Section: General Medicine

Original Research Article

SEVERE NPSLE WITH SEPTIC SHOCK IN KNOWN MCTD WITH LUPUS NEPHRITIS: A FATAL OUTCOME

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ABSTRACT

Background: Neuropsychiatric systemic lupus erythematosus (NPSLE) is a serious, potentially fatal manifestation of SLE and mixed connective tissue disease (MCTD). Coexistent lupus nephritis and multidrug-resistant (MDR) infections further worsen outcomes.

Case: We report a 27-year-old woman with known MCTD and biopsy-proven lupus nephritis on immunosuppression, who presented with fever, severe polyarthritis, right upper-limb cellulitis, recurrent generalized tonic–clonic seizures, and altered sensorium. She progressed to status epilepticus requiring mechanical ventilation and continuous benzodiazepine infusion. Investigations showed active lupus (high dsDNA, low complement), lymphocytic CSF with MRI features of cerebellitis, severe hypoalbuminaemia, progressive pancytopenia and rising urea. Endotracheal aspirate culture isolated MDR Acinetobacter sensitive only to tobramycin. Despite broad spectrum antibiotics, antifungals, pulse steroids, mycophenolate, rituximab and organ-supportive care, she developed refractory septic shock and succumbed.

Conclusion: This case highlights the complex interplay of severe NPSLE, lupus nephritis flare, profound immunosuppression and MDR gram-negative sepsis leading to rapid multiorgan failure. Early recognition, aggressive infection control and close multidisciplinary coordination are imperative to improve outcomes.

Keywords: Neuropsychiatric lupus; Lupus nephritis; Mixed connective tissue disease; Status epilepticus; MDR Acinetobacter; Sepsis.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease characterized by autoantibody production and immune-complex mediated tissue injury. Neuropsychiatric systemic lupus erythematosus (NPSLE) encompasses a broad spectrum of central and peripheral nervous system manifestations including seizures, psychosis, cerebrovascular events and cognitive dysfunction, and occurs in approximately 20–40% of patients.

Mixed connective tissue disease (MCTD) is an overlap syndrome with features of SLE, systemic sclerosis and polymyositis, frequently associated with anti-U1 RNP antibodies and potential multiorgan involvement. Renal involvement in the form of lupus nephritis is a major determinant of long-term prognosis.

Infections remain a leading cause of morbidity and mortality in SLE, particularly in patients receiving high-dose corticosteroids and other immunosuppressive agents. Modern cohorts show that infections account for a substantial proportion of in-hospital deaths among patients with SLE. Multidrug-resistant (MDR) Acinetobacter baumannii has emerged as an important ICU pathogen with high attributable mortality, especially in ventilated and critically ill patients.

We present a fatal case of severe NPSLE with lupus nephritis in a young woman, complicated by MDR Acinetobacterpneumonia and septic shock, to underline the diagnostic challenges and therapeutic

dilemmas in balancing immunosuppression and infection control.

CASE PRESENTATION

A 27-year-old woman (M.F.), resident of Meerut, with a known diagnosis of mixed connective tissue disease and Class IV lupus nephritis, presented to the emergency department with the following complaints:
Multiple joint pains for 15 days
Fever for 15 days
Swelling of the right upper limb with a gaping wound over the right shoulder for 7 days
Multiple generalized seizures for 7 days
Altered mental status for 5 days
She had severe pain involving multiple small and large joints, without obvious swelling or morning stiffness, partially relieved by over-the-counter analgesics (including naproxen). Fever was undocumented, intermittent, associated with chills and rigors, temporarily relieved with antipyretics.
Seven days prior to admission, she developed painful swelling starting over the right shoulder and gradually involving the entire right upper limb, with redness, tenderness and a gaping wound over the shoulder suggestive of cellulitis with soft-tissue infection.
During the same period, she experienced 5–6 episodes/day of generalized tonic–clonic seizures lasting around 10 minutes each, associated with tongue bite, drooling of saliva, clenching of teeth and post-ictal confusion. Over the next 5 days, her mental status progressively deteriorated and at presentation she was drowsy, responding vaguely to commands and not recognizing relatives.

