Neurogenic Bladder in a Patient With Systemic Lupus Erythematosus and Cerebral Involvement

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CENTRAL NERVOUS SYSTEM MANIFESTATIONS

Central nervous system (CNS) manifestations of systemic lupus erythematosus are highly diverse and often have major prognostic consequences.1,2 The prevalence rate of nervous system involvement in SLE is approximately 50%, although the range is large, varying from 18% to 75% of SLE patients.3,4 Neuropsychiatric manifestations, such as psychosis and seizures, are common in SLE. However, neurogenic bladder has rarely been reported in this disorder. Most patients in previous reports have CNS lupus with an upper neuron disorder presenting as a symptom of transverse myelopathy.5,6 We describe the clinical feature of a female patient with neurogenic bladder accompanied with NPSLE of obvious diffuse cortical dysfunction without evidence of spinal cord involvement.

CASE REPORT

A 24-year-old woman was admitted because of voiding difficulty and malar rash for 2 months. She had alopecia, diffuse abdominal pain, fever, and abnormal behavior with tremor and agitation. A neurologic examination showed impaired cognitive function (mini-mental state examination 19/30) despite alert mentality. There was no evidence of sensory or motor deficit.

Her initial laboratory findings showed; white blood cell: 4720/mm³ (lymphocyte 283/mm³), hemoglobin: 7.2 g/dL, platelets: 204,000/mm³, and markedly decreased C3 and C4: [19 mg/dL (normal, 90 – 180 mg/dL) and 3 mg/dL (normal, 9 – 37 mg/dL), respectively]. Urine analysis revealed no RBC, white blood cell, or casts. Repeated urine cultures were negative. Antinuclear antibody (ANA, >1:2560, speckled type), antids DNA antibody (23.5 IU/mL, normal <7 IU/mL), anti-Ro antibody, anti-La antibody, and anti-Smith antibody were positive. Anticardiolipin antibody and lupus anticoagulant were negative. Lumbar puncture showed a clear, colorless cerebrospinal fluid. Analysis of this cerebrospinal fluid showed normal results—protein, 30 mg/dL; glucose, 63 mg/dL; cell count, 1/μL; IgG, 23 mg/dL (serum IgG, 3692 mg/dL); adenosine deaminase 1.5 U/L; and negative oligoclonal band. A 24-hour urine had 1079 mg of protein. A renal biopsy was performed and showed membranous glomerulonephritis.

For evaluation of abdominal pain and obstruction of the urinary tract, abdominal computed tomography was undertaken and demonstrated diffuse bowel wall thickening in the proximal jejunal loop without hydrenephrosis and abnormality of the bladder. Electroencephalogram was normal. Brain magnetic resonance imaging showed no abnormality except diffuse cortical atrophy and ventricular dilatation. To rule out myelopathy, electromyography and nerve conduction velocity were performed, and revealed no evidence of myelopathy. Therefore, spine magnetic resonance imaging was not done. Cardiovascular autonomic nervous function test, including heart rate variation in deep breathing, valsalva maneuver, and orthostatic change, showed abnormality.

On urodynamic study, the volume of residual urine was 1100 mL and less than normal activity of detrusor muscle and flaccid bladder was seen. Because she did not have a voiding sense, free flowmetry was not performed. Based on the revised criteria for SLE, classification with malar rash, renal disorder, hematologic disorder, immunologic disorder, and positive ANA, she was diagnosed as SLE with CNS and autonomic nervous system involvement and neurogenic bladder. Her lupus activity was very high, and systemic lupus erythematosus disease activity index (SLEDAI) was 36 (Table 1). She was treated with high dose corticosteroid (prednisolone, 60 mg a day, orally) and intravenous cyclophosphamide therapy (1 g). After these treatments, most of her symptoms, including cognitive impairment, voiding difficulty, and malar rash, were well controlled and she was discharged. After 7 months of treatment, follow-up urodynamic study showed increased bladder sensation and decreased bladder capacity. She was well with no urinary symptoms at 3.5-year follow-up.

