

CLINICAL VIGNETTE

Seizure improvement following intravenous immunoglobulin in drug-resistant mesial temporal lobe epilepsy associated with systemic lupus erythematosus

Kristijonas Puteikis^{1,2}  | Basma Marzouk^{1,3,4}  | Fabrice Bartolomei^{1,5}  | Stanislas Lagarde^{1,5} 

¹APHM, Timone Hospital, Epileptology and Cerebral Rhythmology, Marseille, France

²Faculty of Medicine, Vilnius University, Vilnius, Lithuania

³Department of Clinical Neurophysiology, Hôpital des Spécialités de Rabat, Ibn Sina University Hospital Center, Rabat, Morocco

⁴Faculty of Medicine and Pharmacy, Mohammed V University of Rabat, Rabat, Morocco

⁵Aix-Marseille Université, INSERM, INS, Institut de Neurosciences des Systèmes, Marseille, France

Correspondence

Stanislas Lagarde, APHM, Timone Hospital, Epileptology and Cerebral Rhythmology, Marseille, France.

Email: stanislas.lagarde@ap-hm.fr

Seizures are a recognized neurological manifestation of systemic lupus erythematosus (SLE), sometimes associated with psychosis.¹ Epilepsy affects 11.5% of patients with SLE, half without structural lesions.² Mesial temporal lobe epilepsy (MTLE) accounts for approximately 40% of cases, while most others are related to cerebrovascular disease.³ Epilepsy is usually controlled with antiseizure medication (ASM) and standard SLE therapy.^{2,3} However, in drug-resistant MTLE, ongoing CNS immune activity may be difficult to assess. We report a right-handed woman with SLE and drug-resistant MTLE, who improved significantly after intravenous immunoglobulin (IVIG).

The patient was diagnosed with SLE at age 18, presenting with cutaneous, articular, and hematologic involvements, and was treated with hydroxychloroquine and corticosteroids. At age 20, she developed status epilepticus with undocumented meningitis on CSF examination. Seizures began thereafter, with MRI showing left mesiotemporal and insular hyperintensities without atrophy. Initial auras involved lightheadedness and dyspnea with preserved consciousness. Later, seizures included

nausea, palpitations, burning chest tightness, fear, visual hallucinations of monsters, hand tremor, staring, loss of consciousness, and postictal confusion. From age 28, semiology evolved toward sudden impaired awareness with oroalimentary, manual, and verbal automatisms, and postictal amnesia. Epilepsy remained drug-resistant despite multiple ASM trials (Figure 1), with 2–4 seizures/month.

At age 28, she underwent presurgical evaluation. 3T MRI showed left hippocampal T1 atrophy and FLAIR hyperintensity, temporal pole FLAIR blurring and amygdala T1 enlargement and FLAIR hyperintensity (Figure S1). FDG-PET showed left anterior temporal hypometabolism, extending to fronto-opercular region (Figure S2). Interictal EEG revealed left basal temporal spikes, with occasional mid-temporal projection (Figure S3A). A seizure recorded after ASM withdrawal began with oroalimentary automatisms, followed by aphasia, manual automatisms, right head-eye version, and bilateral tonic-clonic generalization. Ictal EEG showed left basal temporal theta discharge, spreading to the frontopolar region (Figure S3B). Neuropsychological evaluation found severe

Kristijonas Puteikis and Basma Marzouk contributed equally to this work.