Past medical history

Eighteen months earlier, she had developed polyarthritis and fever. Rheumatologic work-up revealed a strongly positive ANA (129), with anti-U1 RNP, anti-Sm, SSA, Ro52 and SSB positivity. Subsequent renal biopsy showed:
Crescentic glomerulopathy with crescents in 5/15 glomeruli (cellular, fibrocellular and fibrous), with mild mesangial hypercellularity in remaining glomeruli.
Patchy acute tubular injury.
Diffuse immune staining on direct immunofluorescence, consistent with active lupus nephritis.
She was treated with pulse methylprednisolone followed by maintenance mycophenolate mofetil (MMF) with good initial response and reduction in urinary albumin-creatinine ratio. She had been on follow-up with rheumatology/nephrology for lupus nephritis, hypertension and epilepsy since 2024, and had a prior hospitalization at a tertiary centre for sepsis and dengue fever.
There was no documented history of TB, malignancy or chronic liver disease. Drug compliance in the period preceding this admission was suboptimal as per relatives.

Examination on admission

On arrival, she was toxic, febrile and drowsy:
Pulse: 106/min, BP: 112/78 mmHg
Respiratory rate: 22/min
Temperature: 101°F
SpO_2: 97% on 3 L/min oxygen via nasal prongs
Random blood sugar: 102 mg/dL
General examination: Pallor present. No icterus, cyanosis, clubbing or peripheral edema at admission.
Cardiovascular system: S1, S2 heard; no murmurs.
Respiratory system: Bilateral air entry present; no obvious added sounds initially.
Per abdomen: Soft, non-tender, bowel sounds sluggish.
Central nervous system: Drowsy, disoriented, not obeying complex commands. Pupils mid-dilated and sluggishly reactive to light. Tone decreased, deep tendon reflexes globally depressed; plantar responses flexor bilaterally. No obvious neck stiffness noted at presentation (limited assessment due to poor cooperation).
Local examination of the right upper limb revealed diffuse swelling from shoulder to hand, erythema, tenderness and a gaping wound over the right shoulder, consistent with severe cellulitis and soft-tissue infection.
She was admitted to the ICU for further management.

Investigations

Date	Test	Key findings
26/09/2025	CBC + ESR	Hb 8.2 g/dL (↓), TLC 9.46×10³/mm³, Platelets 104×10³/µL (↓), Neutrophils 91% (↑), ESR 12 mm/hr
	RFT + Electrolytes	Urea 62.9 mg/dL (↑), Creatinine 0.7 mg/dL, Na 150 mmol/L (↑), Cl 113 mmol/L (↑), Ca 7.2 mg/dL (↓), Phosphorus 4.8 mg/dL (↑)
	LFT	Total protein 5.0 g/dL (↓), Albumin 2.0 g/dL (↓), ALP 156 U/L (↑), SGOT/SGPT normal
	Procalcitonin	25.4 ng/mL (very high)
	Viral markers	Dengue IgM/IgG, HBsAg, Anti-HCV, HIV – all negative
	Malaria tests	Rapid antigen and peripheral smear – negative
	Typhi Dot	IgM/IgG negative
27/09/2025	CSF analysis	Clear, TLC 20 cells/mm³ (90% lymphocytes), protein 49 mg/dL, sugar 74 mg/dL (slightly high vs blood)
	CSF ADA	0.8 U/L (not suggestive of TB meningitis)
	CSF Gram & AFB stain	No organisms seen
	CSF culture	No growth after 48 h
	Microalbumin/creatinine ratio	4637 mg/g creatinine (severe albuminuria)

	CRP	7.24 mg/dL (elevated)
29/09/2025	Urine R/E	3+ protein, numerous RBCs and pus cells – consistent with active nephritis/UTI
	Procalcitonin	39.7 ng/mL (further elevated)
	CSF CBNAAT (GeneXpert)	MTB not detected
30/09/2025	Blood & urine culture	No growth
03/10/2025	ETT culture & sensitivity	Growth of Acinetobacter spp.; resistant to cephalosporins, carbapenems, fluoroquinolones, aminoglycosides except tobramycin (sensitive); polymyxin B/colistin with intermediate sensitivity
05/10/2025	CBC	Hb 7.6 g/dL (↓), Platelets $130\times10^3/\mu L$ (↓), TLC $8.09\times10^3/mm^3$ with neutrophils 93% (↑)
	RFT + Electrolytes	Ca 7.0 (↓), Cl 113 (↑), phosphorus 4.7 (↑); creatinine 0.8 mg/dL
	LFT	Albumin 1.7 g/dL (↓), ALP 239 U/L (↑), total protein 4.0 g/dL (↓)
	Fungal culture (sputum)	No growth
06/10/2025	Procalcitonin	29.3 ng/mL (persistently high)
10/10/2025	CBC	Hb 6.6 g/dL (↓↓), TLC $1.35\times10^3/mm^3$ (severe leukopenia), Platelets $31\times10^3/\mu L$ (severe thrombocytopenia); peripheral smear showing leuco-erythroblastic picture, toxic granules, nRBCs, thrombocytopenia
	RFT + Electrolytes	Urea 49.6 mg/dL (↑), Creatinine ~1.1 mg/dL (borderline ↑), K 3.3 mmol/L (↓), Ca 6.6 mg/dL (↓)
	LFT	Total protein 3.3 g/dL (↓), Albumin 1.5 g/dL (↓), SGOT 76 U/L (↑), ALP 242 U/L (↑)

