Acute motor-sensory axonal neuropathy associated with systemic lupus erythematosus

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ABSTRACT

Systemic lupus erythematosus (SLE) is an autoimmune disease that involves multiple organs and is generally treated by immunosuppressive agents. Acute motor-sensory axonal neuropathy (AMSAN) is a variant of Guillain-Barré syndrome. The standard therapies are intravenous immunoglobulin or plasmapheresis. An association between AMSAN and SLE is rarely reported. Herein, we describe a case of a 72-year-old man who presented with rapidly progressive paraparesis, dysesthesia, and joint pain with morning stiffness. Initially, he was diagnosed with AMSAN. Intravenous immunoglobulin was given without significant improvement. Subsequent studies indicated the diagnosis of SLE. Therefore, the patient was treated with intravenous methylprednisolone, cyclophosphamide, and then plasmapheresis. At 3 months, he improved from bedridden to wheelchair-bound. Our case demonstrates AMSAN as a rare initial manifestation that can lead to significant disability.

KEYWORDS Acute motor-sensory axonal neuropathy; AMSAN; Guillain-Barré syndrome; systemic lupus erythematosus

Acute motor-sensory axonal neuropathy (AMSAN) is a variant of Guillain-Barré syndrome (GBS), for which the standard treatments are intravenous immunoglobulin and/or plasma exchange. Systemic lupus erythematosus (SLE) is a multisystem immune-mediated disease. Unlike GBS, SLE is generally treated with corticosteroids and immunosuppressive agents. Therefore, the management of this condition is challenging. Herein, we describe the clinical presentation, complex management, and clinical outcome in a case of AMSAN as the first manifestation of SLE.

CASE REPORT

A previously healthy 72-year-old white man presented with rapidly progressive bilateral ascending flaccid weakness and tingling sensation in all four extremities. He became quadriplegic within 3 days. Additionally, joint swelling, pain, tenderness, and morning stiffness were reported in both knees and finger joints. He denied dyspnea, voice change, and swallowing difficulty. He had no history of recent fever, diarrhea, or vaccination. At presentation, he was afebrile (98.8°F) and normotensive (126/65 mm Hg). He had no rash, hair loss, or oral ulcer. There was no superficial

lymphadenopathy. Pain with passive movement and tenderness were noted in both knees and joints of the fingers. Neurological examination showed complete quadriplegia, hypotonia, and areflexia. Hyperesthesia was noted in all extremities. Cranial nerves were intact.

Initial blood work showed an elevated erythrocyte sedimentation rate, C-reactive protein, antinuclear antibody, and anti-double-stranded DNA titers. Antineutrophil cytoplasmic antibody and paraneoplastic antibodies were negative. Urinalysis was negative for protein. Random urine protein was 11 mg/dL. Cerebrospinal fluid examination showed a white blood cell count of 3/μL and protein of 46 mg/dL. A nerve conduction study (*Table 1*) was suggestive for acute diffuse axonal sensorimotor polyneuropathy (motor predominant). Serial complete blood counts showed multiple occasions of lymphopenia (<1000/μL).

Initially, the patient was diagnosed with GBS according to Brighton collaboration diagnostic criteria at level 1 of diagnostic certainty.¹ The electrophysiological study met the criteria for AMSAN subtype.² Therefore, he was initially treated with intravenous immunoglobulin. However, no significant clinical improvement was observed. Given the history of arthritis, lymphopenia, as well as seropositivity of antinuclear antibody and anti-double-stranded DNA,

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Table 1. Nerve conduction studies

