# *Clinical Case Report*

## Guillain–Barré syndrome in a patient with neuropsychiatric systemic lupus erythematosus

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**ABSTRACT**

**Guillain–Barré syndrome is a rare manifestation of neuropsychiatric systemic lupus erythematosus (SLE). Clinical and electrophysiological features of Guillain–Barré syndrome in patients with SLE are different from those in patients without SLE. There is considerable variation in the management and prognosis. We present a patient with Guillain–Barré syndrome and SLE and review the recent knowledge on the various manifestations of neuropsychiatric SLE.**

Natl Med J India 2016;29:14–17

### INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease affecting multiple organ systems. Hebra and Kaposi in 1875 first noted the involvement of the central nervous system in SLE.[1] Neuropsychiatric features are seen in about 56.3% of patients with SLE.[2] Stroke, headache and seizures are the chief presentations.[3] Other manifestations such as Guillain–Barré syndrome (GBS) are rare. We describe a patient with SLE and GBS and review the clinical features, pathogenesis and treatment of neuropsychiatric manifestations of SLE.

### THE CASE

A 20-year-old woman presented to our hospital with a history of fever for 4 months and weakness in all four limbs for one week. The fever was low grade, continuous and not associated with chills or rigors. There was no history of localizing features such as headache, nausea, vomiting, cough, diarrhoea, jaundice, abdominal pain or dysuria. She did not have joint pain, skin rashes, photosensitivity, oral ulcers or excessive hair loss.

One week before presentation she started having difficulty in walking upstairs and standing up from the sitting position. The weakness progressed to involve both upper limbs. At the same time, she noticed that she could not close her eyes fully. At the end of one week, she was unable to walk without support and had difficulty in dressing, mixing her food and performing other daily activities. 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 episodes of weakness earlier. The patient did not have any addictions and gave no history of high-risk sexual behaviour. Her menstrual history was non-contributory. She was married and had two children. There was no history of abortions or stillbirths.

Examination revealed a moderately nourished patient of medium build who was alert, conscious and cooperative. There was an erythematous rash on the cheeks and the nose bridge. There was no icterus, cyanosis, pallor, clubbing, lymphadenopathy or pedal oedema. Her pulse rate was 82 per minute, she was afebrile, blood pressure in the right upper limb in the supine position was 120/80 mmHg and the respiratory rate was 28 per minute, regular. The single breath count was 12.

Examination of the nervous system revealed normal higher mental functions. She was dysarthric and had bilateral lower motor neuron type of facial palsy. Other cranial nerves were normal. Assessment of the motor system showed normal bulk with generalized hypotonia. Muscle power was reduced symmetrically: 3/5 at the shoulders, 4/5 at the elbows and wrists, 4/5 at the hips and 5/5 at the knees. All deep tendon reflexes were absent. Plantar reflexes were bilaterally mute and superficial abdominal reflexes were absent. No objective sensory loss was detected. There were no signs of cerebellar involvement or of meningeal irritation and the skull and spine were normal.

The cardiovascular system was normal and examination of the respiratory system revealed bilateral infrascapular crackles. The abdomen was soft to palpation and there was no organomegaly.

Her random blood sugar was 100 mg/dl, serum bilirubin 0.4 mg/dl, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were 35 and 26 IU/L, respectively, blood urea 27 mg/dl, serum creatinine 1.0 mg/dl, serum sodium 140 mEq/L, serum potassium 3.2 mEq/L, haemoglobin 10 g/dl, and platelet count 110 000/cmm. Urinalysis was normal. Antibodies against HIV, and hepatitis B and C were not present. An ultrasound of the abdomen was normal.

In this young woman, given the history of prolonged fever and photosensitivity along with the finding of a malar rash on examination and polyserositis on investigation, we considered a diagnosis of SLE. An antinuclear antibody (ANA) test by the ELISA technique was positive at 36.41 IU/ml (>25 IU/ml is considered positive). Tests for anti-cardiolipin antibodies were negative.

The recent onset of ascending weakness with flaccid paralysis and areflexia without bowel or bladder involvement were suggestive of GBS. The diagnosis was confirmed by a nerve conduction study, which showed motor sensory axonal polyneuropathy with secondary demyelination.