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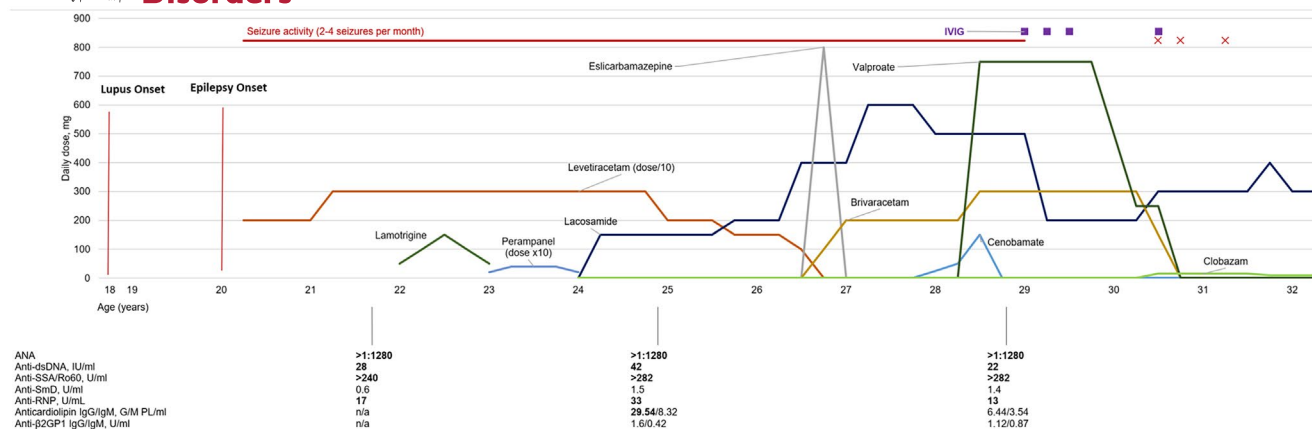


FIGURE 1 Longitudinal treatment and seizure timeline. Daily ASM doses are shown over time; the levetiracetam dose is displayed as a tenth of the actual dose for scale, while the perampanel dose is displayed as 10 times the actual dose. The red line indicates seizure activity over time, red crosses indicate isolated seizures, and purple squares indicate courses of intravenous immunoglobulin (IVIG). Levetiracetam reduction was pursued because of psychiatric comorbidities. Eslicarbamazepine was introduced but discontinued early because of adverse effects. Cenobamate was stopped because of lack of efficacy. Valproate was discontinued prior to a planned pregnancy. One IVIG course consisted of 30g administered over 3 days. Autoimmune serology is shown below the timeline. Values exceeding the laboratory reference range are shown in bold. Reference values were: Anti-dsDNA <15 IU/mL; anti-SSA/Ro60, anti-SmD and anti-RNP <10 U/mL; anticardiolipin IgG <15 GPL/mL; anticardiolipin IgM <15 MPL/mL; anti-β2-glycoprotein I IgG/IgM <8 U/mL. ANA, antinuclear antibodies; anti-dsDNA, anti-double-stranded DNA antibodies; anti-SSA/Ro60, anti-Sjögren's-syndrome-related antigen A/Ro60 antibodies; anti-SmD, anti-Smith D antibodies; anti-RNP, anti-ribonucleoprotein antibodies; anti-β2GPI, anti-beta-2-glycoprotein I antibodies; GPL/MPL, IgG/IgM phospholipid units per mL; n/a, not available.

word-finding, verbal/visual episodic memory, and executive deficits, stable 2 years later, alongside depressive symptoms and mild-to-moderate anxiety.

SLE treatment consisted of prednisone 2.5 mg/day and hydroxychloroquine 400 mg/day, without systemic activity, except subtle cytopenia. CSF analysis revealed intrathecal IgG synthesis (index 0.87), elevated protein (0.63 g/L), albumin quotient (7.66), and free kappa index (67.92). No antineuronal antibodies were detected in serum and CSF (anti-GAD65, LGI1, CASPR2, NMDAR, AMPAR, GABAAR, GABABR, Sox1, Tr, Zic4, Hu, Ri, Yo, CV2, Ma1, Ma2, amphiphysine). Suspecting ongoing neuroinflammation despite systemic control, three IVIG courses were administered at age 29, followed by marked improvement with 1-year seizure remission. Another IVIG course was given after seizure recurrence associated with fatigue and work-related stress. At last follow-up, she remained seizure free for over 1-year, with significantly reduced ASM load (Figure 1).

