Clinical Case Report

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Systemic lupus erythematosus with Guillian–Barre syndrome

A case report and literature review

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Abstract

Introduction: We report a case of systemic lupus erythematosus (SLE) with Guillian–Barre syndrome (GBS) as the first symptom.

Case presentation: A 30-year-old Chinese female with numbness and inductance of lower extremities 2 months previously. The electromyographic and cerebrospinal fluid findings supported inflammatory demyelinating disease, and the renal biopsy findings and rheumatoid-related results considered systemic lupus erythematosus. The patient received treatment with glucocorticoids and cyclophosphamide. Two months after the treatment, the patient's limb numbness and weakness disappeared, and the urinary protein was decreased significantly.

Conclusions: Our case highlights the importance of the early diagnosis and treatment of SLE. Systemic lupus erythematosus is a multifactorial participant autoimmune systemic disease for which the clinical manifestations are complex and diverse. Glucocorticoid and cytotoxic drugs can be used in clinical treatment. If the disease is not diagnosed early, it could also delay treatment. Patients who receive an early diagnosis and appropriate treatment may have a better prognosis.

Data Sources: Data were collected from the patient's electronic medical records and the hospital laboratory medicine database.

Abbreviations: AIDP = acute inflammatory demyelinating polyneuropathy, ANCA = antineutrophil cytoplasmic antibodies, GBS = Guillian–Barre syndrome, LN = lupus nephritis, NPSLE = neuropsychiatric systemic lupus erythematosus, SLE = systemic lupus erythematosus.

Keywords: cyclophosphamide, glucocorticoids, Guillian–Barre syndrome, systemic lupus erythematosus

1. Introduction

Systemic lupus erythematosus (SLE) is a multifactorial autoimmune systemic disease and its causes include genetic, sex hormone, environment, infection, drug, and food factors. There are a variety of autoantibodies that cause systemic multiple system involvement through the immune complex and in other ways. Damaged systems include skin and mucous membranes, joints and muscles, kidneys, the nervous system, blood system, lungs, heart and the digestive system. However, to the best of our knowledge, few cases have been reported in the last 50 years in which the initial manifestation of SLE was Gullian–Barre syndrome (GBS).[1–9]

2. Method

The study was approved by the Research Ethics Committee of the Qilu Hospital of Shandong University. Informed consent was obtained from the patient for the publication of the report.

3. Case report

A 30-year-old Chinese female with no obvious cause appeared with numbness and inductance of lower extremities 2 months previously. It initially manifested as double plantar numbness, which gradually progressed to both legs, and was accompanied by double leg weakness, walking instability and a foot cotton feeling. There was no muscle soreness or beating, no dizziness and headache, no nausea and vomiting, no blurred vision, no difficulty in swallowing and drinking water, and no incontinence. The symptoms of numbness and weakness gradually progressed to the hands, the hands could not bear weight, and the symptoms gradually progressed. For nearly 2 days, the lower extremity weakness symptoms were significantly worse than before, and she was unable to stand firmly alone or squat. She was then admitted to our hospital. Her diet, sleep quality, urination and defecation were normal. Weight loss was 4 kg in the past 2 months. There were no bladder or bowel complaints, and no involuntary movements were noticed. There was no history of dog bite or vaccination. There was no past history of any illness, and she had not had any previous episodes of weakness. The patient did not have any addictions and gave no history of

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high-risk sexual behavior. Her menstrual history was noncontributory. She was married and had 2 children. There was no history of abortions or stillbirths.

Physical examination at admission revealed that she had a temperature of 36.5°C, heart rate of 105 bpm, respiratory rate of 20 breaths/min, blood pressure of 135/90 mm Hg and oxygen saturation of 98% in room air. She had no malar rash, oral ulcer, alopecia, arthritis or muscle inflammation. Neurologic examination indicated that the muscle strength in the legs was of grade 4/5 proximally and distally bilaterally, and there was an absence of deep tendon reflex in both knees and ankles. Paresthesia was observed in the distal limbs, with glove and stocking distributions. Her sense of acupuncture analgesia and vibration at the distal extremities was decreased. The deep tendon reflexes were absent. The bilateral Babinski test was unremarkable. The Romberg sign and heel-knee-tibia test were unstable.

