

Myoclonus as an Anticipatory Symptom of Diffuse Central Nervous System Involvement in Neuropsychiatric Systemic Lupus Erythematosus

Min Jin Lee, Koeun Lee, Jisoo Lee

Division of Rheumatology, Department of Internal Medicine, Ewha Womans University School of Medicine, Seoul, Korea

The clinical manifestations of nervous system involvement in systemic lupus erythematosus (SLE) are highly diverse and their pathogenic mechanisms are incompletely understood. Neuropsychiatric SLE (NPSLE) poses difficulty in making the proper diagnosis, especially in circumstances where its initial symptoms are diffuse neuropsychiatric symptoms. We describe a 43-year old woman who exhibited

a myoclonic jerk of the abdominal wall, followed shortly by acute confusion, which was attributed to SLE. Therapy with high dose corticosteroids completely reversed the symptoms. Myoclonus can be an anticipatory symptom of diffuse neurologic dysfunction in patients with NPSLE.

Key Words. NPSLE, Diffuse neuropsychiatric symptoms, Myoclonus

Introduction

Neuropsychiatric systemic lupus erythematosus (NPSLE) still remains a diagnostic challenge. There is no specific test to confirm the diagnosis. Currently recommended diagnostic work-up for NPSLE is performed to exclude other diagnoses such as infection, and metabolic derangements (1). Symptoms or signs that can predict the development of NPSLE can be useful in clinical settings. We describe a patient who developed sudden emergence of myoclonic movements, followed shortly by acute confusion as initial symptoms of SLE.

Case Report

A 43-year old woman presented with fever of 1 month duration. Swelling of cervical lymph nodes developed 1 week prior to admission. Recently, she felt gloomy, and experienced frequent mood changes. Her past history was unremarkable, except intermittent arthralgia and myalgia for 3 years. The patient was a house wife. She did not smoke nor drink. She was not on any medication. On examination, body temperature of 37.4°C, malar rash, and cervical lymphadenopathy was found. Aside from mild irritability, neurologic examination was

unremarkable. The remainder of the examination was normal. Laboratory tests revealed Hb 14.6 g/dL, WBC 1,700/mm³ (neutrophil 45.2%, lymphocyte 28.6%), and platelet 109,000/mm³. Biochemical tests and urinalysis were within normal limits. C3 was decreased to 74.4 mg/dL. Lupus anti-coagulant was positive with 51.7 secs initial and 52.8 secs at follow up (normal 31.0~44.0 secs). Antinuclear antibody (ANA) was present at a titer of 1 : 80 (speckled type). Anti-Sm, anti-RNP, anti-DNA, anti-SSA, anti-SSB, anti-cardiolipin antibodies were negative. Chest PA was normal with no active lung lesion. Pathologic findings of cervical lymph node showed atypical lymphoid hyperplasia without malignant cells.

On the second hospital day, the patient complained of severe abdominal pain accompanied by muscle spasm. Fever of 38.5°C was accompanied. Physical findings revealed severe involuntary myoclonic jerks of abdominal wall at approximately 10 seconds interval. Cultures of blood and urine, and tests for antibodies to hepatitis B and C viruses, Epstein-Barr virus, and herpes simplex virus were negative. On cerebrospinal fluid (CSF) study, WBC 320/μL (neutrophil 1%, lymphocyte 97%),

<Received : December 1, 2011, Revised (1st: February 10, 2012, 2nd: March 31, 2012), Accepted : April 11, 2012>

Corresponding to : Jisoo Lee, Division of Rheumatology, Department of Internal Medicine, Ewha Womans University School of Medicine, 1071, Anyangcheon-gil, Seoul 158-710, Korea. E-mail : leejisoo@ewha.ac.kr

