DOI:10.4274/tnd.galenos.2019.80708
Turk J Neurol 2020;26:39-41

Stiff Person Syndrome-The Less Common Antibody: A Case Report

Stiff Person Sendromu-Seyrek Saptanan Antikor: Olgu Sunumu

Hüseyin Nezih Özdemir[1], Derya Yöndem[1], Seren Kaplan[2], Figen Gökçay[1]

[1]Ege University Faculty of Medicine, Department of Neurology, Izmir, Turkey

[2]Ege University Faculty of Medicine, Department of Psychiatry, Izmir, Turkey

Abstract

Stiff Person syndrome (SPS) is a rare, disabling syndrome characterized by progressive muscle stiffness and axial rigidity. It may have an autoimmune, paraneoplastic or cryptogenic etiology. A 59-year-old woman presented with stiffness and involuntary spasms in the lower extremities. In a neurologic examination, lower extremity and axial rigidity were revealed. Anti-glutamic acid decarboxylase antibody was negative, anti-amphiphysin was antibody positive. She was diagnosed as having SPS. The symptoms were improved after intravenous immunoglobulin and cancer therapy.

Keywords: Stiff Person syndrome, amphiphysin, rigidity, paraneoplastic

Öz

Stiff Person sendromu (SPS), kaslarda ilerleyici katılık ve aksiyel kaslarda rijidite ile karakterize; nadir görüleni özürlülük oluşturabilen bir sendromdur. Otoimmün, paraneoplastik veya kritojenik etiyolojiye sahip olabilir. Elli dokuz yaşında kadın hasta bacaklarında katılık ve istemsiz spazmlar ile başvurdu. Nörolojik muayenede bacaklarda ve aksiyel kaslarda rijite saptandı. Anti-glutamik asit dekarboksilaz antikoru negatif, anti-amfifizin antikoru pozitifti. SPS tanısı kondu. İntravenöz immünoglobulin ve kanser tedavisinin ardından hastanın bulgularında düzelme izlendi.

Anahtar Kelimeler: Stiff Person sendromu, amfifizin, rijidite, paraneoplastik

Introduction

Stiff person syndrome (SPS) is a rare, disabling syndrome characterized by progressive muscle stiffness and axial rigidity (1). It may have autoimmune, paraneoplastic or cryptogenic etiology (2). Patients with SPS frequently have high blood levels of anti-glutamic acid decarboxylase (anti-GAD) antibody (1). The less common variant is paraneoplastic variant, which can be associated with anti-amphiphysin antibodies (3). Anti-amphiphysin antibody SPS is strongly related to breast cancer, female sex, and neck stiffness (3). Two of the autoimmune and paraneoplastic variants have an immunologic basis (4).

Case Report

A 59-year-old woman with a history of restless leg syndrome was admitted to our department with stiffness and involuntary spasms in the lower extremities. She had lower extremity and back pain caused by the spasms and stiffness. She was also experiencing involuntary jerks in the lower extremities. Her symptoms started three weeks prior to presentation and showed a progressive course. She was nonambulatory because of the stiffness and jerks. The spasms were triggered when she flexed her knees. In a neurologic examination, she was cooperative and oriented. The cranial nerve examination was normal. She had no upper extremity weakness. Lower extremity and axial rigidity were revealed. Her legs and knees were in extension, her ankles were inverted, and her toes were extended (Figure 1). Her blood chemistry and hemogram were unremarkable. Her electroencephalogram was normal. Her cranial and spinal magnetic resonance imaging were normal. She was treated with oral baclofen and diazepam. She partially responded to diazepam, there was a mild improvement in the stiffness. Lower extremity electromyography (EMG) showed sensorial and motor polyneuropathy. The patient was investigated for SPS because of the progressive stiffness in the lower extremities, even though there was no EMG evidence. In blood tests, anti-GAD antibody was negative, anti-amphiphysin was antibody positive. The diagnosis

Address for Correspondence/Yazışma Adresi: Hüseyin Nezih Özdemir MD, Ege University Faculty of Medicine, Department of Neurology, Izmir, Turkey
Phone: +90 538 859 91 38 E-mail: huseyinnezihozdemir@gmail.com ORCID: orcid.org/0000-0002-0651-7276
Received/Geliş Tarihi: 07.07.2019 **Accepted/Kabul Tarihi:** 04.10.2019

©Copyright 2020 by Turkish Neurological Society
Turkish Journal of Neurology published by Galenos Publishing House.