Laboratory data revealed leukopenia 3.16×10^9/L and anemia with hemoglobin at 112 g/L, respectively. Platelets were within the normal limits. The liver function panel results were also within normal limits, except for albumin at 26.4 g/L and hyperlipidemia. Prealbumin was low at 30 g/L and BUN was at 5.32 mmol/. Creatinine was at 43 μmol/L. Urinalysis revealed protein of 3+, and blood tests revealed red blood cells (RBCs) of 13.1/HPF. The erythrocyte sedimentation rate (ESR) and C reactive protein (CRP) level were in the normal range. There was a positive ANA +1:1000, anti-dsDNA, antinucleosome, anti-SSA antibody and low levels of serum complement components (C3, C4). Anticardiolipin antibodies and antineutrophil cytoplasmic antibodies (ANCA) were negative. Serologic tests for HIV, hepatitis B/C, and syphilis were all negative. Cerebrospinal fluid examination revealed albumino-cytological dissociation (total protein: 1370 mg/L and white blood cell: 10×10^6/L). Head computed tomography (CT) revealed no abnormalities. Chest CT showed reduced cardiac cavity density and anemia. Abdominal CT showed that the liver and spleen were larger. A cardiac ultrasound showed mitral valve, mild tricuspid regurgitation. Electrocardiogram (ECG) revealed no obvious abnormalities. Electroneuromyography (ENMG) was highly suggestive of demyelinating polyradiculoneuropathy. The details are described below. Bilateral sural nerve sensory conduction was normal, and bilateral median nerve, ulnar nerve sensory conduction did not lead to a certain waveform, that is, a feeling of separation. Bilateral median nerve, ulnar nerve, and peroneal nerve terminal latency were significantly prolonged, with a slight slowdown in motor conduction velocity. Further, the bilateral ulnar nerve, peroneal nerve slower transmission through the head of the fibulain and the elbow, and the right peroneal nerve conduction block were suggestive of comprehensive demyelination damage. In patients with low motor transmission, a compound muscle action potential (CMAP) amplitude in the normal range compared with their peers and a low volatility do not rule out the possibility of secondary axonal damage. The latency of the detected F wave was significantly prolonged, and the incidence of the F wave in the lower extremities was significantly reduced, suggesting demyelination of the proximal nerve or nerve root. Needle electromechanical tips in some of the distal muscles showed a nerve predominant potential, which suggested that there was movement of fiber axon damage (Table 1). A percutaneous renal biopsy was performed on the patient after hospitalization. The kidney biopsy specimen showed glomerular basement membrane mild diffuse thickening (WHO classification lupus nephritis, class V. Activity index: 1 point, chronic index: 0 points). Immunofluorescence examination showed a glomerular distribution along the mesangial area: IgA ++, IgG+ along the capillary, C3 + along the capillary wall, F +, IgM +, C1q +, Kappa +, Lamda +. HE and special staining showed a total of 14 glomeruli, glomerular capillary wall mild diffuse thickening, mesangial area without proliferation, mesangial cells 1–3/ mesangial area, mesangial matrix without expansion, and endothelial cells without proliferation. Masson staining showed a small amount of hyperhidrosis protein deposition in the capillary wall. Tubular atrophy, part of the renal tubular epithelial cell swelling, granular degeneration, and no clear tube were observed. The renal interstitial area was without edema, fibrosis and lymphocyte and mononuclear cell infiltration. The interstitial small tube wall showed no thickening. Congo red stain was negative (−) (Fig. 1). A final diagnosis of SLE with GBS was made. The patient was initially treated with intravenous pulses of methyl prednisolone 0.5 g daily for 5 days. Maintenance therapy with 48 mg methyl prednisolone once a day, combined with cyclophosphamide treatment 1 g which was provided once a month.

