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"Seizures and Confusion: A Rare Tale of CNS Lupus"

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ABSTRACT
Background: Neuropsychiatric systemic lupus erythematosus (NPSLE) is a rare and severe manifestation of systemic lupus erythematosus (SLE), involving diverse neurological and psychiatric symptoms. Accurate diagnosis and timely intervention remain a clinical challenge due to its multifaceted presentation.
Case Report: A 46-year-old male with a history of lupus nephritis and hypertension presented to the emergency department with two episodes of generalized tonic-clonic seizures, loss of consciousness, and transient postictal confusion. Comprehensive examination revealed no focal neurological deficits or significant systemic abnormalities. Laboratory investigations showed anaemia, mild leukopenia, and renal dysfunction, while imaging revealed small ischemic changes in the brain. Serological markers, including complement levels (C3, C4) and anti-dsDNA antibody titers,supported the diagnosis of NPSLE. Collaborative input from neurology and rheumatology specialists guided the management.
Key Words: Seizures, Neuropsychiatric systemic lupus erythematosus (NPSLE), Rheumatology, Nephrology.

I. INTRODUCTION

Neuropsychiatric lupus, or neuropsychiatric systemic lupus erythematosus (NPSLE), is a significant concern in the Indian context due to its prevalence and impact on patient quality of life. NPSLE encompasses a range of neurological and psychiatric manifestations associated with systemic lupus erythematosus (SLE), a chronic autoimmune disease. In India, the prevalence and clinical outcomes of NPSLE are particularly noteworthy, with studies highlighting the common manifestations and their implications for patient mortality and quality of life.

The following sections provide a detailed overview of the literature on NPSLE in India.

Prevalence and Manifestations

In a study conducted in a tertiary care center in India, 16.6% of SLE patients exhibited NPSLE manifestations, with seizures (6.5%) and cerebrovascular accidents (3.9%) being the most common(Pinto et al., 2022).

Another study in North India reported that neuropsychiatric manifestations significantly affect the quality of life of lupus patients, with a majority being female and diagnosed at a mean age of 27.8 years(Muhammed et al., 2018).

Diagnostic and Prognostic Factors

Diagnostic approaches often include brain MRI and antibody testing, although the specific markers for psychiatric disorders remain under investigation(Rice-Canetto et al., 2024) (Zarzycki et al., 2019).

The presence of lupus anticoagulant and anticardiolipin antibodies was noted in a subset of patients, although no significant difference was found between NPSLE cases and controls(Pinto et al., 2022).

Treatment and Management

Treatment strategies for NPSLE in India involve the use of immunosuppressants and anti-inflammatory medications, with corticosteroids and other agents like cyclophosphamide and mycophenolate mofetil being utilized based on the specific pathways involved(Tan, 2022).

The prognosis of NPSLE varies, with a higher mortality rate observed in Indian patients

compared to those without neuropsychiatric involvement(Pinto et al., 2022).

While the literature provides insights into the prevalence and management of NPSLE in India, challenges remain in the accurate diagnosis and effective treatment of this condition. The variability in clinical presentations and the need for targeted therapeutic approaches underscore the importance of continued research and awareness to improve patient outcomes.

II. DISCUSSION

NPSLE is a complex condition involving multiple pathophysiological mechanisms, including autoantibody-mediated neuronal damage, vascular ischemia, and cytokine-induced inflammation. This case emphasizes the necessity of considering NPSLE in patients with known lupus presenting with unexplained neurological symptoms. Brain imaging and serological markers are pivotal for diagnosis, and a multidisciplinary approach is critical to optimize treatment and outcomes. Early recognition and immunosuppressive therapy, such as corticosteroids or cyclophosphamide, can prevent disease progression and long-term neurological sequelae.In India, the most commonly reported neuropsychiatric symptoms include seizures, headaches, cognitive dysfunction, psychosis, depression, anxiety, movement disorders, and peripheral neuropathy. The exact pathophysiology of NPSLE remains poorly understood, but several mechanisms are proposed: autoantibody-mediated damage, cytokine dysregulation, and vascular pathology.