of SPS was made. The patient was treated with 2 g/kg intravenous immunoglobulin (IVIG), and the symptoms mildly improved. She had no painful cramps but she had muscle stiffness, inversion posture of the ankles, and axial rigidity. She was investigated for paraneoplastic etiology. Breast ultrasound showed a lesion in the right breast. She was referred to general surgery. A tru-cut biopsy was performed. The pathologic findings were compatible with invasive ductal carcinoma. Surgery was performed and the tumor was resected. Three months after the surgery, although she had no jerks and sudden spasms she still had stiffness and was treated with IVIG for a second time. After surgery, she was treated with paclitaxel chemotherapy for a year. At the one-year follow-up after cancer therapy, her symptoms had improved. She had no muscle stiffness and axial rigidity. She could easily flex her knees but the inversion posture of the feet persisted (Figure 2).

Discussion

Lower extremity muscle stiffness and axial rigidity are the typical features of SPS (1). These features may be accompanied by severe and painful spasms of the lower extremities and difficulty in gait (1,2). The onset of the symptoms is acute or subacute (1). Limb weakness, limb posturing resulting from rigidity and hyperreflexia can be found in neurologic examinations (2). In patients with SPS with anti-amphiphysin antibodies, neck, legs, and arms can be affected (3).

Amphiphysin is a presynaptic protein, which regulates endocytosis (4). Antibodies against amphiphysin protein affects the gamma amino butyric acid-related neural pathways and causes hyperexcitability (4). Approximately 10% of patients with SPS have anti-amphiphysin antibodies (5). Anti-amphiphysin antibodies are associated with malignancies, especially breast cancer (5).

Benzodiazepines may be the first-choice treatment (6). Oral baclofen, or for severe cases, intrathecal baclofen can be used (6). Other medication options are valproic acid, levetiracetam, tiagabin, and gabapentin for symptomatic treatment (6). Steroids, IVIG, and plasmapheresis are needed for immunosuppression (6). The primary cause (e.g. cancer) must be treated (6).

In a series, Murinson and Guarnaccia (3) described the features of anti-amphiphysin antibody-positive SPS. In that series, 11 patients had anti-amphiphysin antibody and all were female patients (3). The mean age was 60 years (3). Ten of the 11 patients had breast cancer (3). They emphasized that patients with anti-amphiphysin antibody-positive SPS might be more resistant to IVIG therapy, and they may require plasmapheresis (3). Eight of the 11 patients had continuous motor unit activity in EMG (3).



Figure 1. Her legs and knees were in extension, her ankles were inverted, and her toes were extended



Figure 2. The patient could easily flex her knees; however, the inversion posture of the feet persisted

McKeon et al. (1) published the electrophysiologic findings of 41 patients who underwent EMG in a series of 79 patients. Seven of these 41 patients had no continuous motor activity on EMG (1). This situation was explained by benzodiazepine treatment, masking EMG findings (1).

With typical clinical findings, positive anti-amphiphysin antibody and malignancy in our case the diagnosis of SPS was made. We wanted to share our case because of the limited number of anti-amphiphysin antibody-positive SPS cases in the literature.

Ethics

Informed Consent: Consent form was filled out by the patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: D.Y., S.K., F.G., Concept: S.K., Design: D.Y., Data Collection or Processing: H.N.Ö., Analysis or Interpretation: F.G., Literature Search: H.N.Ö., Writing: H.N.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. McKeon A, Robinson MT, McEvoy KM, et al. Stiff-Man Syndrome and Variants. Arch Neurol 2012;69:230-238.
2. Sarva H, Deik A, Ullah A, Srvert WL. Clinical spectrum of stiff person syndrome: a review of recent reports. Tremor Other Hyperkinet Mov (N Y) 2016;6:340.
3. Murinson BB, Guarnaccia JB. Stiff-person syndrome with amphiphysin antibodies, distinctive features of a rare disease. Neurology 2008;71:1955-1958.
4. Ali F, Rowley M, Jayakrishnan B, Teuber S, Gershwin ME, Mackay IR. Stiff-person syndrome (SPS) and anti-GAD-related CNS degenerations: Protein additions to the autoimmune central neuropathies. J Autoimmun 2011;37:79-87.
5. Murinson BB. Stiff-man syndrome: GABA, GAD, and mechanisms of disease. J Neurosci 2000;6:147-150.
6. Bhatti BA, Gazli ZA. Recent advances and review on treatment of stiff person syndrome in adults and pediatric patients. Cureus 2015;7:427.