Clinical Case Report

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The introspection on the diagnosis and treatment process of a case of Guillain–Barré syndrome (GBS) attributed to systemic lupus erythematosus (SLE)

A case report

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Abstract

Rationale: Systemic lupus erythematosus (SLE) is an autoimmune inflammatory connective tissue disorder. It may cause neurologic damage which is mainly characterized by central and mental system, while peripheral sexual damage is relatively rare in which Guillain–Barré Syndrome (GBS) as the first performance is more rare . GBS is an autoimmune peripheral neuropathy usually triggered by an antecedent bacterial or viral infection, with SLE being a rare cause.

Patient concerns: A 65-year-old male presented to the hospital with progressive numbness and adynamia in extremities. His vital signs were stable. 5 days later, his condition aggravated and mechanical ventilation was necessitated owing to severe dyspnea.

Diagnoses: Based on the clinical symptoms and results of the lumbar puncture and electromyography, he was first diagnosed as GBS, however, after treatment his condition was deteriorate and the blood test showed abnormal immune indices, then renal biopsy was performed, which confirmed the diagnosis of peripheral nervous system in patients with systemic lupus erythematosus (PNS-SLE).

Interventions: Firstly he was treated with intravenous immunoglobulin (IVIG) for 5 days. After his condition deterioration, he was conducted endotracheal intubation and, finally, a tracheostomy was performed. Later on he was treated with steroid therapy for several weeks.

Outcomes: The patient showed remarkable recovery and was able to walk on his own by the time of discharge.

Lessons: PNS-SLE can, by itself, be one of the main causes of morbidity and mortality. Electromyography and renal biopsy should be considered when relevant. Peripheral neuropathy in SLE should be given greater recognition, and rarer forms of presentation should be taken seriously in the differential diagnosis when the clinical picture is atypical. Glucocorticoids may play an important role in the treatment of PNS-SLE.

Abbreviations: CSF = examination of the cerebrospinal fluid, EMG = electromyography, GBS = Guillain–Barré Syndrome, IVIG = intravenous immunoglobulin, NP = neuropsychiatric, NPSLE = neuropsychiatric systemic lupus erythematosus, PNS-SLE = peripheral nervous system in patients with systemic lupus erythematosus, SLE = systemic lupus erythematosus.

Keywords: Guillain–Barré syndrome, intravenous immunoglobulin, neuropsychiatric systemic lupus erythematosus, peripheral nervous system in patients with systemic lupus erythematosus, steroid therapy

1. Introduction

Neuropsychiatric systemic lupus erythematosus (NPSLE) includes 19 neuropsychiatric (NP) syndromes from which 12 involve the central nervous system and 7 the peripheral nervous system (PNS) seen in patients with systemic lupus erythematosus (SLE) in which other causes have been excluded.[1] These symptoms may precede the onset of SLE or may occur at any time during the course of SLE[2,3] in which is not only in the setting of active SLE but also during quiescent.[1] The PNS involvement occurs more frequently in patients who are diagnosed with SLE at older age than those without PNS involvement.[4,5] The prevalence of PNS involvement occurs in 1.5% to 17.7% of patients and over half of them attribute to SLE.[4–9] The most common PN-related symptoms were myasthenia and numbness in affected regions.[10] Its most frequent manifestation is sensory-motor axonal polyneuropathy.[4,6,11] Conversely, the prevalence of Guillain–Barré syndrome (GBS) is very low in all series.[6–9,12–15] GBS is an autoimmune peripheral neuropathy usually triggered by an antecedent bacterial or viral infection. The disease is characterized by a rapidly progressive, symmetrical, and ascending motor paralysis with hypotonia and areflexia. Examination of the cerebrospinal fluid (CSF) demonstrates albuminocytologic dissociation; electrophysiological parameters, such as nerve conduction velocity, H-reflexes, and F waves, indicate sensory-motor demyelinating polyneuropathy. GBS which is also classified under the peripheral involvement in

