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Case Report

Neuropsychiatric systemic lupus erythematosus with normal CSF and EEG: a diagnostic challenge in the setting of antiphospholipid syndrome and vasculitis

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ABSTRACT

Neuropsychiatric systemic lupus erythematosus (NPSLE) is a diagnostically challenging manifestation of SLE. We report a 56-year-old woman with known SLE, antiphospholipid syndrome, vasculitis, and seizure disorder who presented with refractory seizures, hallucinations, and altered sensorium. Despite entirely normal cerebrospinal fluid (CSF) analysis and electroencephalography (EEG), MRI brain revealed an old microhemorrhage in the right thalamocapsular region with diffuse cerebral atrophy, and anti-dsDNA-NcX IgG was positive. A diagnosis of NPSLE was established on this basis. She was treated with intravenous immunoglobulin, intravenous dexamethasone, intravenous cyclophosphamide, and antiepileptic agents, achieving sustained clinical remission at three-month follow-up. This case highlights that normal CSF and EEG do not exclude NPSLE, and that serological and neuroimaging findings must be interpreted together to reach a timely diagnosis and initiate appropriate immunotherapy.

Keywords: Neuropsychiatric systemic lupus erythematosus, NPSLE, Antiphospholipid syndrome, Seizures, Anti-dsDNA antibody, MRI brain, Cerebrospinal fluid, Immunotherapy, Vasculitis

INTRODUCTION

Neuropsychiatric systemic lupus erythematosus (NPSLE) represents one of the most clinically challenging manifestations of SLE, encompassing a wide spectrum of central and peripheral nervous system involvement including seizures, psychosis, cognitive dysfunction, and cerebrovascular disease. The American College of Rheumatology (ACR) has defined 19 distinct neuropsychiatric syndromes attributable to SLE, reflecting the heterogeneity of this condition.[1] Despite its clinical significance, NPSLE remains difficult to diagnose, as no single test is pathognomonic and the diagnosis rests on a combination of clinical, serological, and neuroimaging criteria. The coexistence of antiphospholipid syndrome (APS) with SLE further complicates the neuropsychiatric picture. APS is present in approximately 30-40% of SLE patients and independently contributes to thrombotic events, seizures, and cognitive impairment, making attribution of neurological symptoms to either condition particularly difficult.[2] Vasculitis as an additional comorbidity compounds this diagnostic complexity further.

Cerebrospinal fluid analysis and electroencephalography are routinely performed in the workup of NPSLE; however, both may be entirely normal even in the presence of active neuropsychiatric disease.[3] MRI brain remains the most sensitive neuroimaging modality, with findings including white matter hyperintensities, cortical atrophy, and microhemorrhages reported across the literature. Anti-dsDNA antibodies, particularly the NcX IgG subtype, have been associated with active CNS involvement and

may serve as a serological marker supporting the diagnosis when conventional investigations are unrevealing.[4]

Early recognition and prompt initiation of combination immunotherapy-including corticosteroids, cyclophosphamide and intravenous immunoglobulin have been shown to improve outcomes in severe NPSLE.[5,6] We report a case of NPSLE in a patient with pre-existing antiphospholipid syndrome, vasculitis, and seizure disorder, in whom the diagnosis was established despite normal CSF and EEG, and who achieved sustained remission following combination immunotherapy.

CASE REPORT

A 56-year-old woman with known systemic lupus erythematosus (SLE), antiphospholipid syndrome, vasculitis, and seizure disorder presented to the neurology and internal medicine service with a history of recurrent seizures, auditory and visual hallucinations, altered sensorium, and progressive gait imbalance. She had a background of hypothyroidism, systemic hypertension, diabetes mellitus, and bronchial asthma. There was no history of known drug allergies.

On examination, her blood pressure was 130/84 mmHg and pulse rate was 90 beats per minute. She was conscious and oriented at the time of discharge but had presented in an encephalopathic state during the acute episode. Systemic examination of the cardiovascular and respiratory systems was unremarkable.

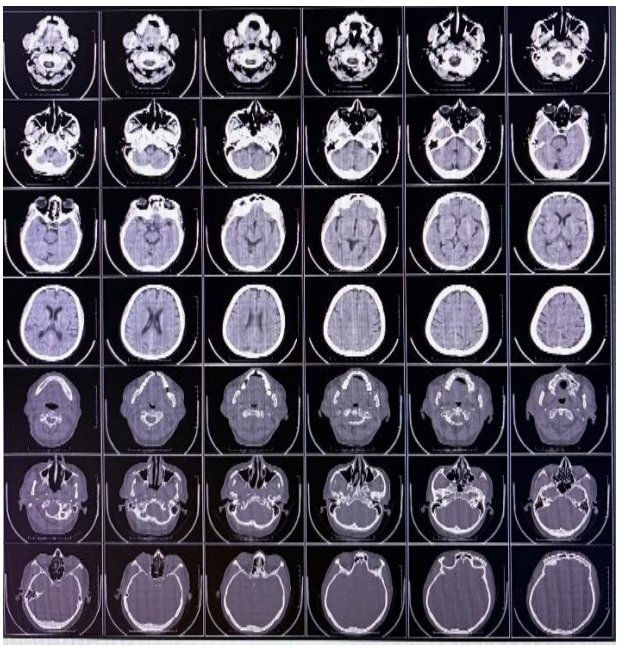

Figure 1: CT brain.