Diagnosis of NPSLE in India faces several challenges, including resource limitations, overlap with other disorders, and cultural and social factors. Treatment approaches involve a multidisciplinary approach, including immunosuppressive therapy, anticoagulation, symptomatic management, and adjunctive therapies like cognitive rehabilitation and psychotherapy.

Research and public health implications suggest that large-scale, multicentric studies are needed to better understand the epidemiology, pathophysiology, and outcomes of NPSLE. The Indian SLE Inception Cohort for Research (INSPIRE) and other initiatives provide valuable data but highlight the need for standardized diagnostic criteria and protocols tailored to the Indian healthcare system.

Adequate public and physician awareness about NPSLE remains suboptimal in India, and educational programs targeting healthcare providers can facilitate early recognition and intervention. Patient education about the potential neurological and psychiatric complications of SLE is crucial for timely care. However, neuropsychiatric lupus is a significant but underappreciated complication of SLE in India. A comprehensive approach involving clinical vigilance, multidisciplinary management, and robust research is essential to improve patient outcomes. Addressing healthcare disparities, enhancing diagnostic capabilities, and fostering collaborations between rheumatologists, neurologists, and psychiatrists will pave the way for better care and quality of life for Indian patients with NPSLE.

Epidemiological Insights

Neuropsychiatric systemic lupus erythematosus (NPSLE) is a significant complication in patients with systemic lupus erythematosus (SLE), characterized by diverse neurological and psychiatric manifestations. Indian studies have reported a prevalence of NPSLE ranging from 19% to 35% among SLE patients, underscoring its critical role in disease morbidity (Singh et al., 2017). The variation in prevalence may be attributed to differences in study design, diagnostic criteria, and patient populations.

Clinical Manifestations

In India, the most commonly reported neuropsychiatric symptoms include:

1. Seizures:Found in approximately 40% of Indian NPSLE patients, seizures often signal central nervous system involvement and may correlate with disease activity (Sundar et al., 2020).
2. Headaches: Observed in 20-40% of cases, lupus headaches are challenging to distinguish from primary headache disorders (Verma et al., 2019).
3. Cognitive Dysfunction:Cognitive impairment, affecting memory, attention, and executive function, is frequently underdiagnosed but has a profound impact on quality of life (Kumar et al., 2021).
4. Psychiatric Symptoms:Psychosis, depression, and anxiety are prevalent, with psychosis being reported in up to 75% of patients in certain cohorts (Sharma et al., 2018).
5. Movement Disorders: Although rare, chorea and other movement abnormalities have been documented in Indian patients.
6. Peripheral Neuropathy:Peripheral nervous system involvement, such as sensory neuropathy, is also observed but less commonly reported.

Pathophysiology and Biomarkers

The exact pathophysiology of NPSLE remains poorly understood, but several mechanisms are

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proposed:

1. **Autoantibody-Mediated Damage:** Autoanti bodies, such as anti-ribosomal P and anti-neuronal antibodies, are implicated in neuronal damage and inflammation.
2. **Cytokine Dysregulation:**Elevated levels of pro-inflammatory cytokines like TNF-α and IL-6 contribute to neuroinflammation.
3. **Vascular Pathology:** Microvascular occlusion, endothelial dysfunction, and vasculitis can lead to ischemic events in the CNS (Mehta et al., 2020).

Challenges in Diagnosis

The diagnosis of NPSLE in India faces several challenges:

1. **Resource Limitations**:Advanced imaging techniques, such as MRI and PET scans, and neuropsychological testing are not uniformly available across all healthcare centers.
2. **Overlap with Other Disorders**:Symptoms like headaches and cognitive dysfunction can overlap with primary neurological or psychiatric disorders, complicating diagnosis.
3.**Cultural and Social Factors**:Psychiatric symptoms are often underreported due to stigma, leading to delays in recognition and treatment (Rao et al., 2019).