2. Autoimmune profile

ANA strongly positive

Anti-dsDNA: >200 IU/mL (strongly positive)

ANA profile: dsDNA strong positive, nucleosome positive, histone positive, SmD1 weakly positive, SSA strong positive, SSB positive, PCNA negative, Scl-70 negative, Jo-1 negative, U1-snRNP borderline

Complement C3: 0.46 g/L (low)

Complement C4: 0.11 g/L (near-normal)

Antiphospholipid profile (β2 glycoprotein, anticardiolipin, phospholipid antibodies): negative

These findings supported active SLE/lupus nephritis rather than antiphospholipid syndrome.

3. Imaging

Contrast-enhanced MRI brain: ill-defined patchy area of altered signal intensity in the right cerebellar hemisphere, reported as likely lupus cerebellitis, with no features of abscess or venous thrombosis.

HRCT chest: Active Infective Etiology

4. Microbiology summary

CSF: cytology lymphocytic; AFB stain, Gram stain, culture, GeneXpert – all negative.

Urine, blood and pus cultures: initially no significant growth.

Endotracheal tube (ETT) aspirate: MDR Acinetobacter spp., resistant to most classes, sensitive only to tobramycin; colistin/polymyxin B intermediate.

Hospital Course and Management

The patient was admitted to the ICU with a working differential of:

Neuropsychiatric lupus (NPSLE) with cerebellitis and status epilepticus

Severe sepsis/early septic shock

Lupus nephritis flare with heavy proteinuria

Right upper-limb cellulitis

She was managed with:

Broad-spectrum intravenous antibiotics (carbapenem-based initially, later escalated based on culture to include agents active against MDR Acinetobacter, including tobramycin and polymyxin as per local protocol)

Intravenous antifungals empirically

Intravenous antiepileptics (levetiracetam, benzodiazepines)

Pulse methylprednisolone followed by maintenance steroids

Continuation/escalation of mycophenolate mofetil

Intravenous fluids and vasopressors as shock evolved

Thromboprophylaxis as permitted by platelet counts

Given persistent disease activity and non-achievement of remission of lupus nephritis, intravenous rituximab was administered as per nephrology recommendation.

Despite therapy, she continued to have frequent generalized seizures that evolved into status epilepticus. In view of tachypnoea, falling oxygen saturation and refractory seizures, she was intubated and placed on mechanical ventilation, and started on continuous benzodiazepine infusion.

In the subsequent days, she developed:

Worsening pancytopenia with leuco-erythroblastic smear, indicating severe marrow stress/suppression.

Persistent high Procalcitonin levels and rising urea with electrolyte derangements, consistent with ongoing severe sepsis and acute kidney injury superimposed on lupus nephritis.

Worsening hypoalbuminemia and cholestatic LFT pattern, suggesting severe catabolic state and systemic inflammation.

The ETT culture grew MDR Acinetobacter; antibiotic regimen was rationalized accordingly. However, she progressed to refractory septic shock, requiring escalating vasopressor support. She eventually developed asystole. Advanced cardiac life support (ACLS) was initiated per protocol, but there was no return of spontaneous circulation, and she was declared dead.

DISCUSSION

NPSLE encompasses a wide range of neurological and psychiatric syndromes including seizures, psychosis, cerebrovascular disease, cognitive dysfunction and cerebellar involvement. Seizures are recognized as one of the more serious NPSLE

manifestations and may occur at or before SLE diagnosis.

In this patient, recurrent generalized seizures, altered mental status, and MRI evidence of cerebellitis, on a background of high dsDNA, low complement and active lupus nephritis, strongly favored NPSLE rather than purely infectious or metabolic encephalopathy. CSF analysis showed mild lymphocytic pleocytosis with normal protein and elevated glucose, and extensive microbiological workup including AFB smear, culture and CSF GeneXpert were negative, making tuberculous or bacterial meningitis unlikely.