Nerves	Amplitude (μ V)			Latency (ms)			Conduction velocity (m/s)		
	R	L	Norm	R	L	Norm	R	L	Norm
Sensory									
Median (second digit)	NR	15.8	>20	NR	3.3	<3.5	NR	39	>50
Ulnar (fifth digit)	6.5	11.3	>17	2.5	3.2	<3.1	39	34	>50
Superficial peroneal	8.1	9.2	>6	2.8	2.2	<4.4	50	64	>40
Sural	5.5	10.5	>6	3.8	3.2	<4.4	37	44	>40
Motor									
Median (APB)									
Wrist	0.4	0.4	>4.0	4.8	5.5	>4.0	28	40	>49
Elbow	0.2	0.3		13.8	11.6				
Ulnar (ADM)									
Wrist	NR	NR		NR	NR		NR	NR	>49
Below elbow	NR	NR		NR	NR				
Above elbow		NR			NR		NR	>49	
Peroneal (EDB)									
Ankle	NR	0.4	>2.0	NR	6.2	<6.5	NR	39	>44
Below fibula	NR	0.4		NR	14.4				
Popliteal		0.2			16.6		45	>40	
Tibial (AHB)									
Ankle	1.9	1.2	>4.0	5.8	4.6	<5.8	11.7	10.3	>41
Knee	0.6	0.8		17.5	14.9				
F-wave									
	Latency (ms)			L-R latency (ms)					
	R	L	Norm	L-R	Norm				
Median	NR	NR	<31		<2.2				
Tibial	40.0	NR	<56		<5.7				

ADM indicates abductor digiti minimi; AHB, abductor hallucis brevis; APB, abductor pollicis brevis; EDB, extensor digitorum brevis; L, left; m/s, meters per second; ms, milliseconds; mV, millivolts; Norm, normal value; NR, no response; R, right; μ V, microvolts.

the diagnosis of SLE was made based on both 1997 American College of Rheumatology criteria and 2012 Systemic Lupus International Collaborating Clinics criteria.^{3–5} Intravenous methylprednisolone and cyclophosphamide were given. Subsequently, the patient's joint pain and sensory symptoms resolved. His motor strength slowly improved.

Later, his weakness started worsening again. A ganglioside antibody panel reported elevated titers of GM1 immunoglobulin (Ig) G and GD1b IgG-IgM antibodies with negative GM1 IgM, GD1a IgG-IgM, and GQ1b GD1a IgG-IgM antibodies. After receiving five cycles of plasma exchange, the patient's neurological deficits began to stabilize and slowly improve. He was discharged to an inpatient rehabilitation facility with low-dose prednisolone. He was still bedridden at discharge. At 3 months, the patient was

able to sit in a wheelchair and perform basic daily activities of living with some assistance.

DISCUSSION

SLE is an immune-mediated disease in which the pathogenesis hinges on loss of tolerance and sustained autoantibody production. In contrast to GBS, which is generally a self-limited monophasic condition, SLE is lifelong. On rare occasions, GBS can be a manifestation of SLE. A meta-analysis of multiple cohort studies disclosed a prevalence of polyneuropathy and mononeuropathy (single or multiplex) of 1.5% and 0.9%, whereas that of GBS is <0.1% of patients with SLE.⁶ Acute motor axonal neuropathy and AMSAN are the axonal variants of GBS. The association of the axonal variants of GBS and SLE has been rarely reported.

Table 2. Reported cases of axonal variants of Guillain-Barré syndrome with systemic lupus erythematosus