A final diagnosis of SLE with GBS was made. The patient was initially treated with intravenous pulses of methyl prednisolone 1 g daily for 5 days. She also received four cycles of plasmapheresis. She was then switched to oral prednisolone 40 mg daily, which was tapered to 5 mg daily over the next one month. Her fever resolved after starting steroids and the muscle strength started improving after the second cycle of plasmapheresis, and by the

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last cycle she had recovered completely. She continues on outpatient follow-up on low-dose prednisolone.

## DISCUSSION

GBS occurs in 0.1% of patients with SLE.[2,4] Classical GBS presents as acute inflammatory demyelinating polyneuropathy but in SLE the majority of patients present with atypical features.[5] In our patient, there was both axonal damage and demyelination of motor and sensory nerves. Acute motor axonal neuropathy (AMAN) and acute motor sensory axonal neuropathy (AMSAN) have been reported earlier in patients with SLE where treatment with glucocorticoids and low-dose pulse cyclophosphamide has been beneficial.[5] Unlike a patient with classical GBS, our patient responded well to steroid therapy.

Apart from GBS, 18 other neuropsychiatric manifestations[6] have been reported in patients with SLE (Table I).[2,7–14] The most common of these is headache.

### *Headache*

The prevalence of headache in patients with SLE is similar to that in the general population with migraine and tension headache being the major diagnoses. It is the most common manifestation of neuropsychiatric SLE.[2] Most headaches in SLE are not related to disease activity. They resolve over time, independent of the treatment of SLE. Lupus headache is a rare entity defined as severe persistent headache non-responsive to narcotic analgesics. It is associated with considerably lower quality of life measures.[15]

### *Mood disorders*

These are seen in 20% of patients with SLE.[2] Depression and anxiety are common features. Characteristically, depression occurs concomitantly with psychosis in neuropsychiatric SLE.

### *Acute confusional state*

In neuropsychiatric SLE, acute confusional state is associated with breakdown of the blood–brain barrier and cerebrospinal fluid (CSF) anti-N-methyl D-aspartate (NMDA) receptor 2 antibodies and anti-Smith (Sm) antibodies.[9]

### *Psychosis*

SLE may present with psychosis. Delusions are the main feature of psychosis and it is also associated with florid skin manifestations.[11] Pathological examination shows grey matter abnormalities. Olanzapine and quetiapine are used in the management of SLE psychosis as they have minimal extra-pyramidal side-effects. However, the diagnosis is confounded by steroid psychosis, which may present with mania and depression.

### *Cognitive dysfunction*

Cognitive deficits in SLE may be due to immune/inflammatory mechanisms in the brain,[16] and improvement with prednisone and hydroxychloroquine has been seen.

### *Cerebrovascular disease*

Seventeen per cent of neuropsychiatric SLE syndromes are cerebrovascular in nature; they may present as ischaemic or haemorrhagic strokes without obvious risk factors.[13] Endothelial dysfunction due to the disease process itself may be the cause of these presentations.[17]

### *Polyneuropathy*

Polyneuropathies are characterized by sensory symptoms such as tingling and numbness, loss of pain and diminished deep tendon reflexes. It is hypothesized that patients with SLE are more susceptible to age-related neurodegeneration, which causes these clinical features.[14]

### *Seizures*

These are more common in patients with SLE than in age-matched adults. They occur early in the disease and are mostly generalized tonic–clonic seizures.[13] They often occur along with psychosis or a neurological deficit.[18] Characteristically, these seizures resolve without anti-epileptic drugs. Sometimes antimalarials may be used.[19]

### *Mononeuropathy*

Mononeuropathy multiplex is the most common presentation of peripheral neuropathy in SLE. It is due to vasculitis of the vasa nervosum of the peripheral nerves. Although various agents such as glucocorticoids, cyclophosphamide, gabapentin, carbamazepine and azathioprine have been used for treatment, steroids appear to be the most beneficial.[20]

### *Autonomic disorder*

Autonomic manifestations of neuropsychiatric SLE present as impaired cardiovascular and respiratory reflexes. These manifestations do not correlate with disease duration or severity or peripheral neuropathy.[21] Complement fixing auto-antibodies directed against autonomic nervous system structures such as nerve growth factor,[7] perivascular lymphocytic infiltrate in sympathetic ganglia, vasculitis of vasa vasorum and secondary amyloidosis appear to cause autonomic dysfunction in SLE.

