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Systemic Lupus Erythematosus With Acute Inflammatory Demyelinating Polyneuropathy: A Case Report and Review of the Literature

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Abstract

We recently encountered a patient with acute inflammatory demyelinating polyneuropathy (AIDP) that was associated with systemic lupus erythematosus (SLE). A 34-year-old Chinese female with a 3-year history of SLE presented with acute bilateral leg weakness and paraparesis, and lost the ability to walk 1 day after noticing bilateral leg numbness and pain for 12 days. Physical examination revealed bilateral facial muscle paralysis, muscle strength in the legs with graded 1/5 proximally and 2/5 distally bilaterally and absence of deep tendon reflex in both knees and ankles. Paresthesia was observed in distal limbs with glove and stocking distribution. Cerebrospinal fluid analysis demonstrated albuminocytologic dissociation. Electrophysiologic survey also indicated sensory-motor demyelinating polyneuropathy. The diagnosis of SLE was established based on her initial symptoms including intermittent fevers, hair loss, oral ulcers, malar rash and arthritis affecting the elbow, wrist and hand joints; positive immunologic findings for antinuclear antibody (ANA), anti-DNA antibody, anti-Smith (anti-Sm) antibody, low serum complement levels, and the kidney biopsy specimen showed glomerular mesangial proliferation with focal endothelial cell proliferation (ISN/PPS 2004 classification lupus nephritis, class III). Treatment with intravenous immunoglobulin, methylprednisolone and cyclophosphamide resulted in clinical and electrophysiological improvement.

Keywords: Systemic lupus erythematosus; Acute inflammatory demyelinating polyneuropathy; Guillain-Barre syndrome

Introduction

Systemic lupus erythematosus (SLE) is a chronic, inflammatory, relapsing-remitting, autoimmune disease characterized by multisystemic involvement with diverse clinical presentations. Neurologic complications are common and frequent in SLE. Central nervous system (CNS) involvement is one of the more common complications that can occur at any stage of the SLE. However, peripheral nervous system involvement in SLE is rare and dominated by distal symmetric axonal polyneuropathy and multiple mononeuropathy [1]. Acute inflammatory demyelinating polyneuropathy (AIDP) or the classic type of Guillain-Barre syndrome (GBS) is very uncommon. Here we report a patient with AIDP that was associated with SLE.

Case Report

A 34-year-old Chinese female presented with a 3-year history of SLE presented with acute bilateral leg weakness and paraparesis, and lost the ability to walk 1 day after noticing bilateral leg numbness and pain for 12 days, accompanied by fever, fatigue, incomplete closure of the eyelids (lagophthalmos) and dysphagia. Three weeks before admission, she had intermittent abdominal pain and watery diarrhea. Her initial symptoms 3 years before her visit had intermittent fevers, hair loss, oral ulcers, malar rash and arthritis affecting the elbow, wrist and hand joints. The laboratory test results at that time were as follows: antinuclear antibody (ANA) titer: 1:320 (+); anti-DNA antibody: (+); anti-Smith (anti-Sm) antibody: (+); serum complement (CH50): 17 (26 - 48) units/mL; C3: 53 (86 - 160) mg/dL; C4: 11 (17 - 45) mg/dL; urinary protein: 1+; 24-h urinary protein (UP): 1.65 g/day and hematuria: -. Her renal function test and hematologic evaluation results were within normal ranges. Renal biopsy was not conducted.

Physical examination at admission revealed that she had a temperature of 38.2 °C, a heart rate of 115 bpm, a respiratory rate of 20 breaths/min, blood pressure of 135/90 mm Hg and an oxygen saturation of 97% on room air. She had malar rash, but there was no clinical evidence of arthritis or muscle inflammation. Neurologic examination indicated she had bilateral facial muscle paralysis, and motor examination revealed muscle strength in the legs with graded 2/5 proximally and distally bilaterally and absence of deep tendon reflex in both knees and ankles. Paresthesia was observed in distal limbs with glove and stocking distribution. The deep tendon reflexes were absent. The bilateral Babinski test was unremarkable. Cardiovas-

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Table 1. Electrophysiological Findings