Reference	Age/gender	Onset of neuropathy (after diagnosis of SLE)	GBS subtype	Ganglioside antibodies	Treatment	Outcome
Ubogu et al ¹⁷	27/F	3 weeks	AMSAN	Negative GM1, asialo-GM1, GD1b, and GQ1b	CS, CP, IVIG	Able to ambulate with minimal assistance, functionally independent at 4 months
Santos et al ¹⁶	28/F	Not mentioned ^a	AMSAN, Bickerstaff encephalitis	Negative GQ1b, GM1, and GM2	PE, IVIG	Death
Yildiz et al ¹⁸	47/F	Initial manifestation	AMAN	Not mentioned	CS, HCQ, CP	Walk with assistance after 3 months
Rajadhyaksha and Mehra ¹⁴	30/F	Initial manifestation	AMAN, PCB variant	Positive GT1a, GQ1b, and GM1b	IVIG, CS, HCQ	Nearly complete recovery in 2 weeks
Santiago-Casas et al ¹⁵	20/F	Initial manifestation	AMAN	Negative	PE, IVIG, CP, CS	Complete recovery in 4 months
Santiago-Casas et al ¹⁵	34/F	1 month prior	AMSAN	Negative	CS, IVIG, CP	Complete recovery in 6 months
Coomes et al ¹³	45/M	2 years prior	AMSAN	Not mentioned	IVIG, PE, CS, MMF	Slow recovery, able to be extubated after several months
Presented case	72/M	Initial manifestation	AMSAN	Positive GM1 IgG and GD1b IgG-IgM	IVIG, CS, CP, PE	Slow improvement, wheelchair bound at 3 months

AMAN indicates acute motor axonal neuropathy; AMSAN, acute motor-sensory axonal neuropathy; CP, cyclophosphamide; CS, corticosteroids; F, female; GBS, Guillain-Barré syndrome; HCQ, hydroxychloroquine; IVIG, intravenous immunoglobulin; M, male; MMF, mycophenolate mofetil; PCB variant, pharyngeal-cervical-brachial variant; PE, plasma exchange; SLE, systemic lupus erythematosus.

^aThe patient was known to have SLE of unknown duration.

Moreover, there is no available standard guideline for treatment of this condition.

Meta-analyses of multiple clinical trials demonstrated the significant benefits of intravenous immunoglobulin and plasma exchange in the treatment of GBS.^{7,8} In contrast, a GBS steroid trial in 1993 and a study in the Netherlands showed that high-dose intravenous methylprednisolone was not beneficial in GBS.^{9,10} Though GBS is mainly caused by the generation of antibodies that cross-react with self-ganglioside, the immunopathogenesis of SLE involves many more mechanisms of both the innate and adaptive immune systems.^{11,12} Therefore, glucocorticoids and other immunosuppressants may be beneficial in this setting.

Additionally, we systematically searched for previous case reports of GBS in the context of SLE. Most cases had demyelinating variant. The seven cases of axonal variant from previous reports^{13–18} and our case are summarized in *Table 2*. Most of the cases of GBS occurred in the early course of SLE and were treated with a variety of immunotherapy regimens. The prognosis was good in most cases with treatment.

In conclusion, AMSAN can be a rare first manifestation of SLE. Furthermore, regimens other than intravenous immunoglobulin and plasma exchange should be considered in patients with GBS or its variant who also have supportive finding of SLE.

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- Sejvar JJ, Kohl KS, Gidudu J. Guillain-Barre syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. *Vaccine*. 2011;29:599–612. doi:10.1016/j.vaccine.2010.06.003.
- Uncini A, Kuwabara S. Electrodiagnostic criteria for Guillain-Barré syndrome: a critical revision and the need for an update. *Clin Neurophysiol*. 2012;123:1487–1495. doi:10.1016/j.clinph.2012.01.025.
- Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum*. 1997;40:1725. doi:10.1002/art.1780400928.
- Petri M, Orbai AM, Alarcon GS, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification

