CASE REPORT

Fulminant Guillain-Barré syndrome in a patient with systemic lupus erythematosus

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SUMMARY

A 45-year-old man with a history of systemic lupus erythematosus presented with progressive weakness and areflexia. Electromyogram revealed reduced motor and sensory amplitudes without demyelinating features. He was clinically diagnosed with the acute motor and sensory axonal neuropathy variant of Guillain-Barré syndrome. Despite intravenous immunoglobulin therapy, he deteriorated with loss of all voluntary motor function and cranial nerve reflexes. Concomitant investigations revealed class V lupus nephritis. Therapy was initiated with plasma exchange, glucocorticoids and further immunosuppression, with gradual neurological recovery. We present the first documented case of fulminant Guillain-Barré syndrome as a neuropsychiatric manifestation of systemic lupus erythematosus, highlighting how immune-mediated polyneuropathy via diffuse deafferentation may mimic the outward appearance of brain death. While glucocorticoids are not indicated in idiopathic Guillain-Barré, when this neurological disorder is a consequence of systemic lupus erythematosus, immunomodulatory treatment should be initiated to prevent neurological deterioration.

BACKGROUND

Guillain-Barré syndrome, or acute inflammatory polyradiculoneuropathy, is characterised by acute ascending progressive weakness, areflexia and dysautonomia.¹ In its severest form, fulminant Guillain-Barré syndrome (GBS) may be mistaken for brain death with flaccid quadriplegia and absent brainstem reflexes due to effectively complete motor, sensory and autonomic denervation. The natural course of fulminant GBS is unknown, as only few reports exist in the literature.² We present the first documented case of fulminant GBS as a neuropsychiatric manifestation of systemic lupus erythematosus (SLE), highlighting how immune-mediated polyneuropathy may mimic the outward manifestations of brain death.

CASE PRESENTATION

A 45-year-old man presented to hospital with new onset proximal upper and lower extremity weakness. His medical history was significant for SLE which was diagnosed 2 years prior following a presentation with polyarthritis, pericarditis, pleuritis, hypocomplementaemia and antinuclear and anti-Smith antibody positivity. He was well controlled on azathioprine 150 mg and prednisone 5 mg daily.

One week prior to presentation, he developed progressive shoulder girdle weakness, followed by distal paraesthesia, proximal lower extremity weakness and inability to ambulate. Neurological assessment revealed reduced power, with a Medical Research Council grade of severe in the deltoids [0/5] and biceps [2/5] symmetrically, and moderate [3–4/5] in all other muscle groups. Bicipital reflexes were absent.

INVESTIGATIONS

Routine biochemical investigations, including creatine kinase, were normal. Urinalysis revealed 1+ protein without blood. C3 and C4 complement titres were depressed at 0.6 and 0.11 g/L, respectively, but unchanged from previous baseline values. Antibody testing redemonstrated positive antinuclear, anti-Smith, anti-RNP and anti-Ro antibody positivity.

Cerebrospinal fluid analysis was normal (white cell count $0 \times 10^6/L$, RBC $1 \times 10^6/L$, protein 370 mg/L); PCR testing was negative for West-Nile virus and herpesviruses. Serum HIV and syphilis tests were negative.

MRI of the brain and spine demonstrated cauda equina nerve root thickening and enhancement but no evidence of intracranial abnormalities. Electromyogram and nerve conduction studies revealed significant reductions in motor and sensory amplitudes without demyelinating features.

DIFFERENTIAL DIAGNOSIS

Given progressive upper and lower extremity weakness with areflexia and absence of cerebrospinal fluid pleocytosis, a clinical diagnosis of GBS was made. The electromyographic features of reduced motor and sensory amplitudes without features of demyelination supported the diagnosis of acute motor and sensory axonal neuropathy, a GBS variant.

TREATMENT

Intravenous immunoglobulin (IVIG, 2 g/kg) was administered. However, the patient's weakness progressed, culminating in quadriplegia and diffuse areflexia. Despite further IVIG, he deteriorated rapidly, developing facial paralysis and respiratory failure requiring endotracheal intubation and mechanical ventilation.