DISCUSSION

Bladder involvement in SLE has generally been considered rare. However, a recent study shows that the proportion of individuals reporting urinary tract symptom is significantly higher in SLE compared with healthy controls (7.9% vs. 1.8%; P < 0.05), although only 10% of patients in their study group had CNS manifestations.7

The etiology of bladder dysfunction in SLE is not yet fully understood. It is thought that infection and various medications such as cyclophosphamide, immune complex-mediated interstitial cystitis, and neurogenic dysfunction can be potential causes.5–13 However, earlier studies on bladder involvement in patients with SLE have focused mainly on lupus cystitis.

Urinary dysfunction with CNS lupus has rarely been reported, and most patients of previous reports had urinary symptoms with transverse myelopathy. Sakakibara et al reported 8 patients with urinary dysfunction. Urinary dysfunction included voiding difficulty and urinary incontinence, and their neurologic manifestations were subacute encephalomyelopathy, subacute myelopathy, and chronic myelopathy. These results suggest that urinary dysfunction can be a feature in SLE patients with myelopathy.5 Chan and Boey reported detrusor hyperreflexia in 5 of 6 patients with transverse myelopathy because of SLE.13

Our patient had obvious diffuse cortical dysfunction, but showed no evidence of spinal cord involvement. Furthermore, her urinary symptoms were a failure of emptying consistent with urodynamic studies that showed detrusor underactivity and notable residual volume. Considering the fact that lupus cystitis often presents with storage symptoms, including frequency, urgency, and pelvic pain, it could be a less likely cause of bladder dysfunction in our patient, even though not confirmed by cystoscopic biopsy.9,14

A recent prospective study shows that, among 9 organ systems, the involvement of CNS has only an independent effect on lower urinary tract symptoms (P = 0.03).7 Of 3 patients with...
complete urinary retention, 2 patients were documented to have transverse myelitis, and 1 had diffuse cortical dysfunction. These findings strengthen our suggestion that cerebral involvement with diffuse cortical dysfunction might be a possible etiologic factor of voiding difficulties in our patients.

Involvement of autonomic nervous system in SLE varies, ranging from 6% to 93% depending on the authors. However, bladder dysfunction secondary to autonomic dysfunction has rarely been reported. There is a report of association between the presence of autoantibodies against sympathetic ganglia and vagus nerve and autonomic dysfunction. Therefore, we cannot rule out the possibility that autonomic dysfunction and cerebral involvement played an important role in impaired detrusor contractility observed in our patient.

The incidence of voiding dysfunction might be underestimated because the multisystem manifestations might overshadow the bladder involvement. However, the voiding difficulty could be the initial manifestation as our patient. In addition, the patient showed relatively high levels of systemic lupus erythematosus disease activity index, similar to a previous study which documented positive correlation between the severity of neurogenic bladder and disease activity of SLE.

Because bladder involvement in CNS lupus is a rare manifestation, treatment guidelines have not yet been established. A previous report of neurogenic bladder as a result of CNS lupus shows a poor response to treatment. However, our patient showed full clinical recovery of bladder symptoms. The good outcome of the patient suggests that earlier identification of CNS SLE as a cause of neurogenic bladder and treatment with immunosuppressive treatment may be important.

TABLE 1. Clinical and Neurological Findings

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Duration of SLE (mo)</th>
<th>SLEDAI</th>
<th>NPSLE</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>24</td>
<td>0</td>
<td>36</td>
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Myelopathy
- Weakness of lower extremity: —
- Decreased sensation: —

Anal reflex: Normal

NCV/EMG: Normal

Autonomic function test: Abnormal

Urinary dysfunction: Retention, voiding difficulty

Urodynamic study: Acontractile detrusor

MRI: Atrophy

Brain: —

Spine: —

SLEDAI, systemic lupus erythematosus disease activity index; NPSLE, neuropsychiatric systemic lupus erythematosus; NCV, nerve conduction velocity; EMG, electromyography; MRI, magnetic resonance imaging; NP, not performed.

REFERENCES