4. Discussion

Systemic lupus erythematosus is a multifactorial autoimmune systemic disease. Causal factors include genetics, sex hormones, environment, infection, drugs, and food. Patients have shown the involvement of a variety of autoantibodies, and the immune complex and other pathways can cause systemic multiple system involvement. Damaged systems include the skin and mucous membranes, joints and muscles, kidneys, nervous system, blood system, lungs, heart and the digestive system. Among these systems, mucocutaneous, musculoskeletal, and renal manifestations are most commonly seen. Nervous system damage, also known as neuropsychiatric systemic lupus erythematosus (NPSLE), includes the central nervous system, the peripheral nervous system, and the autonomic nervous system, which is an important cause of death in SLE patients.[10–12] Common presentations include headaches, cerebrovascular accidents, seizures, depression, and psychosis. Neuropsychiatric manifestations of lupus may precede the onset of lupus and may occur at the time of diagnosis or later in the course of the disease.[11,13] Peripheral nervous system involvement is seen in less than 10% of all nervous system manifestations. [13] Acute inflammatory demyelinating polyneuropathy (AIDP) or the classic type of GBS is very uncommon. [14] Here, we report a patient with GBS that was associated with SLE.

Our patient was immediately given elective electromyography and a cerebrospinal fluid examination after admission. The cerebrospinal fluid showed protein cell separation, and electromyography showed demyelinating polyneuropathy. The diagnosis of GBS was established. Because of family conditions, our patient refused to use immunoglobulin. She was then given intravenous pulses of methyl prednisolone 0.5 g daily for 5 days. Following the rheumatism results, the anti-nuclear antibodies and anti-dsDNA antibody positivity, combined with the anemia and kidney damage, a diagnosis of systemic lupus erythematosus was established. Then, we arranged an ultrasound-guided renal biopsy. The results showed lupus nephritis of the V-type. We then added treatment with cyclophosphamide 1 g (d1 0.4 g, d2 0.6 g), during which the patient was treated with methylprednisolone 48 mg. The numbness of the hands and feet significantly improved compared with the pre-hospital state, and there was only slight numbness at the fingertips. Muscle strength returned to 5/5, and the glove-sock-like feeling disappeared. She was then discharged.

Table 1

Nerve conduction studies and electromyography.

Nerve stimulated	Stimulation site	Recording site	Latency (Moter:onset latency; sensory:peak latency), ms			Amplitude (M: mv; S: uv)			Conduction velocity, m/s			Minimal F latency, ms		
			Left	Right	NL	Left	Right	NL	Left	Right	NL	Left	Right	NL
Medianus nerve (motor)	Wrist	Abductor pollicis brevis	**6.73**	**6.78**	≤4.4	10.3	7.4	≥4						≤31
	Antecubital fossa	Abductor pollicis brevis	10.7	10.9	–	8.3	6.1	–	45.3	43.7	≥49			
	Axilla	Abductor pollicis brevis		16.1	–		5.5	–		44.2				
Ulnar nerve (motor)	Wrist	Abductor digiti minimi	**4.48**	**4.36**	≤3.3	6.3	7.0	≥6				**45.6**	**43.8**	≤32
	Below elbow	Abductor digiti minimi	8.81	8.02	–	6.2	6.8	–	41.6	50.5	≥49			
	Above elbow	Abductor digiti minimi	11.4	10.2	–	6.0	6.8	–	31.0	34.4				
Peroneal (motor)	Ankle	Extensor digitorum brevis	**8.11**	**10.2**	≤6.5	4.0	2.8	≥2						≤56
	Below fibular head	extensor digitorum brevis	14.4	19.1	–	3.2	1.5	–	44.5	40.2	≥44			
	Lateal popliteal fossa	Extensor digitorum brevis	18.6	26.6	–	3.0	1.5	–	20.2	10.7				
Tibial (motor)	Medial ankle	Abductor hallucis brevis	5.04	5.74	≤5.8	7.7	9.3	≥4				**65.5 (53%)**	**be not found**	≤56
	popliteal fossa	Abductor hallucis brevis	12.6	14.0	–	5.0	8.6	–	47.0	41.2	≥41			
Median (antidromic sensation)	Wrist	Digit 2	**be not found**	**be not found**	≤3.5			≥20			≥50			
Ulnar (antidromic sensation)	Wrist	Digit 5	**be not found**	**be not found**	≤3.1			≥17			≥50			
Sural (antidromic sensation)	Posterior-lateral calf	Posterior ankle	2.82	2.94	≤4.4	15.0	18.2	≥6	50.0	48.3	≥40			