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which other causes have been excluded has been rarely associated with SLE.[1] Disorders of peripheral nervous system in patients with systemic lupus erythematosus (PNS-SLE) are a major cause of morbidity.[8] Nervous system involvement in patients with SLE manifests as a nonspecific heterogeneous group of NP symptoms.[16] Currently, there are no known laboratory or radiological biomarkers of NPSLE. Moreover, clinical guidance for diagnosis and therapeutic decision making in these patients is not available.[17] In clinical practice, multidisciplinary diagnostic and therapeutic approach is recommended in these patients based on the suspected cause and the severity of symptoms.[18] NPSLE is typically diagnosed when the patient is symptomatic (based on patient complaints or the physician's assessment).[19] Due to the lack of a gold standard, the attribution of NPSLE represents a clinical challenge; diagnosis is largely based on exclusion of other potential causes. NP events in patients with SLE have a detrimental effect on the quality of life and are associated with a poor prognosis.[8] Here, we report a case of GBS associated with SLE and according to the neurological manifestations, renal biopsy and SLE serology confirm the diagnosis of PNS-SLE, which was seldom seen. At the beginning, after treatment with intravenous immunoglobulin (IVIG), his symptoms did not improve and the patient remained dependent on mechanical ventilation. Partial recovery was only achieved after several weeks of steroid therapy.

2. Case presentation

The study was approved by the ethical committee of First Hospital of Jilin University, China. Written informed consent was obtained the individual participant included in the study.

3. Patient

A 65-year-old man from Changchun, China presented to the emergency department at the First Hospital of Jilin University on August 21, 2015, with progressive numbness and adynamia in his extremities. Approximately 2 weeks prior to hospitalization, the patient had suffered from fever and low back pain. Nine days prior to admission, he experienced dizziness and had headache with metamorphopsia. He was diagnosed with cerebral circulation insufficiency and treated with Ozagrel sodium, salvia miltiorrhza and ligustrazine hydrochloride injection at a local hospital; however, his condition continued to aggravate.

Eight days after the onset of fever, the patient developed numbness in distal lower limbs (from feet to the knees) and in both hands. Three days later, he developed weakness in all extremities; he was unable to get up from a squatting position or to climb stairs. At times, he experienced nasal regurgitation. The patient had no difficulty in speaking or swallowing and had no shortness of breath at that stage. He had a history of rheumatism since approximately 40 years. And he had a history of cerebral infarction and intestinal tuberculosis.

There was a history of blood transfusion during surgery and was infected with HCV, which might have led to a compromised immune system. There was no family history of autoimmune diseases, communicable diseases, or cancer. The patient was allergic to penicillin and alcohol. He worked as a machinist but denied any occupational exposure to mucedine, asbestos, heavy metals, or silica. There was no history of skin rashes, mouth ulcers, hair loss, or photosensitivity.

4. Physical examination and laboratory tests

At admission, his vital signs were stable; he had no dyspnea, and his oxygen saturation was 98% (room air). Systemic examination was unremarkable. There was no edema in the lower extremities. The patient was conscious, coherent, and well oriented. He was able to fully comprehend his condition and surroundings, and his speech remained fluent.

Results of tests on the cranial nerve were normal; however, he experienced diplopia and the right nasal groove was shallow. The muscles in all 4 limbs were hypotonic. On a scale of 1 to 5, the muscle power in the upper extremities was grade 4 and in the lower extremities, grades 2 to 3. Superficial reflexes were normal; there were no deep-tendon jerks but there were ataxia. There was hypoalgesia of hands and distal lower limb from approximately 10 cm below the knee joint.

Laboratory findings on admission included normal complete blood counts (white blood cells [WBCs], 6.44×10^9/L; red blood cells, [RBCs] 4.38×10^{12}/L; and hemoglobin, 130 g/L). Renal function test results were within normal limits (blood urea nitrogen [BUN], 5.81 mmol/L; creatinine, 69.7 μmol/L). With the exception of serum potassium (4.0 mmol/L), his serum electrolyte levels were abnormal (serum sodium, 124.0 mmol/L; serum chloride, 90.9 mmol/L). Vitamin B12 level was elevated at 1107 pmol/L. Erythrocyte sedimentation rate and high-sensitivity C-reactive protein were elevated (67.0 mm/hour and 14.4 mg/L, respectively).

High immunoglobulin G (22.7 g/L) and low complement 3 (C3) (0.79 g/L) were observed. Serum HCV antibody was positive and the HCV RNA detected using fluorescent quantitative polymerase chain reaction showed values above the normal range (2.8 E7↑ IU/mL < 1.0 E3). Rapid HIV test was nonreactive.

Routine urine test showed proteinuria and RBC and cast counts of 628.40 and 0.84 μ/L, respectively. Computed tomography scan of the head showed no signs of intracranial hemorrhage, mass, or other intracranial pathology. Magnetic resonance imaging of the brain and spinal cord was unremarkable.

