CASE REPORT

Minimal Change Nephrotic Syndrome With Stiff-Person Syndrome: Is There a Link?

Ihsan Ergün, MD, M. Cenk Akbostanci, MD, Başol Canbakan, MD, Bilge Koçer, MD, Arzu Ensari, MD, Gökhan Nergizoğlu, MD, and Kenan Keven, MD

• **Stiff-person syndrome is a rare, likely immune-mediated neurological disorder characterized by painful spasms and progressive symmetric rigidity of the axial and proximal limb muscles. Rigidity of truncal muscles and continuous contraction of the agonist and antagonist muscles caused by involuntary motor-unit firing at rest are the hallmarks of stiff-person syndrome. Immunosuppressive therapy has induced remission in patients with stiff-person syndrome. We report a patient with stiff-person syndrome with minimal change nephrotic syndrome (MCNS). The pathophysiologic states of stiff-person syndrome and MCNS are unclear. T-Cell–dependent mechanisms are highly suspected for the pathogenesis of both. The diagnosis of stiff-person syndrome was made on the basis of clinical and laboratory findings, and both MCNS and stiff-person syndrome resolved completely with immunosuppressive therapy. To our knowledge, this is the first case of stiff-person syndrome in association with MCNS in the literature.** ***Am J Kidney Dis*** **46:E11-E14.**

INDEX WORDS: Minimal change disease; nephrotic syndrome; stiff-man syndrome; stiff-person syndrome.

STIFF-PERSON SYNDROME is a rare neurological disorder characterized by painful spasms and progressive symmetric rigidity of the axial and proximal limb muscles. Continuous contraction of the agonist and antagonist muscles caused by involuntary motor-unit firing at rest are the clinical and electrophysiological hallmarks of stiff-person syndrome. The diagnosis of stiff-person syndrome depends on clinical findings and the exclusion of other neurological disorders.[1] Drugs that enhance γ-aminobutyric acid neurotransmission are used for symptomatic treatment. Immunosuppressive therapy, including high doses of steroids, has resolved stiff-person syndrome. Although frequent associations between stiff-person syndrome and other autoimmune disorders, such as type 1 diabetes mellitus, thyroiditis, myasthenia gravis, pernicious anemia, and vitiligo, previously have been described,[2,3] to the best of our knowledge, this is the first case of stiff-person syndrome in association with minimal change nephrotic syndrome (MCNS) for which T-cell–dependent mechanisms are highly suspected in the pathogenesis for both.

CASE REPORT

A 30-year-old man was referred to the hospital for investigation of recent painful spasms and stiffness in his back and proximal extremity muscles. He had felt painful spasms and muscular rigidity on his left shoulder and leg for 2 months. The rigidity was characterized by episodic painful spasms and stiffness. While the stiffness had been spreading to other areas of the body, including the trunk, peripheral edema developed. He had difficulty walking and bending. He was not able to perform his routine daily activities. On admission, blood pressure was 100/70 mm Hg, and physical examination showed 2^{++} pretibial pitting edema. During neurological examination, he had spasms superimposed on rigidity on his trunk and limbs. His gait was slow. His sensorial examination findings and muscle strength were normal. Deep-tendon reflexes were brisk. There was no evidence of myotonia or extrapyramidal or pyramidal dysfunction. During the examination, painful contraction of the trunk and limb muscles was noticed in both agonist and antagonist muscles. Electrophysiological study showed contractions of the agonist and antagonist muscles and continuous motor-unit activity in the lumbar paraspinal, rectus abdominis (Fig 1), bilateral anterior tibial, and gastrocnemius muscles at rest.

Laboratory findings on admission were as follows: hemoglobin, 13.9 g/dL (139 g/L); total leukocyte count, 8,600/μL; serum creatinine, 0.7 mg/dL (62 μmol/L); sedimentation rate, 17 mm/h; and C-reactive protein, 3.54 mg/L (normal range, 0 to 5 mg/L). He had proteinuria (protein, 8.9 g/d), hypoalbuminemia (albumin, 2.4 g/dL [24 g/L]), and hyperlipidemia (total cholesterol, 287 mg/dL [7.42 mmol/

From the Departments of Nephrology, Neurology, and Pathology, Ankara University School of Medicine, Ibni Sina Hospital, Ankara, Turkey.

Received December 22, 2004; accepted in revised form March 14, 2005.

Originally published online as doi:10.1053/j.ajkd.2005.03.009 on May 18, 2005.