L/R	Muscle	Insertion activity	Electromyography							
			Spontaneous activity				Voluntary motor unit potentials			
			Fibrillation potentials	Positive sharp wave	Fasciculation	Duration		Amplitude	Polyphasia	Recruitment
L	Bicips	NL	–	–	–	NL		NL	NL	NL
L	First dorsal interosseous	NL	–	–	–	–	13 ms ↑30%	↑ 2.5 mv	NL	↓↓
R	Medial vastus	NL	–	–	–	–	NL	NL	NL	NL
R	Tibialis anterior	NL	–	–	–	–	15 ms ↑30%	↑ 5 mv	↑ 40%	↓↓↓

NL = normal.

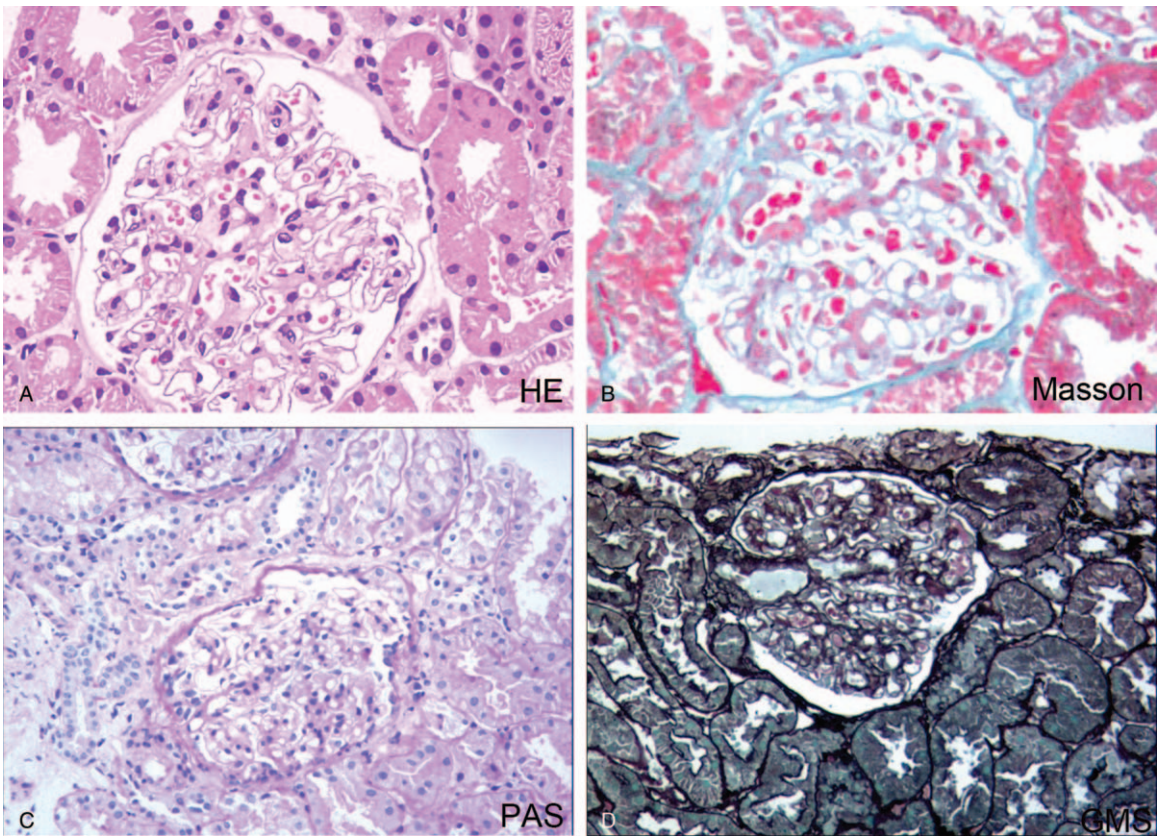

Figure 1. Histologic features of section of kidney biopsy. Glomerular capillary wall mild diffuse thickening, mesangial area without proliferation (×400).

Various forms of lupus related polyneuropathy have been reported in 10–20% of patients with SLE.[15] However, GBS which is a demyelinating polyneuropathy, is a rare complication in lupus.[16,17] The prevalence of SLE with GBS has been reported to be between 0.6% and 1.7%.[18,19] GBS as a presenting feature of SLE remains uncommon, with only a few cases reported in the last half-century; the first case was reported in 1964.[18] The diagnosis of our patient with Guillain-Barre syndrome was based on limb symmetry, flaccid paralysis, gloves, socks, nest-like sensory loss, cerebrospinal fluid with protein cell separation, and electromyography showing demyelinating polyneuropathy. In our patient, the diagnosis of SLE was made with the presence of renal involvement, anemia, positive ANA, and positive ds-DNA antibodies, meeting the minimum 4 of 11 criteria for a diagnosis of SLE by the American College of Rheumatology. In addition to these findings, the renal biopsy was consistent with class V Lupus nephritis (LN).

The pathogenesis of GBS as a manifestation of active SLE is not clear, but both cell-mediated and humoral processes may play a significant role.[17] The current study considered the following aspects: Vascular occlusion, which was mainly due to vascular endothelial hyperplasia, but occlusive endometrial fibrosis and thrombosis and other non-inflammatory vascular lesions were factors. Vascular occlusion is mainly caused by lupus erythematosus mental system damage in the focal regions. If there is multiple small blood vessel occlusion, there can also be a wide range of performances. Autoantibodies are also involved. There