### *Myelopathy*

Lupus myelopathy is a rare disease seen in young patients with

TABLE I. Neuropsychiatric manifestations of systemic lupus erythematosus

| Common disorders | Reported prevalence (%) | Variable and rare disorders | Reported prevalence (%) |
|---|---|---|---|
| Headache | 28[2] | Autonomic dysfunction | 0.1–90[2,7] |
| Mood disorder | 27[2] | Myelopathy | 1–2[8] |
| Acute confusional state | 26[9] | Cranial neuropathy | 0.1–1[10] |
| Psychosis | 25–55[11] | Guillain–Barré syndrome | 0.1 |
| Cognitive dysfunction | 20–50[2,12] | Plexopathy | Rare |
| Cerebrovascular disease | 17[13] | Aseptic meningitis | Rare |
| Polyneuropathy | 15[14] | Demyelinating syndrome | Rare |
| Seizure disorder | 10[2] | Movement disorders | Rare |
| Mononeuropathy | Common | Myasthenia gravis | Rare |

SLE.[8] It presents with bilateral leg weakness, sensory loss, and bowel and bladder dysfunction. Analysis of the CSF is unremarkable. Peripheral white matter degeneration of the cord termed 'subpial leukomyelopathy' has been seen in these patients. These are small lesions at multiple cord levels producing a summating and often perplexing clinical effect. Infarcts and haematomas of the cord are also seen in SLE.[22] Pulse intravenous methyl prednisolone followed by cyclophosphamide may be useful in lupus myelopathy if started early. Patients with abnormal MRI signals in the spinal cord have poorer outcomes.[23]

*Cranial neuropathies*

The eighth cranial nerve is involved most commonly in SLE. The third, fourth and sixth cranial nerves are also involved in that order. Vasculitis, antibody-mediated demyelination, local inflammatory cytokine-related damage and neural ischaemia due to migroangiopathic thrombi have been proposed as potential pathogenetic mechanisms. Methyl prednisolone, cyclophosphamide and rituximab have been found useful in SLE-related cranial neuropathies.[10]

*Plexopathy*

SLE-related plexopathy may be the initial manifestation of a neuropathy. The disorder generally responds well to steroid therapy.[24]

*Aseptic meningitis*

Rarely, recurrent aseptic meningitis is seen with non-steroidal anti-inflammatory drug use in SLE.[25,26] It is characterized by high protein levels in the CSF and increased serum acute phase reactants. Chronic aseptic meningitis, characterized by chronic inflammation of the ventricular ependyma is a rare feature of neuropsychiatric SLE.[27]

*Demyelinating syndrome*

Atypical demyelinating syndromes such as tumefactive demyelination and neuromyelitis optica have been reported with SLE.[28] Elevated anti-ribosomal P protein and anticardiolipin antibodies in these patients damage neural tissue leading to these rare phenotypes.[29]

*Movement disorders*

These are rare features of neuropsychiatric SLE. Chorea has been reported in 4% of cases. Hemiballismus, parkinsonism, dystonia and myoclonus have also been reported.[13,30] Immune mediation via anti-neuronal membrane antibodies,[3] vasculopathy and coagulopathy have all been implicated in these diseases.[13] Prednisolone and hydroxychloroquine have been found to be useful in the management of SLE-related movement disorders.

*Myasthenia gravis*

It is a rare neurological disease seen in patients with SLE.[31] Deficiency and dysfunction of CD4+ CD25+ lymphocytes predispose to myasthenia and SLE. Myasthenia may develop before or after SLE has been diagnosed.[32] Patients may have symptoms of myasthenia without overt manifestations of SLE, but serology for SLE may be positive.[31] These patients may not respond to steroids and may require intravenous immunoglobulins or plasmapheresis.