Following the initial workup, the patient was diagnosed with GBS, and a trial of IVIG at 0.4 g/kg/day was given for a period of 5 days. Approximately 3 days after the start of treatment, the patient experienced difficulty in falling asleep accompanied by aggravation of numbness and weakness in the extremities, and inability to cough. A lumbar puncture yielded clear CSF; CSF examination showed WBC count of 3.0×10^6/L with a predominance of monocytes; protein concentration was 1.77 g/L (albuminocytologic dissociation); and glucose concentration was 3.60 mmol/L. The CSF results were not consistent with a diagnosis of GBS.

Electromyography (EMG) study of the median, ulnar, peroneal, and tribal nerves revealed gross reduction in motor nerve conduction velocity; distal latency was grossly prolonged in all nerves, while F waves were absent in all the nerves. H-reflexes were absent on both sides, and sensory nerve action potential was absent in the ulnar nerves (Tables 1–3).

Table 1

Motor nerve conduction velocity.

Nerve	Latency, ms	Amplitude, mv	Conduction velocity, m/s	F wave
Ulnar	3.19↑	2.9↓/3.4↓	43.9↓/41.9↓	–
Median	7.90↑	2.3↓/2.0↓	37.9↓	–
Tibial	6.44↑	3.8↓/2.3↓	38.7↓	–
Peroneal	5.36↑	4.7↓	37.6↓	–

The median, ulnar, peroneal, and tribal nerves revealed gross reduction in motor nerve conduction velocity; distal latency was grossly prolonged in all nerves. F waves were absent in all the nerves.

Table 2

Sensory nerve–conduction velocity.

Nerve	Latency, ms	Amplitude, mv	Conduction velocity, m/s
Ulnar	2.65	2.7↓	41.5↓
Median	2.70	4.5↓	48.1
Superficial	2.09	10.1	52.6
Sural	1.62	5.7	61.7

The median, ulnar nerves revealed reduction in sensory conduction velocity.

Table 3

Right tibial nerve H reflex.

	M-Lat, ms	H-Lat, ms	H/M amp
Knee gastrocnemius muscle	6.4	–	–

H-reflexes were absent on both sides.

After IVIG treatment, the weakness progressed (muscle power in the upper extremities was grade 3 and that in the lower extremities was at grade 2) and the patient had difficulty swallowing, coughing, and breathing. We then conducted endotracheal intubation and, finally, a tracheostomy was performed.

Taking into consideration the patient's history of rheumatism, tests for immune indices were performed; the results were as follows: anti-ds-DNA positive titer: 1:10; homogeneous pattern positive titer: 1:1000; and cytoplasmic particle type positive titer: 1:1000. anti-SSA, anti-SSB, anti-Sm, anti-Nrnp/Sm, and anti-Jo-1 were negative.

Based on these results, SLE was suspected. Renal biopsy (Fig. 1) showed focal glomerulonephritis and positive IgA, IgM, C1q, and C3, which confirmed the diagnosis of SLE.

Considering the patient's condition and the diagnosis of SLE, we opted for a trial of steroid therapy. The patient showed a remarkable response to 2 weeks of aggressive therapy and began to recover. We were able to withdraw the artificial breathing apparatus, and the patient was able to take a few steps by himself upon discharge.

5. Discussion

PNS-SLE is one of the main causes of morbidity and mortality.[17] There are 7 types of peripheral neuropathy associated with SLE in which includes acute inflammatory demyelinating polyradiculoneuropathy, autonomic disorder, mononeuropathy, myadthenia gravis, neuropathy, plexopathy, and polyneuropathy. The most common type of PNS-SLE was polyneuropathy with sensory involvement, followed by mononeuropathy. GBS associated with SLE is relatively rare. The prevalence of peripheral neuropathies associated with SLE is variable (range 1.5%–17.7%) and about 60% attributable to SLE.[4–9] In nearly half of them, PNS-SLE involvement was the only manifestation of the SLE flare when it appeared.[5] The pathogenesis is unclear, although it has been linked to vascular disease of the small arteries that supply the affected nerves.[20,21] GBS is a heterogeneous condition with several variant forms. This acute monophasic progressive disease presents with symmetrical muscle weakness and absent or attenuated deep-tendon reflexes.