Treatment Approaches

Management of NPSLE in India involves a multidisciplinary approach. Key strategies include:

1. **Immunosuppressive Therapy:** Corticosteroids and immunosuppressants like cyclophosphamide and mycophenolate mofetil are the mainstays of treatment.
2. **Anticoagulation**: For patients with antiphospholipid syndrome, anticoagulants such as warfarin or heparin are prescribed to prevent thrombotic events.
3. **Symptomatic Management:** Anticonvulsants for seizures, antidepressants for mood disorders, and antipsychotics for psychosis are used to address specific symptoms.
4. **Adjunctive Therapies**:Cognitive rehabilitation and psychotherapy are increasingly recognized as valuable components of care (Chatterjee et al., 2022).

Future Research and Public Health Implications

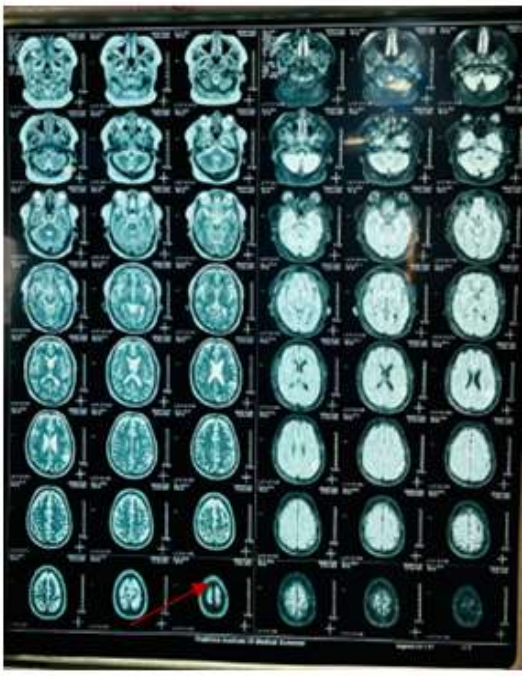
Given India's diverse population, there is a need for large-scale, multicentric studies to better understand the epidemiology, pathophysiology, and outcomes of NPSLE. The Indian SLE Inception Cohort for Research (INSPIRE) and other initiatives provide valuable data but highlight the need for standardized diagnostic criteria and protocols tailored to the Indian healthcare system.

Role of Awareness and Education

Public and physician awareness about NPSLE remains suboptimal in India. Educational programs targeting healthcare providers can facilitate early recognition and intervention. Additionally, patient education about the potential neurological and psychiatric complications of SLE is crucial for timely care.

III. CONCLUSION

Neuropsychiatric lupus is a significant but underappreciated complication of SLE in India. A comprehensive approach involving clinical vigilance, multidisciplinary management, and robust research is essential to improve patient outcomes. Addressing healthcare disparities, enhancing diagnostic capabilities, and fostering collaborations between rheumatologists, neurologists, and psychiatrists will pave the way for better care and quality of life for Indian patients with NPSLE.This case highlights the importance of a high index of suspicion for NPSLE in lupus patients presenting with neurological symptoms. Timely diagnosis through clinical, radiological, and serological correlation, along with a collaborative approach to management, is essential to improving prognosis in these patients.



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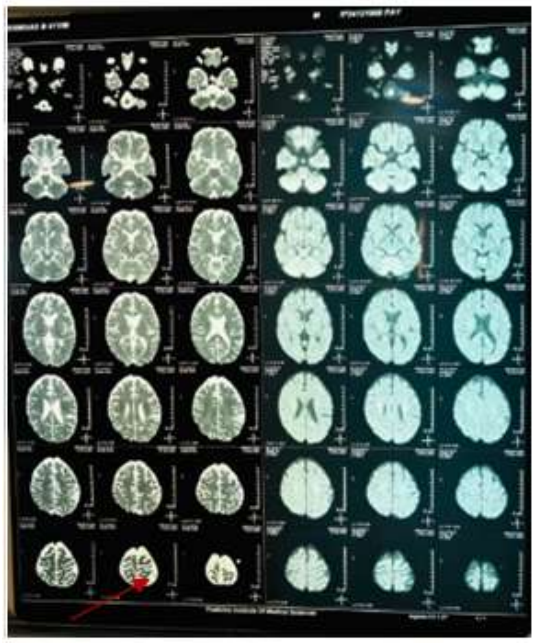

Figure-1 . MRI scan of the brain demonstrating the clinical findings .

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