EULAR recommendations emphasize early recognition and treatment of NPSLE, often with high-dose corticosteroids and cyclophosphamide or other immunosuppressives in severe cases. In our patient, the need for intensive immunosuppression (pulse steroids, MMF, rituximab) occurred in the setting of an already high infectious risk, creating a difficult therapeutic balance.

Infections are a leading cause of mortality in SLE worldwide, often surpassing active disease as a cause of death. Major infections frequently occur within the first years after diagnosis and are associated with high disease activity and intensive immunosuppressive regimens. In this patient, persistent very high Procalcitonin, septic profile and growth of MDR Acinetobacter from ETT aspirate supported severe nosocomial pneumonia/sepsis as a major driver of deterioration.

MDR Acinetobacter baumannii has emerged as a major ICU pathogen with high mortality. In-hospital mortality associated with MDR Acinetobacter infections ranges from 26–50% or higher, especially in ventilated patients, those with pneumonia, bacteremia or septic shock. Delays in appropriate antimicrobial therapy, carbapenem resistance and critical illness are key predictors of poor outcome. In this case, the patient already had multiorgan involvement (kidney, CNS, hematologic), profound hypoalbuminemia and severe marrow suppression, all of which are known to worsen prognosis in sepsis.

The progressive pancytopenia with leuco-erythroblastic smear likely reflected a combination of sepsis-induced marrow suppression, consumptive coagulopathy, nutritional depletion and possibly evolving macrophage activation syndrome (MAS), although ferritin and other MAS markers were not detailed. Hematologic abnormalities including cytopenias are common in SLE and have been associated with worse outcomes.

Another critical issue in the management of this patient was timing and intensity of immunosuppression. On one side, active lupus nephritis and NPSLE demanded escalation (pulse steroids, rituximab); on the other side, the development of MDR sepsis made further immunosuppression hazardous. Evidence-based guidelines for such complex scenarios are limited, and most decisions rely on expert consensus, careful risk–benefit assessment and close interdisciplinary coordination.

This case illustrates how, in a young patient with otherwise potentially treatable autoimmune disease, the combination of severe NPSLE, active nephritis, MDR gram-negative sepsis and progressive pancytopenia can culminate in a rapidly fatal course despite aggressive ICU care.

CONCLUSION

Severe NPSLE in the context of active lupus nephritis and MCTD represents a high-risk clinical situation. The coexistence of profound immunosuppression and MDR Acinetobacter sepsis in our patient led to rapid clinical deterioration, refractory shock and death. This case underscores: the need for early recognition and aggressive treatment of NPSLE, meticulous infection surveillance in immunosuppressed patients, prompt, appropriate antimicrobials for MDR organisms, and close collaboration between rheumatology, nephrology, neurology and critical care teams.

Better risk stratification tools and clear guidance on balancing immunosuppression versus infection risk are urgently needed in such complex scenarios.

Learning Points

Neuropsychiatric lupus should be suspected in SLE/MCTD patients presenting with new-onset seizures or cerebellar signs, particularly when supported by MRI and serologic activity markers.

Infections, especially with MDR gram-negative organisms, are a leading cause of death in SLE and are magnified by aggressive immunosuppression.

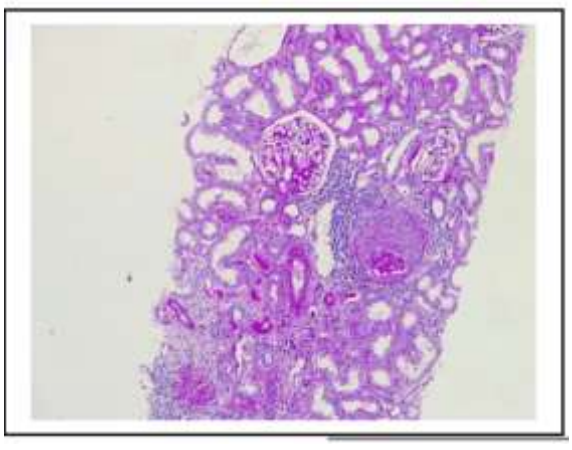
Persistent high Procalcitonin, marrow suppression and worsening organ dysfunction are poor prognostic markers in lupus patients with sepsis.

Management of severe NPSLE with concurrent MDR sepsis requires individualized multidisciplinary decision-making and frequent reassessment of the intensity of immunosuppression.

Ethical Considerations

Written informed consent could not be obtained from the relatives; however, all possible steps have been taken to anonymize the patient's identity (use of initials, removal of identifying details) in accordance with journal and institutional ethical standards.

Histopathology Image (Kidney Biopsy)



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