	Lat (SD), ms	Amp (SD), mV	CV (SD), m/s	Amp (SD), %
Motor nerve				
Right medianus				
Wrist-APB	4.5 (3.9)	0.2 (-2.7)		
Elbow-wrist	9.5	0.2	35.4	34
Left ulnaris				
Wrist-ADM	3.8 (-6.2)	0.1 (-4.5)		
Ab elbow-wrist	8.5	0.6	47.8 (-1.7)	435 (52)
Right tibialis				
Ankle-AHB	9.4 (15.7	0.1		
PF-ankle	25.7	0.1	23.4	351
Left tibialis				
Ankle-AHB	9.0 (14.6)	0.0		
PF-ankle	24.0	0.1	27.3	352
Right peroneus				
Ankle-EDB	7.9 (8.3)	0.2 (-2.1)		
CF down-ankle	17.0	0.2	34.2	3
Left peroneus				
Ankle-EDB	9.0 (9.8)	0.1 (-2.1)		
CF down-ankle	18.7	0.3	32.4	415
Sensory nerve				
Right medianus				
Dig II-wrist	2.6 (-0.7)	16	53.7	
Left ulnaris				
Dig V-wrist	2.8 (0.1)	12	46.5	
Right peroneus super				
Ankle-foreleg	4.1	4.0	35.0 (-3.2)	
Left peroneus super				
Ankle-foreleg	3.9	5.9	33.4 (-3.6)	

cular, respiratory and abdominal examinations were normal. The autonomic and sphincter functions related to urination and defecation were preserved.

This time, abnormal laboratory findings included ESR 46 mm, CRP 8.5 mg/L, positive ANA +1:640 (< 1:160), anti-SSA, anti-SSB antibody and low levels of serum complement components (CH50, C3, C4). Anti-dsDNA and anticardiolipin antibodies were negative or within the normal range. Anti-ganglioside antibodies were negative. Viral and bacterial serology and antiganglioside antibodies were negative. Serologic tests for HIV, hepatitis B/C and cytomegalovirus were all negative. Cerebrospinal fluid examination revealed albuminocytological dissociation (total protein, 154.3 mg/dL and white blood cell, 3/mm^3, respectively). Abdominal ultrasound exam, chest radiograph and ECG revealed no obvious abnormalities. Brain magnetic resonance imaging did not show any pathologic lesions. Electroneuromyography (ENMG) was highly suggestive of demyelinating polyradiculoneuropathy with prolonged distal motor latencies, decreased amplitudes of compound muscle action potential, slow nerve conduction velocities, absence of F waves and delayed M-wave, without acute denervation (Table 1). A percutaneous renal biopsy was performed on the patient after hospitalization. The kidney biopsy specimen showed glomerular mesangial proliferation with focal endothelial cell proliferation (ISN/PPS 2004 classification lupus nephritis, class III). Immunofluorescent study findings for IgA, C1q, C3 (diffuse capillary loops, mesangial area, 2+), IgM (diffuse capillary loops, mesangial area, +), and IgG (segmental capillary loops, mesangial area, +) were positive. Light microscopy revealed segmental glomerular sclerosis, mild to moderate glomerular mesangial expansion, mesangial cells and matrix hyperplasia, infiltration of mononuclear cells and neutrophils, capillary endothelial cells proliferation, capillary loops wall thickening, and lumens stenosis. Masson trichrome (Masson) staining and periodic Schiff methenamine (PASM) staining showed the deposition of complex red deposits in