Three weeks following presentation, peripheral sensation diminished, and communication became limited to blinking. By 1 month, all voluntary

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Table 1 Reported cases of Guillain-Barré and Lupus

Citation	Age/ gender	Timing	SLE features	Antibodies	GBS variant	Treatment	Outcome
Chaudhuri <i>et al</i> ⁶	40 M	Concurrent	Seizure, class V nephritis, leucopenia	ANA, dsDNA	AIDP	Plasma exchange, steroid, CP	Partial: 16 wk
Robson <i>et al</i> ⁸	33 F	Concurrent	Neuropsychiatric, vasculitis, haemolytic anaemia, thrombocytopenia, lymphopenia, complements	ANA, dsDNA, cardiolipin	AIDP	Steroid, CP	Partial: 8 wk
Matsuki <i>et al</i> ²⁰	61 F	Concurrent	Arthralgia, pericardial effusion, anaemia, leucopenia	ANA, dsDNA, Ro, La, GM1	AMSAN	Plasma exchange, steroid, mizoribine	Partial: 8 wk
Vaidya <i>et al</i> ⁷	23 M	Concurrent	Class V nephritis, complements	ANA, dsDNA, Smith	AIDP	Plasma exchange, CP, steroid	Complete: undefined
Miyagawa <i>et al</i> ⁹	13 F	SLE first (6 years prior)	Chilblain, oral ulcers, leucopenia	ANA, dsDNA, Ro, La	AIDP	Plasma exchange, IVIG, steroid	Complete: 20 wk
Stahl <i>et al</i> ¹⁰	56 F	SLE first (1 year prior)	Alopecia, arthritis, myelitis, oral ulcers, anaemia, leucopenia, thrombocytopenia	ANA, dsDNA, histone	AIDP	IVIG, steroid, CP, plasma exchange, CSF filtration	Complete: undefined
Van Laarhoven <i>et al</i> ²³	20 F	Concurrent	Malar rash, pericardial/pleural effusions, class IV nephritis, haemolytic anaemia, complements	ANA, Smith, RNP	Unspecified	IVIG, CP, steroid	Complete: 24 wk
Lewis and Gibson ¹¹	26 M	SLE first (5 years prior)	Arthralgia, lymphadenopathy, myositis, necrotizing vasculitis, pericardial/pleural effusions, class I nephritis	ANA, dsDNA, Smith, RNP, cardiolipin	AIDP	IVIG, steroid, CP, azathioprine	Complete: 10 days. *Recurred in 8 months, died
Hsu <i>et al</i> ¹²	28 F	Concurrent	Pleuritis, lymphopenia, complements	ANA, dsDNA, Ro, La	AIDP	Plasma exchange, steroid	Partial: 2 wk
Yildiz <i>et al</i> ¹³	47 F	Concurrent (*history of discoid lupus)	Alopecia, oral ulcer, malar rash, anaemia, leucopenia, thrombocytopenia	ANA	AMAN	Steroid, CP, HCQ	Partial: 12 wk
Rajadhyaksha and Mehra ²²	30 F	Concurrent	Arthralgia, oral ulcers, class II nephritis, anaemia, complements	ANA, dsDNA, Smith, GT1a, GQ1b, GM1b	AMAN and pharyngeal-cervical-brachial	IVIG, steroid, HCQ	Complete: 2 wk
Santiago-Casas <i>et al</i> ¹⁴	20 F	Concurrent	Lymphopenia, proteinuria	ANA, dsDNA	AMAN	Plasma exchange, IVIG, CP, steroid, HCQ	Complete: 16 wk
Santiago-Casas <i>et al</i> ¹⁴	34 F	SLE first (1 year prior)	Arthritis, lymphopenia	ANA, dsDNA	AMSAN	IVIG, steroid, CP, HCQ, azathioprine	Complete: 24 wk
Ha-ou-nou <i>et al</i> ¹⁵	44 M	Concurrent	Malar rash, proteinuria, lymphopenia, complements	ANA, dsDNA	AMAN	IVIG, steroid	Died
Okoh <i>et al</i> ²¹	41 F	Concurrent	Pericardial/pleural effusions, class III/V nephritis leucopenia, complements	ANA, dsDNA, Smith, GQ1	Miller-Fisher	Plasma exchange, IVIG, steroid, CP, MMF	Complete: 18 wk
Fazio <i>et al</i> ¹⁶	44 F	Concurrent	Lymphadenopathy	ANA, dsDNA, Smith, RNP, β -2 glycoprotein	AIDP	IVIG, HCQ	Partial: undefined
Nadri and Althaf ¹⁷	23 F	Concurrent	Class V nephritis	ANA, dsDNA	AIDP	Plasmapheresis, IVIG, steroid, MMF	Partial: 24 wk
Ali <i>et al</i> ¹⁸	38 F	Concurrent	Oral ulcers, proteinuria, complements	ANA, dsDNA, Ro, lupus anticoagulant	AIDP	IVIG, steroid, CP, HCQ	Partial: undefined
Li and Wang ¹⁹	34 F	SLE first (3 years prior)	Alopecia, arthritis, malar rash, oral ulcers, class III nephritis, complements	ANA, dsDNA, Smith	AIDP	IVIG, steroid, CP	Partial: undefined
Li and Wang ¹⁹	65 M	Concurrent	Arthralgia, class III nephritis, complements *concomitant HCV diagnosis	ANA, dsDNA, ANCA	Unspecified	IVIG, steroid	Partial: 2 wk

