intravenously. In addition, there is a report that sodium valproate, Vigabatrin, is helpful in a small number of patients.⁶⁾

Antibodies to GAD are detected in the serum and cerebrospinal fluid in 50% to 60% of patients diagnosed with SPS.⁷⁾ Although the etiology of the syndrome is controversial, it is believed to be associated with immunity,¹⁾ because the syndrome is often comorbid, with other autoimmune diseases, and is associated with an increase in anti-GAD antibodies, which inhibit the synthesis of several autoimmune antibodies and δ -aminobutyric acid. The frequent comorbidity of SPS with other autoimmune diseases, such as type I diabetes mellitus or thyroiditis, and the response to immunotherapies strongly suggest an autoimmune pathogenesis.¹⁾ However, to the best of our knowledge, no studies have yet been conducted to determine whether antibodies are involved in the pathogenesis.⁷⁾ During electrophysiologic studies in SPS patients, the nerve conduction test is usually normal, and continuous motor unit action potential during resting is important in needle EMG. This is usually observed in the thoracolumbar spinal muscles and rectus abdominis muscle. These EMG findings are characterized by the disappearance of diazepam during sleep, spine anesthesia, or general anesthesia.⁸⁾

SPS has an established autoimmune basis; however, no immune therapy has consistently been effective in altering the disease course.⁹⁾ Further investigation is needed to determine the relative contribution of T cells and antibody production to the disease as well as the role of the complement system. The low prevalence of this disease makes clinical trials untenable, but enhanced understanding of neuroimmunological diseases may enable make rational therapeutic choices. Diazepam is widely used to increase the suppressive effect of gamma-aminobutyric acid, and in some cases, it is necessary to increase the dose to 100 mg/day due to disease progression or habituation. SPS can be serious or disabling if left untreated and can lead to total body rigidity. However, treatment response and prognosis are good; hence, early recognition of the disorder and initiation of therapy is important.¹⁰⁾

In conclusion, only few patients present with problems of increased muscle tension. In the differential diagnosis of these patients, a spinal cord lesion, radiculopathy, or muscle disease is usually suspected. However, when the muscle tension is different from typical stiffness and abnormal findings of the upper motor nerve cannot be found during examination, SPS is rarely consid-

ered. Therefore, if we understand the characteristic clinical features and EMG findings of SPS, diagnosis of patients with abnormalities in muscle tension can be done more accurately. We believe that through accurate diagnosis and disease management, symptoms in patients can be alleviated.

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