Pathogenesis of SLE-related epilepsy is multifactorial and may involve structural, ischaemic, inflammatory and treatment-related mechanisms.^{1,4} Ischemic injury is mainly related to antiphospholipid antibodies,⁵ whereas inflammation may involve blood-brain barrier disruption, anti-dsDNA/NMDA receptor cross-reactivity, cytokines, complement activation.^{1,6} Case reports described neuropsychiatric SLE with anti-LGI1,⁷ AMPA-R⁸ or NMDA-R⁹ autoimmune encephalitis, supporting systematic antineuronal antibody testing. Hippocampal

neuropil reactivity in SLE-related epilepsy supports also CNS-directed autoimmunity.¹⁰ Immunotherapy for drug-resistant SLE-associated epilepsy remains controversial and is not generally recommended without systemic activity.⁵ Cyclophosphamide was historically used for severe presentations,¹¹ while rituximab and obinutuzumab have also shown efficacy.^{4,12} Epilepsy-specific data are scarce, one study reported seizure-freedom in 3/5 patients after cyclophosphamide.¹³

In our patient, the initial status epilepticus and MRI hyperintensity were compatible with limbic encephalitis. Later semiological changes and mesiotemporal MRI hyperintensity may have reflected a shift from chronic to acute neuroinflammation. Negative antibody testing did not exclude an immune-mediated process, although the first criterion for probable antibody-negative autoimmune encephalitis¹⁴ was undocumented. Persistent intrathecal IgG synthesis and prolonged seizure remission after IVIG support immune-mediated seizure maintenance.

This vignette suggests that intensified immunotherapy may benefit selected patients with SLE-associated drug-resistant epilepsy. Seizures in SLE should prompt evaluation for acute symptomatic causes, including treatment-related complications (opportunistic infections, posterior reversible encephalopathy syndrome) and structural lesions, particularly cerebrovascular injury. If no cause is identified, persistent neuroinflammation should be assessed using systemic SLE activity, CSF markers, and neuroimaging. When evidence supports inflammatory

pathophysiology, immunotherapy escalation may be meaningful. Future studies should report neurological and seizure outcomes after immunomodulatory treatment in neuropsychiatric SLE.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to disclose.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

PREVIOUS PRESENTATIONS

This work has not previously been presented at a meeting.

ORCID

Kristijonas Puteikis  <https://orcid.org/0000-0001-8527-3902>

Basma Marzouk  <https://orcid.org/0000-0002-7886-1631>

Fabrice Bartolomei  <https://orcid.org/0000-0002-1678-0297>

Stanislas Lagarde  <https://orcid.org/0000-0003-2916-1302>

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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Test yourself

1. Which features most strongly support an immune-mediated contribution in a patient with drug-resistant focal epilepsy associated with SLE?
 - A. Hippocampal sclerosis on MRI
 - B. Focal hypometabolism on FDG-PET
 - C. Intrathecal IgG synthesis
 - D. Neuronal autoantibodies
 - E. Uncontrolled systemic activity of the disease
2. Which statement best describes chronic epilepsy in systemic lupus erythematosus?
 - A. It is less frequent in patients with associated antiphospholipid syndrome
 - B. It is always associated with active systemic lupus manifestations
 - C. It may occur without an identifiable structural lesion
 - D. It excludes neuropsychiatric systemic lupus erythematosus
 - E. It is typically diagnosed only during acute encephalopathy
3. In a patient with SLE receiving immunotherapy who presents with new-onset seizures, which causes should be investigated?
 - A. Opportunistic CNS infection
 - B. Posterior reversible encephalopathy syndrome (PRES)
 - C. Vascular lesion
 - D. Metabolic imbalance
 - E. Neuronal autoantibodies

Answers may be found in the [Supporting Information](#).