are currently four kinds of anti-neuronal antibodies: antilymphocytic antibodies, anti-phospholipid antibodies (including cardiolipin antibodies and lupus anticoagulants), and anti-ribosomal P protein antibodies. These antibodies are often present in the plasma and cerebrospinal fluid, and they cause more extensive neurological damage. Other cytokines, such as α-interferon and interleukin-6 levels, are considered to play a role in the pathogenesis.

Corticosteroids, cyclophosphamide, plasmapheresis, and immunoglobulin have been used in AIDP or GBS with SLE according to the previous literature. The combination of corticosteroids and cyclophosphamide is considered the first-line treatment option in a review of the literature.[6] In addition to renal biopsy, consistent with class V LN, our treatment was to give hormone and cyclophosphamide treatment after the intravenous pulses of methyl prednisolone at 0.5 g daily for 5 days. Compared with her prehospital state, our patient had only slight numbness at the fingertips, her muscle strength returned to 5/5, the glove-sock-like feeling disappeared, and she was discharged. Subsequently, the patient was hospitalized once a month to take cyclophosphamide and check the related indicators in parallel. In the second hospitalization, the numbness of the hands and feet had completely disappeared, and the quantitative proteinuria was reduced compared with her previous levels.

5. Conclusions

Controlled clinical trials are lacking because GBS-like acute axonal neuropathies are rare in SLE patients. However, their association has been strongly supported by reports in the

literature. Our study confirmed that the early application of hormones and cyclophosphamide is effective for treatment. However, the pathogenesis of both diseases still requires more clinical research.

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Author contributions

YG and ZG participated in its design and drafted the manuscript. ZG collected the clinical and imaging data. JZ collected and analyzed the pathological data. JL collected and analyzed electromyography data. ZH, XL, and TP helped to draft the manuscript. All authors read and approved the final manuscript.
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