pISSN: 2093-940X, eISSN: 2233-4718

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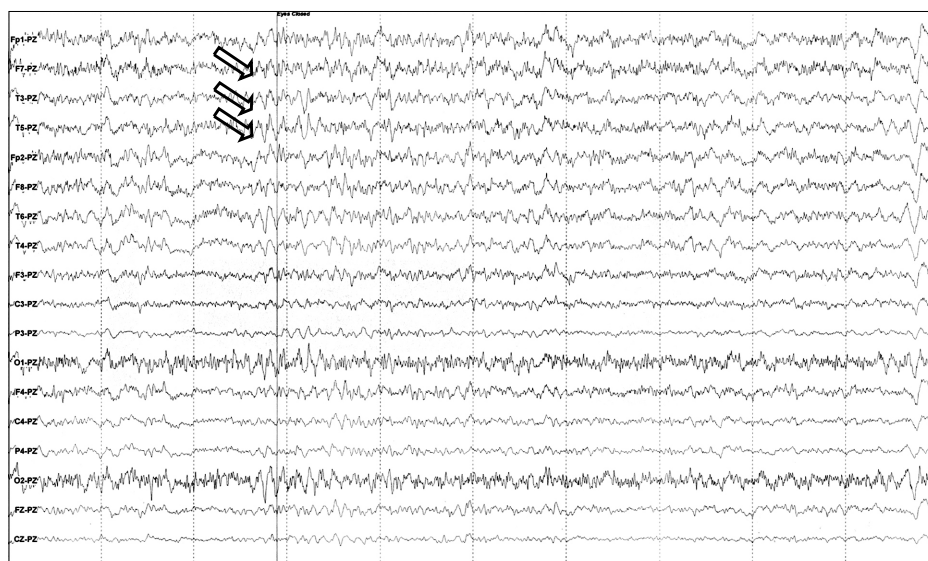


Figure 1. Electroencephalogram was characterized excessive beta wave (arrows) at the anterior and temporal zone.

total protein 26 mg/dL, and glucose 60 mg were detected. CSF was negative for cryptococcal antigen, herpes simplex virus, enterococcus, and *Mycobacterium tuberculosis*. Electroencephalogram showed excessive beta waves (Figure 1). Brain and spine MRI showed nonspecific high signal intensity in both subcortical white matters of the front lobes without abnormalities in the spine. Two days after, she developed acute confusion. Based on malar rash, hematologic disorder, immunologic disorder, and ANA positivity, diagnosis of SLE was made. Because of no evidence of infection was found, acute confusional state was assessed as a symptom of NPSLE. SLEDAI score was assessed as 14. 125 mg/day of methylprednisolone was administered promptly. Clonazepam 0.5 mg/day was administered to control the myoclonus. In 3 days, confusion abated and she recovered clear consciousness with full orientation. However, myoclonus continued for 10 days although its severity was lessened. At the time of discharge, the patient was fully conscious, oriented, without any neurologic deficit. Six months later, the patient was doing well without any symptoms of SLE or NPSLE.

Discussion

NPSLE should be considered as a possible differential diagnosis for rapid onset neuropsychiatric symptoms even in previously healthy individuals. Before making the diagnosis of NPSLE, secondary causes of neuropsychiatric symptoms such as infections, metabolic or endocrine disturbances should be vigorously excluded. However, timely diagnosis of NPSLE is important, since treatment delay is associated with poor prognosis (1). The patient we described presented with rapidly evolving neuropsychiatric symptoms of myoclonus and acute

confusional state. Although she had symptoms and signs suggestive of active SLE, the diagnosis of NPSLE was difficult, since she was not previously diagnosed with SLE. CSF examination and MRI findings were non-specific, but no definite evidence for CNS infection such as herpes viral infection or tuberculosis was found. Treatment with high dose corticosteroids promptly reversed the symptoms without neurologic damage.

Myoclonus is a movement disorder characterized by sudden, brief, involuntary muscle jerks. Myoclonus most often occurs in context of variety of neurological and nonneurological disorders including autoimmune diseases such as SLE (2). However, movement disorders other than chorea have been less well characterized in SLE (3). Only one case of myoclonus as a symptom of NPSLE has been described previously (4). Recent advances in understanding of immune mediated mechanisms suggest a common pathogenetic mechanisms mediated by autoantibodies. Anti-glutamate-receptor antibodies was suggested to play an important role in movement disorders as well as NPSLE (5). N-Methyl-D-aspartate receptors (NMDARs) are receptors for the neurotransmitter glutamate, the major excitatory neurotransmitter of the brain critically important for many brain functions. Antibodies to NMDAR modulate NMDAR activation by synergizing with the natural agonist glutamate to increase excitatory postsynaptic potentials, causing overexcitability of the neurons (6). Alterations in NMDAR activity can produce uncontrolled movement, seizures, coma, and hallucinations (7). In SLE, presence of anti-NMDAR antibodies in the CSF were shown to correlate with acute, diffuse central nervous system (CNS) manifestations of NPSLE that include seizure disorders, acute

confusional state, and psychosis (8). The patient we described developed acute confusional state shortly after the development of myoclonus. Close clustering of two NPSLE symptoms of myoclonus and acute confusion may implicate common pathogenic mechanisms.

Summary

Although not included in the ACR case definition of NPSLE, myoclonus can occur as a part of diffuse CNS involvement and may be associated with diffuse neurologic dysfunction of NPSLE.

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