GBS is a rare manifestation of SLE, which falls under the category of PNS-SLE.[15,22–25] GBS, as the initial presentation of SLE, has been reported in only a few cases to this day.[15,22] The exact pathophysiology of this relationship is largely unknown; however, cross-reactivity between the auto-antibodies associated with SLE and those formed against myelin tissue is believed to be involved.[26] In addition, immune-suppression associated with SLE is an aggravating factor which exacerbates the neuronal inflammation in these patients.[25] The older people were more likely to suffer from PNS-SLE than those without peripheral neuropathies.[4] Although there is no clear recommendation for the treatment of PNS-SLE, induction treatment with glucocorticoids with or without immunosuppressant agents are indicated if the PNS-SLE appears in the context of lupus activity.[27] Overall, global response (complete and/or partial) to treatments was achieved in 77.4% of patients in some studies without differences between the types of PNS-SLE involvement.[5,6] Our patient was also in the context of lupus activity and partial recovered with the treatment with glucocorticoids.

In our present report, we described a case of GBS associated with SLE which finally diagnosed as PNS-SLE. The clinical features, the results of the CSF, magnetic resonance imaging, and EMG supported the diagnosis and treated with IVIG at the beginning. However, he was not sensitive to the IVIG and the condition aggravated. He had no definite history of infection such

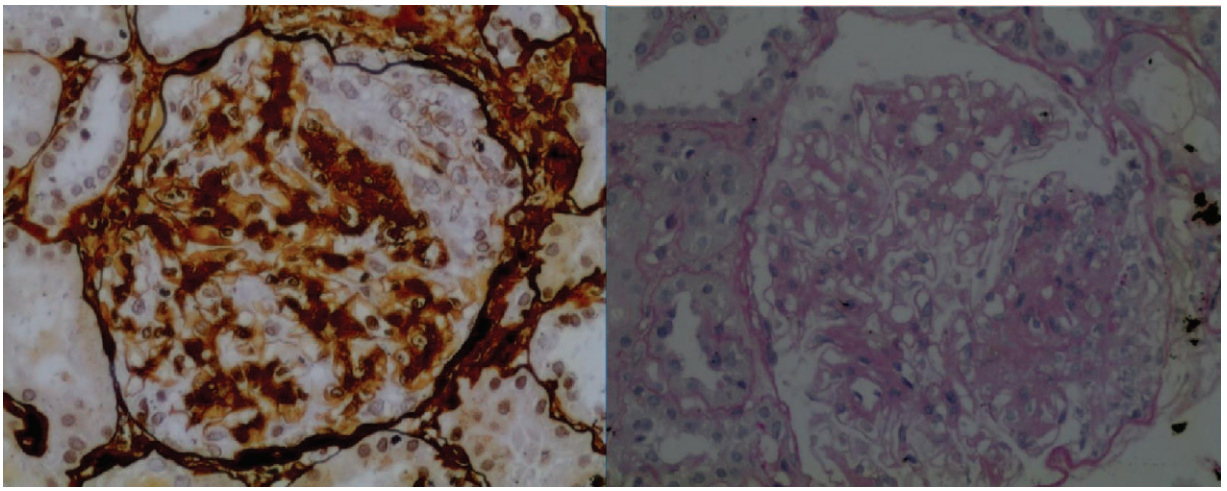

Figure 1. Histopathological examination of renal biopsy specimen showing focal lupus nephritis (ISN/PPS 2004 classification lupus nephritis).

as influenza or diarrhea but had a history of rheumatism and infected with HCV, moreover the serological examination of rheumatic immunity was positive, so we considered that the GBS might be attributed to SLE not other causes. Then the renal biopsy was conducted and finally confirmed our conjecture.

Our patient was initially diagnosed with GBS, which was confirmed by CSF analysis, EMG, and nerve-conduction studies, as well as by clinical observation. However, he had no history of infection and premonitory symptoms which excluded other causes and according to the renal biopsy, the diagnosis of PNS-SLE was confirmed. When the GBS patients lack definite history of infection, care should be taken not to overlook the possibility of connective tissue disease as the etiology of peripheral neuropathy, because it may easily be attributed to other causes. And this may also explain why after use the IVIG the symptoms of our patient did not improve. Because of the differences in pathogeny and epidemiology, the treatment effect was different. Pulsed glucocorticoid therapy (eg, prednisone and methylprednisolone) is the treatment of choice for the management of SLE. Cyclophosphamide is yet another immunosuppressive agent used to control manifestations of SLE.[23] Although, immune suppressants and interferon should be used to treat SLE and HCV, respectively, these may result in an increase in viral replication and the standard therapy with interferon might have neurological side effects, such as nerve palsy and peripheral neuropathy.[28] After assessment the pros and cons, we did not use the immune suppressants and interferon. Luckily, he was picking up after using glucocorticoids.

Our experience with this patient showed that GBS might attribute to SLE. A high index of suspicion for SLE in such cases may help avoid any unnecessary delay in diagnosis and help improve prognosis of the patient.

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