AIDP, acute inflammatory demyelinating polyneuropathy; AMAN, acute motor axonal neuropathy; AMSAN, acute motor and sensory axonal neuropathy; ANA, antinuclear antibody; complements, hypocomplementaemia; CP, cyclophosphamide; CSF, cerebrospinal fluid; dsDNA, double-stranded DNA; GBS, Guillain-Barré syndrome; HCQ, hydroxychloroquine; IVIG, intravenous immunoglobulin; MMF, mycophenolate mofetil; RNP, ribonucleoprotein; SLE, systemic lupus erythematosus; wk, week; yr, year.

motor function was absent. Soon thereafter, reflex cranial nerve functions were lost including pupillary, corneal, vestibulo-ocular, cough and gag reflexes. Ventilator triggering and discernible autonomic response to painful stimuli were also absent, despite the absence of sedation or analgesia. At this stage, while the patient manifested the outward appearance of clinical brain death, a proximate cause of irreversible coma was absent; rather, diffuse deafferentation via profound peripheral

nervous system damage was hypothesised to mimic a comatose state. Nevertheless, to definitively exclude central nervous system (CNS) injury, further testing was pursued. Repeat MRI demonstrated a structurally intact brain but now displayed decreased venous haemoglobin deoxygenation—a radiological finding typically observed in neuronal states of metabolic inactivity. Electroencephalography demonstrated unreactive stage-2 sleep, suggestive of a hypometabolic state, potentially

on the basis of reduced CNS activity when devoid of peripheral stimulation.

Due to the severity of disease progression, plasma exchange was initiated. Initial clinical improvement soon followed, with gradual return of facial movements and communication via blinking. Concomitant surveillance investigations revealed a dramatic rise in proteinuria; repeat urinalysis demonstrated 4+ protein and subsequent 24 hours urine collection identified 15.2 g of protein/24 hours. Renal biopsy confirmed class V lupus nephritis. Glucocorticoids were therefore initiated with a pulse of methylprednisolone 1 g/day for 3 days, followed by 1 mg/kg of prednisone daily in addition to mycophenolate mofetil.

OUTCOME AND FOLLOW-UP

Neurological recovery continued slowly, with return of sensation and increasing facial movements. After a protracted ventilator-dependent flaccid quadriplegia, he had gradual partial neurological recovery and after several months was successfully extubated. Given the chronicity of his clinical course, his diagnosis was revised to chronic inflammatory demyelinating polyneuropathy. His clinical recovery subsequently regressed, and he developed recurrent respiratory failure requiring reintubation. Intensified immunosuppression with rituximab B-cell depletive therapy was initiated. Over the following month, partial neurological recovery again occurred followed by successful extubation. With ongoing immunosuppression with rituximab, mycophenolate mofetil and corticosteroids in addition to intensive physiotherapy, the patient's strength and function continued to slowly recover.