Fatigue, memory impairment and personality changes have also been reported in SLE.[13]

*Conclusion*

Neuropsychiatric disease may manifest in an atypical manner in patients with SLE. Immunosuppressive drugs used in SLE predispose to infections with atypical presentations and some drugs themselves cause neuropsychiatric manifestations. Our patient, who had GBS and SLE, had an atypical presentation. Patients with neuropsychiatric symptoms should be screened for SLE as their treatment differs from that in patients without SLE.

## ACKNOWLEDGEMENTS

We thank the Department of Radiology, Guntur Medical College, Guntur for their support in the analysing the radiological images.

## REFERENCES

1 Hebra F, Kaposi M. *On diseases of the skin, including the exanthema.* London:New Sydenham Society; 1875:1–247.
2 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.
3 Ozcan ME, Altýnöz MA, Karadeli HH, Asil T, Koçer A. A 17-year-old female with systemic lupus presents with complex movement disorder: Possible relationship with antiribosomal p antibodies. *Case Rep Neurol Med* 2013;**2013:**590729.
4 Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF, *et al.* The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982;**25:**1271–7.
5 Santiago-Casas Y, Peredo RA, Vilá 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:** 324–7.
6 The American College of Rheumatology nomenclature and case definitions for neuropsychiatric lupus syndromes. *Arthritis Rheum* 1999;**42:**599–608.
7 Maule S, Quadri R, Mirante D, Pellerito RA, Marucco E, Marinone C, *et al.* Autonomic nervous dysfunction in systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA): Possible pathogenic role of autoantibodies to autonomic nervous structures. *Clin Exp Immunol* 1997;**110:**423–7.
8 Dai YJ, Liu Q, He J, Li ZG. [Myelopathy associated with systemic lupus erythematosus: A clinical analysis of 10 cases and review of literature.] *Zhonghua Nei Ke Za Zhi* 2013;**52:**213–17.
9 Hirohata S, Sakuma Y, Yanagida T, Yoshio T. Association of cerebrospinal fluid anti-Sm antibodies with acute confusional state in systemic lupus erythematosus. *Arthritis Res Ther* 2014;**16:**450.
10 Aslam F, Bannout F, Russell EB. Cranial nerve palsies: Sarcoidosis to systemic lupus erythematosus. *Case Rep Rheumatol* 2013;**2013:**175261.
11 Pego-Reigosa JM, Isenberg DA. Psychosis due to systemic lupus erythematosus: Characteristics and long-term outcome of this rare manifestation of the disease. *Rheumatology (Oxford)* 2008;**47:**1498–502.
12 Nayak RB, Bhogale GS, Patil NM, Chate SS. Psychosis in patients with systemic lupus erythematosus. *Indian J Psychol Med* 2012;**34:**90–3.
13 Joseph FG, Lammie GA, Scolding NJ. CNS lupus: A study of 41 patients. *Neurology* 2007;**69:**644–54.
14 Jasmin R, Sockalingam S, Ramanaidu LP, Goh KJ. Clinical and electrophysiological characteristics of symmetric polyneuropathy in a cohort of systemic lupus erythematosus patients. *Lupus* 2015;**24:**248–55.
15 Hanly JG, Urowitz MB, O'Keeffe AG, Gordon C, Bae SC, Sanchez-Guerrero J, *et al.* Headache in systemic lupus erythematosus: Results from a prospective, international inception cohort study. *Arthritis Rheum* 2013;**65:**2887–97.
16 Denburg SD, Carbotte RM, Denburg JA. Cognition and mood in systemic lupus erythematosus: Evaluation and pathogenesis. *Ann N Y Acad Sci* 1997;**823:**44–59.
17 Moraes-Fontes MF, Lúcio I, Santos C, Campos MM, Riso N, Vaz Riscado M. Neuropsychiatric features of a cohort of patients with systemic lupus erythematosus. *ISRN Rheumatol* 2012;**2012:**989218.
18 Ramsey-Goldman R, Alarcón GS, McGwin G, Petri M, Vilá LM, Edberg JC, *et al.* Profile Study Group. Time to seizure occurrence and damage in PROFILE, a multi-ethnic systemic lupus erythematosus cohort. *Lupus* 2008;**17:**177–84.
19 Hanly JG, Urowitz MB, Su L, Gordon C, Bae SC, Sanchez-Guerrero J, *et al.* Seizure disorders in systemic lupus erythematosus results from an international, prospective, inception cohort study. *Ann Rheum Dis* 2012;**71:**1502–9.
20 Bhowmik A, Banerjee P. Mononeuritis multiplex complicating systemic lupus erythematosus. *Indian Pediatr* 2012;**49:**581–2.
21 Shalimar, Handa R, Deepak KK, Bhatia M, Aggarwal P, Pandey RM. Autonomic dysfunction in systemic lupus erythematosus. *Rheumatol Int* 2006;**26:**837–40.
22 Provenzale J, Bouldin TW. Lupus-related myelopathy: Report of three cases and review of the literature. *J Neurol Neurosurg Psychiatry* 1992;**55:**830–5.
23 Kovacs B, Lafferty TL, Brent LH, DeHoratius RJ. Transverse myelopathy in systemic lupus erythematosus: An analysis of 14 cases and review of the literature. *Ann Rheum Dis* 2000;**59:**120–4.