- criteria for systemic lupus erythematosus. *Arthritis Rheum.* 2012;64:2677–2686. doi:[10.1002/art.34473](https://doi.org/10.1002/art.34473).
5. Tan EM, Cohen AS, Fries JF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum.* 1982;25:1271–1277. doi:[10.1002/art.1780251101](https://doi.org/10.1002/art.1780251101).
 6. Unterman A, Nolte JE, Boaz M, Abady M, Shoenfeld Y, Zandman-Goddard G. Neuropsychiatric syndromes in systemic lupus erythematosus: a meta-analysis. *Semin Arthritis Rheum.* 2011;41:1–11. doi:[10.1016/j.semarthrit.2010.08.001](https://doi.org/10.1016/j.semarthrit.2010.08.001).
 7. Chevet S, Hughes RA, Annane D. Plasma exchange for Guillain-Barre syndrome. *Cochrane Database Syst Rev.* 2017;(2):CD001798.
 8. Hughes RA, Swan AV, van Doorn PA. Intravenous immunoglobulin for Guillain-Barre syndrome. *Cochrane Database Syst Rev.* 2012;(7):CD002063.
 9. Guillain-Barre Syndrome Steroid Trial Group. Double-blind trial of intravenous methylprednisolone in Guillain-Barre syndrome. *Lancet.* 1993;341:586–590.
 10. van Koningsveld R, Schmitz PIM, Meché FGA, Visser LH, Meulstee J, van Doorn PA. Effect of methylprednisolone when added to standard treatment with intravenous immunoglobulin for Guillain-Barre syndrome: randomised trial. *Lancet.* 2004;363:192–196. doi:[10.1016/s0140-6736\(03\)15324-x](https://doi.org/10.1016/s0140-6736(03)15324-x).
 11. Tsokos GC, Lo MS, Costa Reis P, Sullivan KE. New insights into the immunopathogenesis of systemic lupus erythematosus. *Nat Rev Rheumatol.* 2016;12:716–730. doi:[10.1038/nrrheum.2016.186](https://doi.org/10.1038/nrrheum.2016.186).
 12. van den Berg B, Walgaard C, Drenthen J, Fokke C, Jacobs BC, van Doorn PA. Guillain-Barre syndrome: pathogenesis, diagnosis, treatment and prognosis. *Nat Rev Neurol.* 2014;10:469–482. doi:[10.1038/nrneurol.2014.121](https://doi.org/10.1038/nrneurol.2014.121).
 13. Coomes EA, Haghbayan H, Spring J, Mehta S. Fulminant Guillain-Barre syndrome in a patient with systemic lupus erythematosus. *BMJ Case Rep.* 2019;12:bcr-2018-226634. doi:[10.1136/bcr-2018-226634](https://doi.org/10.1136/bcr-2018-226634).
 14. Rajadhyaksha A, Mehra S. Pharyngeal-cervical-brachial variant of Guillain-Barre syndrome with predominant bulbar palsy as the initial presentation of systemic lupus erythematosus and lupus nephritis: a case report. *Int J Rheum Dis.* 2012;15:e162–164. doi:[10.1111/j.1756-185X.2012.01761.x](https://doi.org/10.1111/j.1756-185X.2012.01761.x).
 15. Santiago-Casas Y, Peredo RA, Vila LM. Efficacy of low-dose intravenous cyclophosphamide in systemic lupus erythematosus presenting with Guillain-Barre syndrome-like acute axonal neuropathies: report of two cases. *Lupus.* 2013;22:324–327. doi:[10.1177/0961203313476358](https://doi.org/10.1177/0961203313476358).
 16. Santos DPA, Spitz M, Oliveira P, et al. Overlap of Bickerstaff encephalitis and Guillain-Barre syndrome in a patient with systemic lupus. *Arq Neuropsiquiatr.* 2009;67:904–905. doi:[10.1590/S0004-282X2009000500025](https://doi.org/10.1590/S0004-282X2009000500025).
 17. Ubogu EE, Zaidat OO, Suarez JI. Acute motor-sensory axonal neuropathy associated with active systemic lupus erythematosus and anticardiolipin antibodies. *J Clin Rheumatol.* 2001;7:326–331. doi:[10.1097/00124743-200110000-00014](https://doi.org/10.1097/00124743-200110000-00014).
 18. Yildiz OK, Balaban H, Senel S, Cevik S. Acute lumbosacral polyradiculoneuropathy heralding transformation to systemic lupus erythematosus in a patient with discoid lupus. *Lupus.* 2011;20:972–974. doi:[10.1177/0961203310392427](https://doi.org/10.1177/0961203310392427).