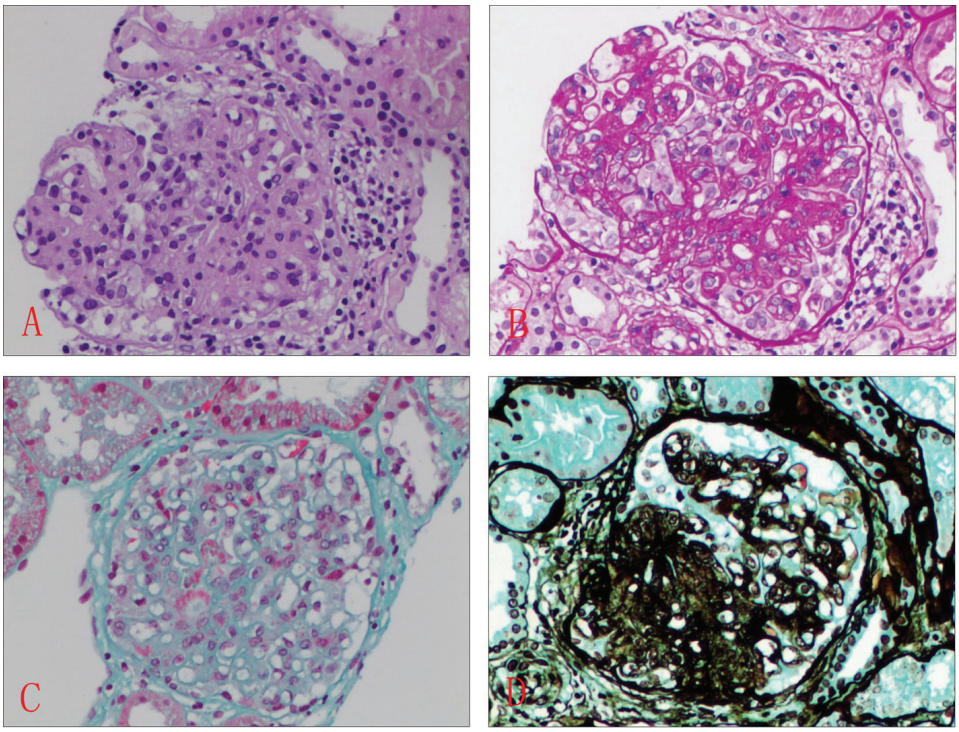

Figure 1. Histologic features of section of kidney biopsy. Glomerular mesangial proliferation with focal endothelial cell proliferation. (A) H&E, × 400; (B) PASM, × 400; (C) Masson, × 400; (D) Gomori methenamine silver (GMS), × 400

the glomerular endothelial cells mesangial region, mild renal tubular interstitial lesions and mononuclear cell infiltration, segmental degeneration of small arteries (Fig. 1). There was no obvious tubular atrophy and interstitial fibrosis in the kidney. Timely management involved plasma exchange followed by intravenous gammaglobulin infusion (0.4 g/kg daily for 5 days), and continuation of high-dose systemic corticosteroids, two 1.0 g pulses of methylprednisolone. Cyclophosphamide therapy was continued with 400 mg intravenously every second week for 2 months.

Discussion

Peripheral neuropathy (NP) is a known and underestimated complication in SLE. Only a few previous studies have reported frequent occurrence of NP in SLE, with incidences from 1.5% to 27.8% [2-7]. NP usually develops during the course of the SLE, especially in the advanced stage of the SLE, and very rarely from the outset of the SLE [8, 9]. AIDP is the most prevalent form of GBS. The prevalence of SLE in AIDP or GBS has been reported to be 0.6-1.7% [2, 10]. Our review of the literature finds that AIDP or GBS with SLE was more common in females (73.3%, 11/15) than males (26.7%, 4/15), and cerebrospinal fluid albuminocytological dissociation was present in 66.7 % (9/15) of cases, and more importantly, usually occurred in early course of the SLE (Table 2) [8, 9, 11-23], even as the first manifestation of SLE [8, 16-21]. We reported the AIDP patient with SLE occurring early in the course of lupus, which was consistent with the previously reported ones [16].

The pathogenesis of AIDP or GBS with SLE is not clearly understood [22, 23]. There is some considerable speculation that cell-mediated and humoral processes, or immunological cross-reactivity, or the presence of auto-reactive antibodies resulted in subsequent damage to the peripheral nervous system [22, 23]. Further studies are needed to elucidate the underlying reasons for AIDP or GBS with SLE.

The previous literature reported four treatment options have been used in AIDP or GBS with SLE, including corticosteroids, cyclophosphamide, plasmapheresis and immunoglobulin. Although clinical trials have demonstrated that corticosteroids treatment has no beneficial effect on GBS during the past decades [24, 25], steroid therapy is still the more frequently used treatment modality for SLE with neuropsychiatric manifestations. The combination of corticosteroids and cyclophosphamide was considered the first-line treatment option in a review of the literatures (Table 2) [19]. The efficacy of plasmapheresis and immunoglobulin for AIDP or GBS with nephritis lupus is controversial [19]. Varying responses have been noted with each patient encountered and no consensus guidelines have yet been established.