Investigations revealed a positive antinuclear antibody (ANA) and positive anti-dsDNA-NcX IgG, consistent with active SLE. Cerebrospinal fluid (CSF) analysis was entirely normal colourless, clear, with no cells seen, microprotein 5.67 mg/dl, and sugar 64 mg/dl. Electroencephalography (EEG) was also normal. CT brain (January 2025) demonstrated mild generalised cerebral atrophy. MRI brain (January 2026) showed an old microhemorrhage in the right thalamocapsular region and diffuse cerebral atrophy.[7] MRI venogram and MR angiography of brain and neck vessels were within normal limits, with no evidence of dural venous sinus thrombosis or critical stenosis. Echocardiography showed preserved left ventricular systolic function (LVEF 65%) with Grade I diastolic dysfunction and mild pulmonary hypertension.

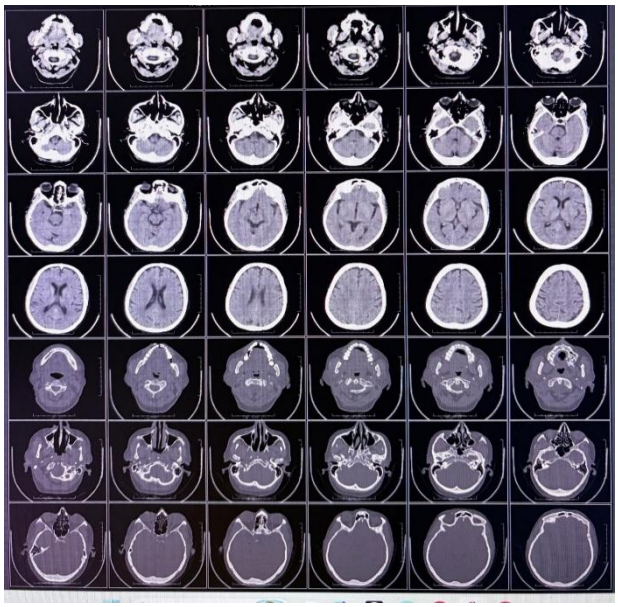

Figure 2: MRI brain

She was diagnosed with NPSLE on the basis of clinical features, positive serology, and neuroimaging findings, in the setting of pre-existing antiphospholipid syndrome and vasculitis. She was treated with intravenous immunoglobulin, intravenous dexamethasone, intravenous cyclophosphamide, and antiepileptic therapy (levetiracetam, lacosamide and clobazam).[8] She responded well to treatment and was discharged in a stable, conscious, and oriented state. At three-month follow-up, she remained in sustained clinical remission.

DISCUSSION

This case illustrates the diagnostic challenges inherent to NPSLE, particularly when conventional investigations fail to provide confirmatory evidence. Our patient presented with refractory seizures, hallucinations, and altered sensorium yet both CSF analysis and EEG were entirely normal. This finding is consistent with published data demonstrating that CSF abnormalities are present in fewer than 30% of NPSLE cases, and that a normal CSF does not exclude active neuropsychiatric disease.[1,3] Similarly, EEG lacks both sensitivity and specificity for NPSLE and should not be used as a standalone diagnostic tool.

The diagnosis in our patient was supported by positive anti-dsDNA-NcX IgG serology and MRI brain findings of an old microhemorrhage in the right thalamocapsular region with diffuse cerebral atrophy. Microhemorrhages in NPSLE are attributed to small vessel vasculopathy and antiphospholipid antibody-mediated thrombotic microangiopathy.[4,7] The coexistence of antiphospholipid syndrome made vascular contributions to the neuropsychiatric presentation particularly likely, and disentangling SLE-mediated from APS-mediated neurological injury remains one of the most difficult clinical problems in this population.[2] The overlap of multiple autoimmune conditions SLE, antiphospholipid syndrome, and vasculitis in a single patient creates a clinically complex picture in which each condition may independently contribute to seizures, cognitive change, and psychiatric symptoms.[9] Attribution of individual symptoms to a specific underlying condition is often not possible, and management must therefore target the shared immunological substrate rather than each diagnosis in isolation.

Regarding treatment, our patient received combination immunotherapy comprising intravenous immunoglobulin, intravenous dexamethasone, and intravenous cyclophosphamide, alongside antiepileptic therapy. This approach is supported by evidence from controlled trials demonstrating superiority of cyclophosphamide over methylprednisolone alone in severe neurological manifestations of SLE.[5,6] The excellent and sustained clinical response at three months reinforces the importance of early and aggressive immunotherapy in severe NPSLE.

This case also draws attention to the clinical value of anti-dsDNA antibody testing in neuropsychiatric workup when standard investigations are unrevealing. While anti-dsDNA antibodies are a marker of overall SLE disease activity, their elevation in the context of acute neuropsychiatric symptoms combined with characteristic MRI findings can provide the diagnostic confidence needed to initiate immunotherapy without delay.[10,11]

CONCLUSION

NPSLE can present with refractory seizures and psychiatric symptoms despite normal CSF and EEG. In such cases, positive anti-dsDNA-NcX IgG serology combined with MRI brain findings can secure the diagnosis and guide timely treatment. Clinicians should not exclude NPSLE on the basis of normal conventional investigations alone. Early combination immunotherapy results in excellent outcomes, as demonstrated in this case.

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