24 Bloch SL, Jarrett MP, Swerdlow M, Grayzel AI. Brachial plexus neuropathy as the initial presentation of systemic lupus erythematosus. *Neurology* 1979;**29:**1633–4.
25 Samuelson CO Jr, Williams HJ. Ibuprofen-associated aseptic meningitis in systemic lupus erythematosus. *West J Med* 1979;**131:**57–9.
26 Faurie P, Pérard L, Hot A, Desmurs-Clavel H, Fassier T, Boibieux A, *et al.* [Recurrent aseptic meningitis secondary to nonsteroidal anti-inflammatory drugs in a patient with lupus]. *Rev Med Interne* 2010;**31:**e1–e3.
27 Lancman ME, Mesropian H, Granillo RJ. Chronic aseptic meningitis in a patient with systemic lupus erythematosus. *Can J Neurol Sci* 1989;**16:**354–6.
28 Hardy TA, Chataway J. Tumefactive demyelination: An approach to diagnosis and management. *J Neurol Neurosurg Psychiatry* 2013;**84:**1047–53.
29 Baraczka K, Lakos G, Sipka S. Immunoserological changes in the cerebro-spinal fluid and serum in systemic lupus erythematosus patients with demyelinating syndrome and multiple sclerosis. *Acta Neurol Scand* 2002;**105:**378–83.
30 Martino D, Chew NK, Mir P, Edwards MJ, Quinn NP, Bhatia KP. Atypical movement disorders in antiphospholipid syndrome. *Mov Disord* 2006;**21:**944–9.
31 Bekircan-Kurt CE, Tuncer Kurne A, Erdem-Ozdamar S, Kalyoncu U, Karabudak R, Tan E. The course of myasthenia gravis with systemic lupus erythematosus. *Eur Neurol* 2014;**72:**326–9.
32 Hrycek A. Systemic lupus erythematosus and myasthenia gravis. *Pol Arch Med Wewnêtrznej* 2009;**119:**582–5.

FORM IV

(See Rule 8)

| | |
|---|---|
| 1. Place of publication | All India Institute of Medical Sciences<br>New Delhi 110029 |
| 2. Periodicity | Bi-monthly |
| 3. Printer's name<br>(Whether citizen of India)<br>Address | Dr Peush Sahni<br>Indian citizen<br>All India Institute of Medical Sciences<br>New Delhi 110029 |
| 4. Publisher's name<br>(Whether citizen of India)<br>Address | Dr Peush Sahni<br>Indian citizen<br>All India Institute of Medical Sciences<br>New Delhi 110029 |
| 5. Editor's name<br>(Whether citizen of India)<br>Address | Dr Peush Sahni<br>Indian citizen<br>All India Institute of Medical Sciences<br>New Delhi 110029 |
| 6. Names and addresses of individuals who own the newspaper and partners or shareholders holding more than one per cent of the total capital | All India Institute of Medical Sciences<br>New Delhi 110029 |

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15 February 2016

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Signature of publisher