AIDP or GBS with SLE is rare in SLE patients. Controlled clinical trials are largely lacking which results in various non-standardized treatment regimens. However, the association of them has been strongly evidenced by reported literatures, which translates into significant implications for their management and long-term outcomes. Our findings suggest prompt diagnosis and treatment, early in the course of illness, is of critical importance for a positive clinical outcome.

Table 2. Previous Reports About GBS or AIDP With SLE

Author	Age/sex	GBS and SLE	Organ involvement	Auto-Ab(+)	Treatment (effect +, -)
Hsu et al [18]	28/F	Early	PNS, pleurisy, lymphopenia	ANA, anti-dsDNA, anti-Ro/SS-A, anti-La/SS-B	Prednisolone, PE, (+)
Chaudhuri et al [20]	40/M	Early	PNA, lymphopenia, seizure, membranous glomerulonephritis	ANA, anti-dsDNA	Prednisolone, cyclophosphamide, PE, (+)
Santiago-Casas et al [22]	20/F	Early	PNA, lymphopenia, proteinuria	ANA, anti-dsDNA	Cyclophosphamide, glucocorticoids, PE, IVIG, (+)
Santiago-Casas et al [22]	34/F	Early	PNS, arthritis, lymphopenia	ANA, anti-dsDNA	Glucocorticoids, IVIG, cyclophosphamide, (+)
Miyagawa et al [13]	9/F	Late	PNS, chilblain or erythema multiforme, oral ulcers	ANA, anti-dsDNA, anti-Ro/SS-A, anti-La/SS-B	Corticosteroids, PE, IVIG, (+)
Robson et al [23]	33/F	Early	Hemolytic anemia, thrombocytopenia, retinal vasculitis, PNS, CNS	ANA, anti-dsDNA	Glucocorticoids, cyclophosphamide, (+)
Vaidya et al [16]	23/M	Early	PNS, WHO class V lupus nephropathy	ANA, anti-dsDNA	Glucocorticoids, cyclophosphamide, PE, (+)
Millette et al [21]	23/F	Early	PNS, cranial nerve	ANA, anti-dsDNA, anti-Smith, anti-RNP	Glucocorticoids, (+)
Okoh et al [8]	41/F	Early	Leukopenia, pericardial and pleural effusions, proteinuria, and hematuria	ANA, anti-dsDNA, anti-Smith	Cyclophosphamide, glucocorticoids, PE, IVIG, mycophenolate mofetil, (+)
van Laarhoven et al [19]	20/F	Early	Facial exanthema pleural and pericardial, proteinuria, autoimmune hemolytic anemia	ANA, anti-Smith, anti-RNP	IVIG, cyclophosphamide, glucocorticoids, (+)
Rajadhyaksha et al [17]	30/F	Early	Oral ulcers, arthralgias, bulbar palsy, cranial nerve, class II mesangio proliferative lupus nephritis nerve	ANA, anti-dsDNA, anti-Smith, GT1a, GQ1b, GM1b	IVIG, glucocorticoids, (+)
Ha-Ou-Nou et al [11]	44/M	Early	Lymphopenia, proteinuria, thrombocytopenia	anti-dsDNA	Corticosteroids, IVIG, (-)
Stahl et al [14]	56/F	Early	Thrombocytopenia, stomatitis, hair loss, arthritis	ANA, AHA	IVIG, cyclophosphamide, corticosteroids, (-)
Lewis and Gibson [12]	21/M	Late	Arthritis, pleuro-pericarditis, proteinuria	ANA, anti-dsDNA, anti-RNP, ACA	Cyclophosphamide, IVIG, prednisolone, (+)
Yildiz et al [9]	47/F	Late	Discoid rash, photosensitivity, oral ulcers, leucopenia, lymphopenia	ANA	Corticosteroid, cyclophosphamide, (+)
Matsuki et al [15]	61/F	Early	Arthritis, oral ulcers, pericarditis, lymphopenia	ANA, anti-dsDNA, anti-Ro/SS-A, anti-GMl	Methylprednisolone, mizoribine, immunoadsorption, PE, (+)

PE: plasma exchange; IVIG: intravenous immunoglobulin; ANA: antinuclear antibody; anti-dsDNA: anti-double-stranded DNA; anti-SS-A: anti-Ro antibodies; anti-SS-B: anti-La antibodies; AHA: anti-histone antibodies; ACA: anti-cardiolipin antibodies; PNS: peripheral nervous system; anti-Smith: anti-Smith antibodies.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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