Address reprint requests to Ihsan Ergün, MD, Department of Nephrology, Ankara University School of Medicine, Ibni Sina Hospital, Sihhiye, 06100, Ankara, Turkey. E-mail: ihsanerg@yahoo.com or iergun@medicine.ankara.edu.tr

0272-6386/05/4601-0031$30.00/0

doi:10.1053/j.ajkd.2005.03.009

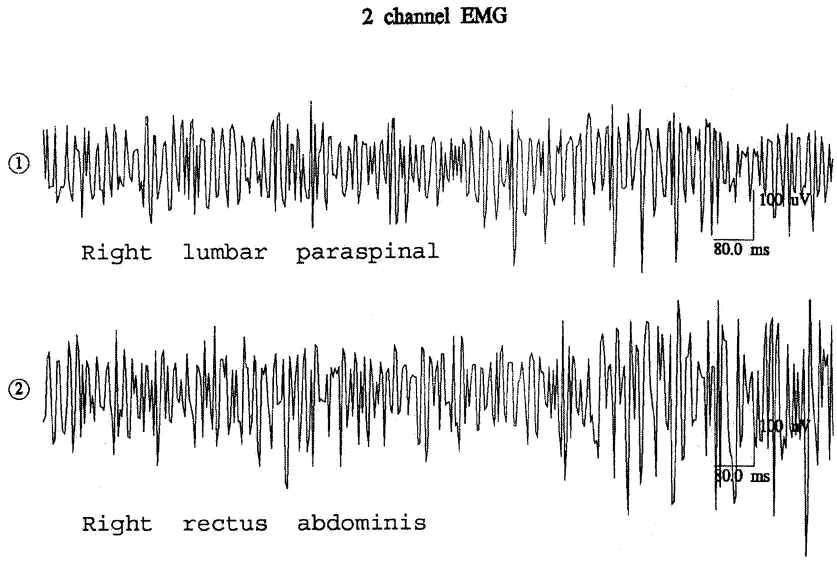

Fig 1. Electromyographic activity of the patient at rest. Spontaneous spasms in the right lumbar paraspinal and rectus abdominis muscles.

L]; triglyceride, 274 mg/dL [3.09 mmol/L]). Urine microscopic examination showed no erythrocytes or casts. Serum lactate dehydrogenase (142 U/L) and creatine phosphokinase (32 U/L) levels were normal. Test results for antinuclear antibody, antineutrophil cytoplasmic antibody, hepatitis B virus surface antigen, hepatitis C virus antibody, and human immunodeficiency virus antibody were negative. Other biochemical parameters, complement levels (C3c and C4), and cerebrospinal fluid were normal. Immune electrophoresis showed no evidence of a paraprotein.

A renal biopsy was performed for nephrotic syndrome. Evaluation of light microscopy was normal, with negative immunofluorescence findings, and electron microscopy showed diffuse foot-process fusion without electron-dense deposits, compatible with minimal change disease. The diagnosis of stiff-person syndrome was based on the patient's history, neurological examination, and electrophysiological findings. To exclude a malignancy, a computed tomographic scan of the thorax, magnetic resonance image of the brain, ultrasonographic evaluation of the abdomen, gastroscopy, and colonoscopy were performed, and all showed normal results.

After the diagnosis, diazepam, 10 mg/d, was administered, and neurological symptoms regressed partially. After documentation of MCNS, 3-day methylprednisolone (500 mg/d) pulse therapy was initiated, followed by oral prednisolone (1 mg/kg/d) with cyclophosphamide (2 mg/kg/d). Oral prednisolone therapy was continued for a month with the same dose, then tapered slowly to 0.3 mg/kg/d. Month 2, nephrotic syndrome remitted partially, and month 3, proteinuria completely disappeared. Control serum albumin level was 4 g/dL (40 g/L). After remission, the cyclophosphamide dose was tapered to 1 mg/kg/d. Oral prednisolone and cyclophosphamide therapy was continued for 6 months, then stopped. Neurological symptoms and findings completely disappeared after pulse therapy, with normalization of electromyographic findings (Fig 2). Diazepam therapy was discontinued after 6 months. No recurrence was noticed during 1 year after cessation of the therapy.

DISCUSSION

Stiff-person syndrome is a rare central nervous system disorder characterized by progres-

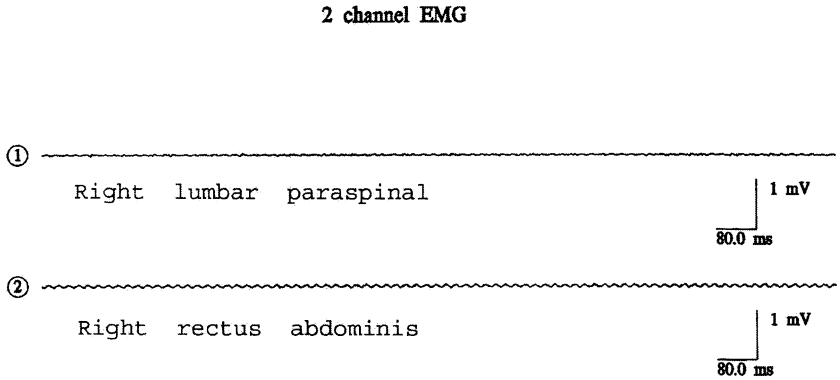

Fig 2. Electromyographic activity of the patient at rest. Return to normal.