DISCUSSION

GBS, or acute inflammatory polyradiculoneuropathy, is characterised by acute ascending progressive weakness, areflexia and dysautonomia.¹ Involvement of the diaphragm and accessory respiratory muscles may necessitate ventilatory support.¹ Several subtypes exist, including the classic acute inflammatory demyelinating polyneuropathy, and the rarer variant of acute motor sensory axonal neuropathy seen in this case.¹ Albuminocytological dissociation (increased cerebrospinal fluid protein without pleocytosis) is seen in two-thirds of cases.¹ Electrodiagnostic studies in demyelinating variants demonstrate decreased conduction velocity, prolonged latency and conduction blocks, whereas axonal forms display decreased motor and sensory amplitudes. Spinal imaging may reveal thickened and enhanced nerve roots and cauda equina, but cerebral imaging and electroencephalography should be unremarkable.¹

The only proven therapies for GBS are IVIG and plasma exchange; previous meta-analyses indicate no benefit from corticosteroids.^{3,4} However, GBS is also recognised as a potential neuropsychiatric manifestation of SLE.⁵ Current guidelines indicate that when neuropsychiatric manifestations occur in the context of generalised SLE activity or when specific neurological manifestations reflect an underlying inflammatory process, such as peripheral neuropathy, pulse glucocorticoids should be used.⁵

Review of the literature reveals that cases of GBS in the context of SLE have predominantly presented with acute inflammatory demyelinating polyneuropathy followed by the acute motor axonal neuropathy variant.^{6–19} Rare cases of acute motor sensory axonal neuropathy,^{14,20} Miller-Fisher syndrome²¹ and pharyngeal-cervical-brachial syndrome²² have also been reported. While standard GBS therapies such as plasma exchange and IVIG are often applied, in the majority of cases of concurrent SLE and GBS, additional immunosuppressive or

immunomodulatory therapies have been employed, including corticosteroids, cyclophosphamide, azathioprine,¹⁴ mycophenolate mofetil¹⁷ and/or hydroxychloroquine.^{13,14,16,18,22} In some cases, patients did not respond to traditional GBS therapies, but had significant clinical improvement following immunosuppressive therapy.^{10,14,23} Table 1 outlines previous cases of GBS complicating SLE, including patient demographics, SLE features, autoantibodies, GBS variant, treatment and outcomes.

Although GBS is not known to involve the CNS, our patient demonstrated a profound level of unconsciousness, with MRI and electroencephalographic findings hinting at an effective 'hibernation' of central neuronal metabolism.²⁴ Was the unconsciousness in this patient mediated solely by their apparent complete peripheral nervous deafferentation? Such a theory would posit that external sensory input is a *sine qua non* for the maintenance of consciousness and is potentially supported by the patient's rapid return to consciousness once sensory input was restored with immunomodulatory therapy.

To our knowledge, this patient represents the first reported case of fulminant GBS mimicking brain death as a neuropsychiatric manifestation of SLE, with initial clinical response to sequential therapy with IVIG, plasma exchange and glucocorticoids. Contrasting with idiopathic GBS, the underlying pathophysiological process in this case may have been mediated by SLE activity and glucocorticoids may have altered the clinical course of the disease.

Learning points

- ▶ Fulminant Guillain-Barré syndrome may be a severe neuropsychiatric manifestation of systemic lupus erythematosus.
- ▶ Diffuse deafferentation from Guillain-Barré syndrome should be considered in the differential diagnosis for a patient with the outward manifestations of brain death.
- ▶ While glucocorticoids are not indicated in idiopathic Guillain-Barré, in the context of systemic lupus erythematosus glucocorticoids and immunosuppressive treatment should be considered.

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